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Risikobeurteilung von Bodenschadstoffen in Haus- und Familiengärten gemäss Anhang 3, Ziffer 2 AltlV für die menschliche Gesundheit

SCAHT

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ANHANG 312

1 Methodik

1.1 Ausgangslage, Problematik, Zielsetzung

Im Zusammenhang mit der grossflächigen Quecksilberbelastung von Hausgärten in Wohngebieten im Kanton Wallis hatte das SCAHT bereits 2014 im Auftrag des BAFU einen Prüfwert von 2 mg/kg Hg für Quecksilber gemäss VBBo[1] hergeleitet. Im März 2015 wurde Anhang 3, Ziffer 2, AltlV[2] entsprechend revidiert.

Das BAFU hat dem SCAHT im September 2014 den Auftrag erteilt, für 16 weitere Schadstoffe gemäss Anhang 3, Ziffer 2 AltlV die Bodensanierungswerte vor dem Hintergrund einer möglichen direkten Bodenaufnahme durch Kinder zu überprüfen. Die leichtflüchtigen chlorierten Kohlenwasserstoffe (LCKW) waren nicht Gegenstand dieses Auftrags (Vertrags-Nr: 00.0143.PZ / N342-0159). Das BAFU hat eine Prioritätenliste zur Überarbeitung der bestehenden Sanierungswerte der 16 Schadstoffe erstellt (**Tabelle 1-1**).

Tabelle 1-1: Priorisierung der Überprüfung der Bodensanierungswerte gemäss Anhang 3, Ziffer 2 AltlV[2].

Priorität	Stoff	Bodensanierungswert gemäss Anhang 3, Ziffer 2 AltlV
1	Kupfer	1000 mg Cu/kg
2	Cadmium	20 mg Cd/kg
3	Zink	2000 mg Zn/kg
4	Polycyclische aromatische Kohlenwasserstoffe (PAK)	100 mg/kg
5	Benzo[a]pyren	10 mg/kg
6	Blei	1000 mg Pb/kg
7	Antimon	50 mg Sb/kg
8	Polychlorierte Biphenyle (PCB)	1 mg/kg
9	Arsen	50 mg As/kg
10	Chrom (VI)	100 mg CrVI/kg
11	Nickel	1000 mg Ni/kg
12	Benzol	1 mg/kg
13	Monocyclische aromatische Kohlenwasserstoffe (BTEX)	500 mg/kg
14	Silber	500 mg/kg
15	Aliphatische Kohlenwasserstoffe C_5-C_{10}	5 mg/kg
16	Aliphatische Kohlenwasserstoffe C_{11}-C_{40}	500 mg/kg

[1] **VBBo:** Verordnung über Belastungen des Bodens vom 1. Juli 1998 (Stand am 1. Juni 2012)

[2] **Anhang 3:** Konzentrationswerte für die Beurteilung der Sanierungsbedürftigkeit von Böden; **Ziffer 2:** Standorte bei Haus- und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen; **AltV** (Altlasten-Verordnung): Verordnung über die Sanierung von belasteten Standorten vom 26. August 1998 (Stand am 1. März 2015).

1.2 Risikocharakterisierung

Die Anzahl wissenschaftlicher Publikationen zu toxikologischen Fragestellungen wächst ständig und wissenschaftliche Sachverhalte werden häufig kontrovers diskutiert. Das SCAHT stützt seine Risikobewertung deshalb wenn möglich auf die Ergebnisse der Risikobeurteilung international anerkannter Gremien und Behörden, wie z. B. der Europäischen Lebensmittelsicherheitsbehörde (EFSA).

1.2.1 Mehrstufenmodell

Zur effizienten Beurteilung des Gesundheitsrisikos für den Menschen durch die Exposition gegenüber Schadstoffen im Boden schlägt das SCAHT einen Mehrstufenprozess vor. Im ersten Schritt werden standardisierte Annahmen zu spezifischen Parametern der Risikoabschätzung gemacht, die grundsätzliche Aussagen zum möglichen Gesundheitsrisiko einzelner Schadstoffe erlauben.

Um Entscheidungsfindungsprozesse im Kontext des Risikomanagements zu unterstützen, können diese Annahmen in weiteren Schritten im Rahmen einer verfeinerten Szenarioplanung modifiziert werden. In einem ersten Schritt wird angenommen, dass die orale Exposition den relevantesten Aufnahmepfad für Kontaminanten aus dem Boden darstellt.

Die Beurteilung des Gesundheitsrisikos durch die direkte Aufnahme von Schadstoffen aus dem Boden erfolgt nach den allgemeinen Grundsätzen der Risikobewertung. Dabei wird ein mögliches Gesundheitsrisiko durch einen Abgleich des Gefährdungspotentials eines Schadstoffes mit der Exposition gegenüber dem betreffenden Stoff abgeschätzt. Die Identifizierung einer möglichen Gefährdung der menschlichen Gesundheit erfolgt im Rahmen toxikologischer und/oder epidemiologischer Studien.

1.2.2 Risikocharakterisierung von Stoffen mit Schwellenwert für toxikologische Effekte - NOAEL-Verfahren

Für die meisten toxischen Wirkungen wird davon ausgegangen, dass sie einem Schwellenwert unterliegen; d. h. der gesundheitsschädliche Effekt tritt nur ein, wenn eine bestimmte Dosis (Schwelle) überschritten wird; Expositionen unterhalb dieser Dosis rufen keinerlei schädlichen Effekt hervor. Für Stoffe mit solchen Schwellenwert-Wirkungen können sichere Grenzwerte abgeleitet werden.

Um aus einer Studie an Tieren einen Grenzwert für Menschen abzuleiten, geht man von einem Referenzwert, dem so genannten NOAEL ("No Observed Adverse Effect Level") aus. Der NOAEL ist die höchste Dosierung ohne schädliche Wirkung im Tierversuch. Um eine unschädliche Dosis für den Menschen zu bestimmen, wird dieser NOAEL durch einen Sicherheitsfaktor geteilt, der Unterschiede zwischen Tier und Mensch (Faktor 10x) und Unterschiede zwischen den einzelnen Menschen (Faktor 10x) berücksichtigen soll. Meist wird dafür ein Faktor von 100 verwendet (10 x 10). So ist gewährleistet, dass auch besonders empfindliche Personen, wie Kinder, Schwangere oder ältere Menschen geschützt sind. Je nach vorhandener toxikologischer Datengrundlage können die standardmässig verwendeten Sicherheitsfaktoren vergrössert oder verkleinert werden.

Typische gesundheitlich unbedenkliche Grenzwerte für Expositionen gegenüber Chemikalien können je nach regulatorischem Umfeld verschiedene Namen tragen:

- PTDI oder "Provisonal Tolerable Daily Intake" oder vorläufig duldbare tägliche Aufnahmemenge: Dieser Wert gibt die Menge eines Stoffes an, die Verbraucher täglich und ein Leben lang ohne erkennbares Gesundheitsrisiko aufnehmen können. Der PTDI stellt einen Grenzwert für die Langzeit-Exposition von VerbraucherInnen dar. Häufig wird anstelle der duldbaren täglichen Aufnahmemenge eine wöchentliche Aufnahmemenge angegeben ("Provisonal Tolerable Weekly Intake" oder PTWI).

- DNEL steht für „Derived No Effect Level“ und ist die aus toxikologischen Daten abgeleitete Expositionshöhe eines Stoffes, unterhalb welcher die menschliche Gesundheit nicht beeinträchtigt wird und oberhalb welcher ein Mensch nicht exponiert werden sollte.

Kommt die Expositionsbeurteilung für einen Stoff zu dem Schluss, dass die Exposition der Bevölkerung gegenüber der Chemikalie den gesundheitlich unbedenklichen Referenzwert nicht überschreitet, dann ist ein gesundheitliches Risiko unwahrscheinlich. Überschreitet die Exposition den zulässigen Referenzwert, dann ist eine Gesundheitsbeeinträchtigung möglich, wobei das Ausmass des Gesundheitsschadens umso grösser ist, je grösser der Unterschied zwischen dem gesundheitlich unbedenklichen Referenzwert und der tatsächlichen Exposition ist (siehe Box 1).

BOX 1: Grundsätze der Risikobewertung

Gefahrenpotential x Exposition = Gesundheitsrisiko

Referenzwert = duldbare Aufnahmemenge

Exposition < Referenzwert ➔ Gesundheitsrisiko unwahrscheinlich

Exposition > Referenzwert ➔ Gesundheitsrisiko möglich

1.2.3 Risikocharakterisierung von Stoffen ohne Schwellenwert für toxikologische Effekte - BMDL-Verfahren

Nicht alle gesundheitsschädlichen Wirkungen unterliegen einem Schwellenwertmechanismus. Für einige Substanzen existiert nach heutigem wissenschaftlichen Kenntnisstand keine Dosis ohne toxikologische Wirkung. Jede noch so kleine Menge einer solchen Substanz kann gesundheitsschädlich sein. Ein Beispiel für Substanzen ohne Schwellenwertmechanismus sind genotoxische Kanzerogene. Idealerweise sollte der Mensch mit solchen Stoffen überhaupt nicht in Kontakt kommen. Im Spannungsfeld von Erwartungen an den Gesundheitsschutz, Wissen und Wissenslücken sowie technologischer und ökonomischer Machbarkeit lässt sich dieser Anspruch aber selten in vollem Umfang erfüllen.

Zur Risikocharakterisierung von Stoffen ohne Schwellenwert-Wirkungen wie z. B. genotoxischen Kanzerogenen kann eine Dosis mit schädlicher Wirkung (sog. Benchmark Dose Response, BMR) berechnet werden. Genotoxische Substanzen verursachen Änderungen im genetischen Material von Zellen. Sie können die Anzahl und Struktur der Chromosomen beeinflussen oder einzelne Gene verändern (Mutationen). Viele dieser genotoxischen Effekte lösen in der Folge Krebs aus. Bei diesen sog. genotoxischen Kanzerogenen wird grundsätzlich eine Wirkungsweise ohne Schwellenwert unterstellt. Dies bedeutet, dass auch sehr niedrige Dosierungen eines Stoffes ihre schädigende Wirkung entfalten können, wobei die Wahrscheinlichkeit der Krebsentstehung von der Dosis abhängig ist. Im Tierversuch kann man allerdings bei extrem niedrigen Dosen oft keine toxikologischen Effekte messen.

Hier hilft das Benchmark-Dose-Verfahren (BMD). Durch eine Extrapolation der Dosis-Wirkungs-Kurve in den Niedrigstdosisbereich kann man die Stärke der krebserzeugenden Wirkung auch für sehr kleine Dosen abschätzen, die im Tierversuch nicht getestet werden konnten. Dieser BMD-Wert dient dann als Ausgangspunkt zur Bestimmung der unteren 95% Vertrauensgrenze, die als “Benchmark

Dosis Level“ (BMDL) bezeichnet wird. Der BMDL-Wert beschreibt diejenige Dosis, bei der ein bestimmter toxikologischer Effekt einer bestimmten Stärke mit 95% Sicherheit nicht beobachtet wird. Ein Problem bei der Anwendung des BMD-Verfahrens ist die Frage nach dem zusätzlichen Risiko, das man zulässt im Vergleich zur Hintergrundbelastung (sog Benchmark-Response: BMR). BMR-Werte von 1%, 5% und 10% werden am häufigsten verwendet, weil sie am besten den Dosisbereich zwischen NOAEL und LOAEL im Tierversuch repräsentieren (der NOAEL ist die höchste Dosierung ohne schädliche Wirkung im Tierversuch und der LOAEL ist die niedrigste Dosis mit schädlicher Wirkung im Tierversuch). Für welchen der BMR-Werte man sich im Rahmen der Risikobeurteilung entscheidet, hängt vom betrachteten toxikologischen Endpunkt ab und unterliegt vielfach einer Expertenmeinung.

Typische gesundheitlich wenig bedenkliche Grenzwerte für Expositionen gegenüber Chemikalien sind:

- Benchmark-Dosis (BMD) steht für die Dosis, die einen bestimmten toxikologischen Effekt in exponierten Versuchstieren oder Menschen verursacht, der in der nicht exponierten Kontrollgruppe nicht beobachtet wird.
- DMEL steht für „Derived Minimal Effect Level“ und ist die aus toxikologischen Daten abgeleitete Expositionshöhe eines Stoffes, unterhalb welcher die menschliche Gesundheit wenig beeinträchtigt wird.

1.2.4 Risikocharakterisierung von Stoffen mit langer biologischer Halbwertszeit - Body Burden

Stoffe die eine lange biologische Halbwertszeit besitzen, reichern sich im Körper an, wenn pro Zeiteinheit mehr Stoff aufgenommen wird als der Körper ausscheidet. Bei täglicher Aufnahme solcher Stoffe über die Hintergrundbelastung in Nahrung und Luft wächst die Körperlast (Body Burden) stetig an. Die Körperlast beschreibt die Stoffmenge, die sich bis zu einem bestimmten Zeitpunkt im Leben im Körper angesammelt hat und langfristig im Körper vorhanden ist. Sie ist für die Risikocharakterisierung von Stoffen mit langer biologischer Halbwertszeit relevanter als die einzelne aufgenommene Dosis.

1.2.5 Integrative Risikobewertung – Berücksichtigung der Hintergrundbelastung

Die Gesundheitsbewertungsmethode des SCAHT beruht auf einer Einzelstoffbewertung mit teilweise integrativem Ansatz (siehe Box 2). Für jeden einzelnen Schadstoff wird das Ausmass der Exposition durch das Verschlucken kontaminierter Böden mit der unvermeidlichen Hintergrundbelastung des Menschen durch die Schadstoffe in der Umwelt verglichen. Mögliche Expositionsquellen für Schadstoffe im Alltag sind die Atemluft, die Nahrung und das Trinkwasser. Für Kleinkinder kann die Aufnahme von Schadstoffen über den Hausstaub ein relevanter Expositionspfad sein. Die Belastung des Hausstaubs korrelliert i.d.R. mit der Belastung des Bodens in Familiengärten (Alloway 2004). Durch die Berücksichtigung dieser Hintergrundbelastung kann das zusätzliche Gesundheitsrisiko durch Verschlucken von kontaminierten Böden gewichtet werden im Vergleich zum Gesundheitsrisiko durch die unvermeidbare Schadstoffbelastung aus der Umwelt.

Diese Gewichtung erlaubt eine Priorisierung möglicher Risikominimierungsmassnahmen hinsichtlich ihrer Schutzwirkung für die menschliche Gesundheit. Bodensanierungsmassnahmen tragen nur dann wesentlich zu einer Minimierung des Gesundheitsrisikos bei, wenn das Gesundheitsrisiko durch Verschlucken von Boden gross ist im Vergleich zum Gesundheitsrisiko durch die Aufnahme der Schadstoffe über die Nahrung und Atemluft.

BOX 2: Integrative Risikobewertung und Risikomanagement

Gesamtexposition = Exposition Boden + Hintergrundexposition (z.B. Nahrung, Atemluft)

Gesamtexposition > Referenzwert ➔ Gesundheitsrisiko

Exposition Boden >> Hintergrundexposition ➔ Bodensanierung sinnvoll

Exposition Boden << Hintergrundexposition ➔ Bodensanierung nicht zielführend

1.2.6 Risikomanagement von Stoffen ohne Schwellenwert für toxikologische Effekte - ALARA-Prinzip

Wenn für einen Stoff aus toxikologischer Sicht kein sicherer Schwellenwert abgeleitet werden kann, bis zu dem ein gesundheitliches Risiko praktisch ausgeschlossen ist, sollte für die Festlegung des Sanierungswerts im Boden von Familiengärten das ALARA-Prinzip zur Anwendung kommen.

Wenn bereits die Hintergrundexposition (beispielsweise Nahrung und Trinkwasser), den gesundheitlich unbendenklichen Referenzwert überschreitet, bleibt rein rechnerisch kein Spielraum für eine zusätzlische Exposition über den Boden, und auch in diesem Fall sollte für die Festlegung des Sanierungswerts das ALARA-Prinzip zur Anwendung kommen (siehe Box 3).

ALARA steht für „As Low As Reasonably Achievable“ und bedeutet, dass die Exposition gegenüber einem Stoff so weit wie vernünftigerweise erreichbar reduziert werden soll.

BOX 3: Bedingungen zur Anwendung des ALARA-Prinzips

Wenn kein sicherer Schwellenwert für eine Substanz vorhanden ist
➔ Bodensanierung gemäss ALARA

oder

Wenn Hintergrundexposition >> Referenzwert
➔ Bodensanierung gemäss ALARA

Risikomanager kritisieren in der Anwendung des ALARA-Prinzips, dass dieser Ansatz keine Informationen liefert, die ihnen eine Differenzierung nach Prioritäten erlaubt. Offen bleibt auch die Frage, was als „so gering wie vernünftigerweise erreichbar“ anzusehen ist. Ein „Ranking“ von Risiken wäre aber für das Risikomanagement hilfreich für die Prioritätensetzung. Dieses „Defizit“ für die Risikobewertung von genotoxischen und kanzerogenen Substanzen ohne Schwellenwert kann durch die Anwendung des MOE (Margin of Exposure)-Ansatzes ausglichen werden.

1.2.7 Priorisierung von Risikomanagementmassnahmen - MOE-Prinzip

MOE (Margin of Exposure) ist ein von Risikobewertern verwendetes Instrument zur Abwägung möglicher Sicherheitsbedenken und zur Priorisierung von Risikominimierungsmassnahmen. Es wurde ursprünglich von der EFSA angewendet, um genotoxische Kanzerogene, also Substanzen ohne

sicheren Schwellenwert für toxikologische Endpunkte, in Lebensmitteln zu beurteilen. Mittlerweile ist die Anwendung jedoch auf andere Bereiche und toxikologische Endpunkte ausgeweitet worden.

Der MOE-Ansatz verwendet als Referenzpunkt, die Dosierung einer Substanz, die in Tierstudien oder im Rahmen epidemiologischer Untersuchungen eine geringe, aber messbare Reaktion des Körpers verursacht hat (der sog. Benchmark Dose Level, BMDL). Dieser Referenzpunkt wird dann mit den Schätzungen zur Schadstoffaufnahme über die Nahrung, Umgebungsluft usw. verglichen.

Der MOE berechnet sich, indem der Referenzpunktpunkt durch die geschätzte menschlichen Exposition dividiert wird (MOE = BMDL / Exposition) (EFSA 2005, p. 16). Je niedriger die MOE für eine bestimmte Substanz, desto wahrscheinlicher ist das Gesundheitsrisiko, das von der Substanz ausgeht und umso dringlicher sind Risikominimierungsmassnahmen.

Bei einem MOE unter 10'000 für kanzerogene Effekte geht die EFSA häufig von einem nicht mehr gesellschaftlich akzeptablen Gesundheitsrisiko aus und fordert Risikominimierungsmassnahmen. Für nicht kanzerogene Effekte würde ein MOE unter 100 die Notwendigkeit von Risikominimierungsmassnahmen anzeigen (siehe Box 4).

BOX 4: MOE (Margin of Exposure)-Ansatz zur Priorisierung von Risikominimierungsmassnahmen für kanzerogene und nicht kanzerogene Stoffe.

MOE = BMDL / tatsächliche Exposition

$MOE_{Genotoxische\ Kanzerogene} > 10000$ ➔ Gesundheitsrisiko akzeptabel
➔niedrige Priorität für Riskominimierungsmassnahmen

$MOE_{Nichtgenotoxische\ Kanzerogene} > 100$ ➔ Gesundheitsrisiko akzeptabel
➔niedrige Priorität für Riskominimierungsmassnahmen

1.2.8 Schutzziel

Das Schutzziel der Risikobeurteilung durch das SCAHT sind Kinder. Kinder sind im Hinblick auf eine direkte Aufnahme von Schadstoffen aus dem Boden besonders gefährdet. Ausserdem können sie besonders empfindlich auf mögliche Schadstoffe reagieren. Dieser Sachverhalt muss bei der Risikobewertung von Schadstoffen und bei der Festlegung von Referenzwerten berücksichtigt werden. Ob für Kinder ein zusätzlicher Sicherheitsfaktor berücksichtigt werden soll, wird kontrovers diskutiert.

Das SCAHT verzichtet in seiner Risikobewertung auf die Einführung eines zusätzlichen Sicherheitsfaktors. Bei der Ableitung der gesundheitsbezogenen Referenzwerte aus den Daten toxikologischer Studien werden bereits Extrapolationsfaktoren („Sicherheitsfaktoren") angewandt, die u. a. individuelle Empfindlichkeitsunterschiede gegenüber toxischen Wirkungen innerhalb der menschlichen Bevölkerung berücksichtigen. Damit wird einer grösseren Empfindlichkeit von Kindern, alten Menschen und Kranken Rechnung getragen. Darüber hinaus stehen häufig auch toxikologische Daten zur Reproduktions- und Entwicklungstoxizität zur Verfügung, die eine besondere Empfindlichkeit im Kindesalter berücksichtigen. Des weiteren berücksichtigen die Annahmen zur Expositionsabschätzung des SCAHT die spezifische Situation der Kinder. Zum Beispiel können Kinder bezogen auf ihr Körpergewicht das 3- bis 4-fache eines Erwachsenen essen. Darüber hinaus beschränkt sich ihre Nahrung auf ein kleineres Sortiment an Lebensmitteln, das weniger oder stärker

belastet sein kann als das der Erwachsenen. Das SCAHT wertet deshalb zur Abschätzung der Hintergrundexposition durch die Nahrung, soweit vorhanden, nur kinderspezifische Daten aus. Hinweisen zu besonders kritischen toxikologischen Endpunkten, wie z. B. den möglichen negativen Auswirkungen einer Exposition gegenüber Fremdstoffen in den ersten Lebensphasen hinsichtlich der späteren Entwicklung, wird bei der Empfehlung von Risikominimierungsmassnahmen durch das SCAHT gesondert Rechnung getragen (siehe auch BfR 2003).

1.2.9 Parameter zur standardisierten Risikobeurteilung

1.2.9.1 Alter

Kleinkinder im Alter von 1-3 Jahren sind besonders gefährdet. Aufgrund des Spielverhaltens von Kindern kann das Verschlucken von Staub und Boden ein wichtiger Expositionspfad gegenüber Schadstoffen sein. Das gilt vor allem für kleinere Kinder, die grössere Mengen Boden und Staub aufnehmen als andere Teile der Bevölkerung, insbesondere in Hinblick auf die aufgenommene Menge relativ zur Körpermasse.

⇒ **Das SCAHT führt standardmässig eine Risikobeurteilung für Kleinkinder im Alter von 1-3 Jahren aus und begründet seine Annahme wie folgt:**

- Sowohl die WHO (WHO 2014) als auch die USEPA (USEPA 2005) kommen zu dem Schluss, dass Kleinkinder im Vergleich zu anderen Altersgruppen die grössten Mengen von Boden verschlucken. Das belegt auch eine Reihe von früheren Schlüsselstudien zum Gesundheitsrisiko von Kindern durch Schadstoffaufnahme aus dem Boden (z. B. Calabrese et al 1989, 1997, 1999; Stanek et al 1990, 2001; Stanek and Calabrese 1995), die sich auf Kleinkinder konzentriert haben.
- Während die orale Phase, bei der Säuglinge ihre Umgebung mit dem Mund erkunden, bereits zwischen dem 3. und 5. Lebensmonat beginnt, gewinnt die aktive Spielphase (im Familiengarten) erst ab dem ersten Lebensjahr an Bedeutung. Die Hand-zu-Mund-Aktivitäten, die zur Bodenaufnahme führen, nehmen aber zwischen dem 2. und 6. Lebensjahr wieder ab (**Tabelle 1-2**). Hand-zu-Mund-Aktivitäten sind demnach im ersten und zweiten Lebensjahr am stärksten ausgeprägt. Das SCAHT wählt aber Kleinkinder im Alter von 1-3 Jahren für die Risikobeurteilung aus. Dadurch wird die Altersgruppe mit den ausgeprägtesten Hand-zu-Mund-Aktivitäten erfasst, und die Risikobeurteilung für Kleinkinder im Alter von 1-3 Jahren bietet hinreichend Schutz auch für ältere Kinder bietet. Aus praktischen Gründen ist eine Fokussierung auf die Altersgruppe von 1-2 Jahren nicht möglich. Die WHO empfiehlt die Einteilung in verschiedene Alters- und Gewichtsklassen (**Tabelle 1-3**), die eine Einteilung in die Altersgruppe von 1-3 Jahren ermöglicht. Die EFSA folgt dieser Einteilung der Altersgruppen, weshalb vorhandene Daten zur Hintergrundbelastung mit Schadstoffen durch die Nahrung oder Atemluft diesem Raster folgen.

Tabelle 1-2: Relevante Aktivitäten für die Bodenaufnahme in den einzelnen Lebensphasen der Kinder (WHO 2014)

Table 3
Examples of factors considered in deriving age groups reflecting behavioral development.

Age group	Characteristics relevant to oral and dermal exposure
Birth to <3 months	Breastfeeding and bottle feeding. Hand-to-mouth activities
3 to <6 months	Solid food may be introduced. Contact with surfaces increases. Object/hand-to-mouth activities increase
6 to <12 months	Food consumption expands. Floor mobility increases (surface contact). Children are increasingly likely to mouth non-food items
12 to <24 months	Children consume full range of foods. They participate in increased play activities, are extremely curious and exercise poor judgment. Breastfeeding and bottle feeding cease
2 to <6 years	Children begin wearing adult-style clothing. Hand-to-mouth activities begin to moderate
6 to <11 years	There is decreased oral contact with hands and objects as well as decreased dermal contact with surfaces
11 to <16 years	Smoking may begin. There is an increased rate of food consumption
16 to <21 years	High rate of food consumption begins

Tabelle 1-3: Einteilung der Altersgruppen laut WHO (2014)

Table 6
WHO-recommended tiered set of early life age groups.

Life stage descriptor	Tier 1 age groups
Preconception	Preconception
Fetal	Prenatal
Newborn (neonatal)	Birth to <1 month
Infant	1 to <3 months
	3 to <6 months
	6 to <12 months
Toddler	1 to <2 years
Early childhood	2 to <3 years
	3 to <6 years
Middle childhood	6 to <11 years
Early adolescence	11 to <16 years
Late adolescence	16 to <21 years

1.2.9.2 Körpergewicht

Das durchschnittliche Körpergewicht während der Expositionsdauer ist entscheidend für die Risikobeurteilung. Gesundheitlich unbedenkliche Referenzwerte geben die duldbare Menge an Schadstoff bezogen auf das Körpergewicht an. Für die Risikobeurteilung sind realitätsnahe Annahmen zum Körpergewicht einzelner Altersklassen entscheidend.

Das SCAHT bezieht sich auf die Klassifizierung von Altersgruppen gemäss der WHO (2014), die von der amerikanischen Umweltschutzbehörde übernommen wurde. **Tabelle 1-4** listet die entsprechenden empfohlenen Werte für das Körpergewicht der einzelnen Altersklassen (USEPA 2011).

Tabelle 1-4: Empfohlene Altersstufen und Körpergewichte (USEPA 2011)

Table 8-1. Recommended Values for Body Weight

Age Group	Mean (kg)	Multiple Percentiles	Source
Birth to <1 month	4.8		
1 to <3 months	5.9		
3 to <6 months	7.4		
6 to <11 months	9.2		
1 to <2 years	11.4	Table 8-3 through Table 8-5	U.S. EPA analysis of NHANES, 1999–2006 data
2 to <3 years	13.8		
3 to <6 years	18.6		
6 to <11 years	31.8		
11 to <16 years	56.8		
16 to <21 years	71.6		
Adults	80.0		

Das SCAHT folgt ausserdem der Empfehlung der USEPA, einen durchschnittlichen Mittelwert für das Körpergewicht während der zu betrachtenden Expositionsphase ("time-weighted average body weight") gemäss USEPA-Methode zu berechnen (**siehe Box 5**). Für Kleinkinder im Alter 1- 3 Jahren ergibt sich auf Basis der USEPA Daten ein zeitlich gemitteltes Körpergewicht von 12.6 kg:

BOX 5: USEPA-Methode zur Berechnung des durchschnittlichen Mittelwerts für das Körpergewicht während der zu betrachtenden Expositionsphase (time-weighted average body weight)(USEPA 2011).

Mittleres Körpergewicht eines 1 - 3-Jährigen:

(11.4 kg x 1 Jahr) + (13.8 kg x 1 Jahr) / 2 Jahre = 12.6 kg

⇒ **Das SCAHT verwendet standardmässig ein Gewicht von 12.5 kg.**

1.2.9.3 Bodenaufnahmerate

Ob das Verschlucken von kontaminiertem Boden ein Gesundheitsrisiko darstellt, hängt wesentlich von der verschluckten Menge an schadstofbelastetem Boden ab. Es gibt zahlreiche Publikationen, die versuchen die Menge an Boden abzuschätzen, die Kinder zu sich nehmen.

Auffällig ist, dass die Angaben zur Bodenaufnahmerate stark variieren (USEPA 2011, Kapitel 5.5, Seite 5-31), mit Werten von weniger als 50 mg/Tag bis zu Werten weit über 1000 mg/Tag (e.g. Calabrese et al., 1989), und z.T. Standardabweichungen aufweisen, die ein Vielfaches grösser sind als die durchschnittliche Bodenaufnahme (Hough 2010).

Die USEPA hat in einer Meta-analyse Studien zur Bodenaufnahmerate analysiert (USEPA 2011, Table 5-22, Seite 5-49), einschliesslich der bis dahin als sog. Schlüsselstudien bezeichneten und kommt zu dem Schluss, dass viele Studien aus heutiger Sicht als wenig verlässlich einzustufen sind (USEPA Exposure Factors Handbook Kapitel 5 “Soil and Dust Ingestion“), weil die angewandten Methoden sich in der Zwischenzeit verändert haben, z.B. die Anwendung von Tracer-Technologie zur genaueren Bestimmung der Bioverfügbarkeit oder die verbesserte Modellierung der Biokinetik.

Zur genaueren Illustration der Unsicherheiten bei der Bestimmung der Bodenaufnahmeraten sind im Folgenden exemplarisch die Ergebnisse einer Studie von Stanek und Calabrese (1995) aufgelistet.

Stanek and Calabrese (1995) estimated annual soil ingestion distribution based on daily soil ingestion values in 64 children aged 1-4 yrs old participating in the 1989 Amherst soil ingestion study (see Tabelle 1-5). It was reported that the estimated median of the 64 children daily soil ingestion as averaged over 365 days was 75 mg/day, while the upper 95%ile was 1751 mg/day (siehe **Tabelle 1-5**); findings indicated that more than 10% of the subjects ingested on the average approximately 1200 mg/day. Stanek and Calabrese (1995) also estimated the percent of children with soil ingestion exceeding daily rates for given periods of the year (siehe **Tabelle 1-6**). They showed that 33% of the children will ingest >10000 mg of soil on 1-2 days per year, and 16% of children are expected to ingest >1000 mg of soil on 35-40 days per year.

Tabelle 1-5: Soil ingestion estimates on 64 children over 365 days based on fitting a log-normal distribution model to daily soil ingestion values.

(Quelle: Stanek and Calabrese 1995, Tabelle 8)

Soil ingestion estimates for children	Rate of soil ingestion
Range of median soil ingestion estimates of 64 subjects over 365 days	1-103 mg/day
Median soil ingestion of 64 subjects[a]	14 mg/day
Range of upper 95% soil ingestion estimates of 63 subjects over 365 days[b]	1-5263 mg/day
Median of the upper 95% soil ingestion estimates of the 64 subjects over 365 days	252 mg/day
Range of estimated total number of grams of soil ingested per year by 63 subjects[b]	0.365-828.16 g/year
Range of average daily soil ingestion values for the 63 subjects over 365 days[b]	1-2268 mg/day
Median of the 64 subjects daily average soil ingestion[a]	75 mg/day
The upper 95% of the average daily soil ingestion for 64 subjects[a]	1751 mg/day
The upper 90% of the average daily soil ingestion for 64 subjects[a]	1190 mg/day

[a] With subject estimates equal to the average soil ingestion over 365 days.
[b] Subject exhibiting soil pica excluded.

Tabelle 1-6: Estimated percent of children with soil ingestion exceeding daily rates for given time periods per year

(Quelle: Stanek and Calabrese 1995, table 9)

Estimate number of days per year with soil ingestion	Daily rate of soil ingestion				
	>200 mg	>500 mg	>1000 mg	>5000 mg	>10000 mg
1-2 days	86%	72%	63%	42%	33%
7-10 days	72%	53%	41%	20%	9%
35-40 days	42%	31%	16%	1.6%	1.6%

Bei der USEPA selbst kann man über die Jahre einen Trend zu niedrigeren Bodenaufnahmemengen feststellen. Im Jahr 2002 wurden noch Aufnahmemengen von 100 - 400 mg pro Tag angenommen (USEPA 2002). Die USEPA hat ihre Werte aber im Jahr 2008 nach erneuter Begutachtung einzelner Studien (Calabrese et al 1989) nach unten korrigiert. Seit 2008 geht die Richtlinie der USEPA für alle Kinder ab dem ersten Lebensjahr von einer durchschnittlichen täglichen Gesamtaufnahmemenge von Erde und Staub in Höhe von 100 mg/Tag aus (USEPA 2011; USEPA 2014a). Für den oberen Bereich der Bodenaufnahmemenge empfiehlt die USEPA 200 mg/Tag (**Tabelle 1-7**).

Auch andere Institutionen gehen von niedrigeren täglichen Aufnahmemengen als 250 mg/Tag. BfR und UBA (BfR 2008) nehmen eine mittlere Aufnahmemenge von 20-100 mg/Tag an und rechnen nur im „worst Case"-Szenario mit Aufnahmemengen von 100-500 mg/Tag (BfR 2008). Health Canada (HC 2004) geht standardmässig von einer Aufnahmemenge von 80 mg/Tag aus. Die Niederlande (Oomen et al. 2008), Health Australia (2001) und das Umweltministerium in Neuseeland (MfE 2011) rechnen mit 100 mg/Tag. Ähnlich niedrigere Werte werden auch von Van Holderbeke et al. (2008) vorgeschlagen, nämlich eine durchschnittliche kombinierte Aufnahmemenge von Hausstaub und Boden in Höhe von maximal 100 mg/Tag aber eher 40-80 mg/Tag.

Tabelle 1-7: USEPA Empfehlungen zur täglichen Bodenaufnahme (USEPA 2011)

Table 5-1. Recommended Values for Daily Soil, Dust, and Soil + Dust Ingestion (mg/day)

	Soil[a]				Dust[b]		Soil + Dust	
Age Group	General Population Central Tendency[c]	General Population Upper Percentile[d]	High End Soil-Pica[e]	High End Geophagy[f]	General Population Central Tendency[g]	General Population Upper Percentile[h]	General Population Central Tendency[c]	General Population Upper Percentile[h]
6 weeks to <1 year	30				30		60	
1 to <6 years	50		1,000	50,000	60		100[i]	
3 to <6 years		200				100		200
6 to <21 years	50		1,000	50,000	60		100[i]	
Adult	20[j]			50,000	30[j]		50	

[a] Includes soil and outdoor settled dust.
[b] Includes indoor settled dust only.
[c] Davis and Mirick (2006); Hogan et al. (1998); Davis et al. (1990); van Wijnen et al. (1990); Calabrese and Stanek (1995).
[d] Özkaynak et al. (2011); Stanek and Calabrese (1995b); rounded to one significant figure.
[e] ATSDR (2001); Stanek et al. (1998); Calabrese et al. (1997b; 1997a; 1991; 1989); Calabrese and Stanek (1993); Barnes (1990); Wong (1988); Vermeer and Frate (1979).
[f] Vermeer and Frate (1979).
[g] Hogan et al. (1998).
[h] Özkaynak et al. (2011); rounded to one significant figure.
[i] Total soil and dust ingestion rate is 110 mg/day; rounded to one significant figure it is 100 mg/day.
[j] Estimates of soil and dust were derived from the soil + dust and assuming 45% soil and 55% dust.

⇒ **Das SCAHT geht nach Rücksprache mit USEPA-Kollegen (USEPA 2014b) von einer täglichen Aufnahmemenge in Höhe von 250 mg pro Tag aus. Diese Menge stellt die kombinierte Gesamtexposition gegenüber Staub und Boden dar.**

⇒ **Dieses Vorgehen wird begründet durch die Tatsache, dass die Belastung des Hausstaubs in den Innerräumen mit der Belastung der Böden in den Familiengärten korreliert, die Hausstaubexposition im Standardszenario des SCAHT aber nicht gesondert berücksichtigt wird.**

1.2.9.4 Bioverfügbarkeit aus dem Boden

Beim Verschlucken von Bodenpartikeln gibt die gemessene Schadstoffmenge im Boden nur die **externe Exposition** an. Für eine möglichst realitätsnahe Risikobewertung ist diese Schadstoffmenge, nicht ausschlaggebend. Vielmehr muss die **interne Exposition,** d.h. die Schadstoffmenge die tatsächlich vom Körper aufgenommen/absorbiert wird**,** bei der Risikobeurteilung berücksichtigt werden. Nur die interne Exposition ist ein Mass für die **absolute orale Bioverfügbarkeit von Schadstoffen aus dem Boden** und beschreibt den Anteil der Schadstoffe, der nach dem Verschlucken von Boden tatsächlich aus dem Verdauungstrakt über die Blutgefässe des Magen- und Darmtrakts in den Blutkreislauf aufgenommen/absorbiert wird.

Werden Schadstoffe aus dem Boden nicht komplett absorbiert, ist die externe Exposition grösser als die interne Exposition. In diesem Fall würde eine Risikobeurteilung, die auf der externen Exposition basiert ein mögliches Gesundheitsrisiko überschätzen.

Zur Beschreibung der **absoluten oralen Bioverfügbarkeit** nach Verschlucken von Schadstoffen aus dem Boden **existieren unterschiedliche Konzepte (siehe Abbildung 1.1. und Box 6).**

1.2.9.4.1 Bioccessibility- und Bioavailabilitykonzept

Die **absolute orale Bioverfügbarkeit** nach Verschlucken von Schadstoffen aus dem Boden setzt sich aus **zwei Teilkomponenten** zusammen, die die beiden Phasen bei der Aufnahme von Schadstoffen nach dem Verschlucken von kontaminiertem Boden in den Körper beschreiben (siehe **Abbildung 1-1**): die sog. **„Bioaccessibility"** und **„Bioavailability"**. Während im Englischen zwischen diesen beiden Phasen unterschieden wird, existiert im Deutschen ganz allgemein nur der Begriff der Bioverfügbarkeit, der keine Unterscheidung der beiden Phänomene zulässt.

In **Abbildung 1-1 sind diese beiden Prozesse** schematisch dargestellt. Demnach kann die **absolute orale Bioverfügbarkeit** nach Verschlucken von Schadstoffen aus dem Boden durch das Produkt des Bioaccessability-Faktors und des Bioabsorability-Faktors beschrieben werden.

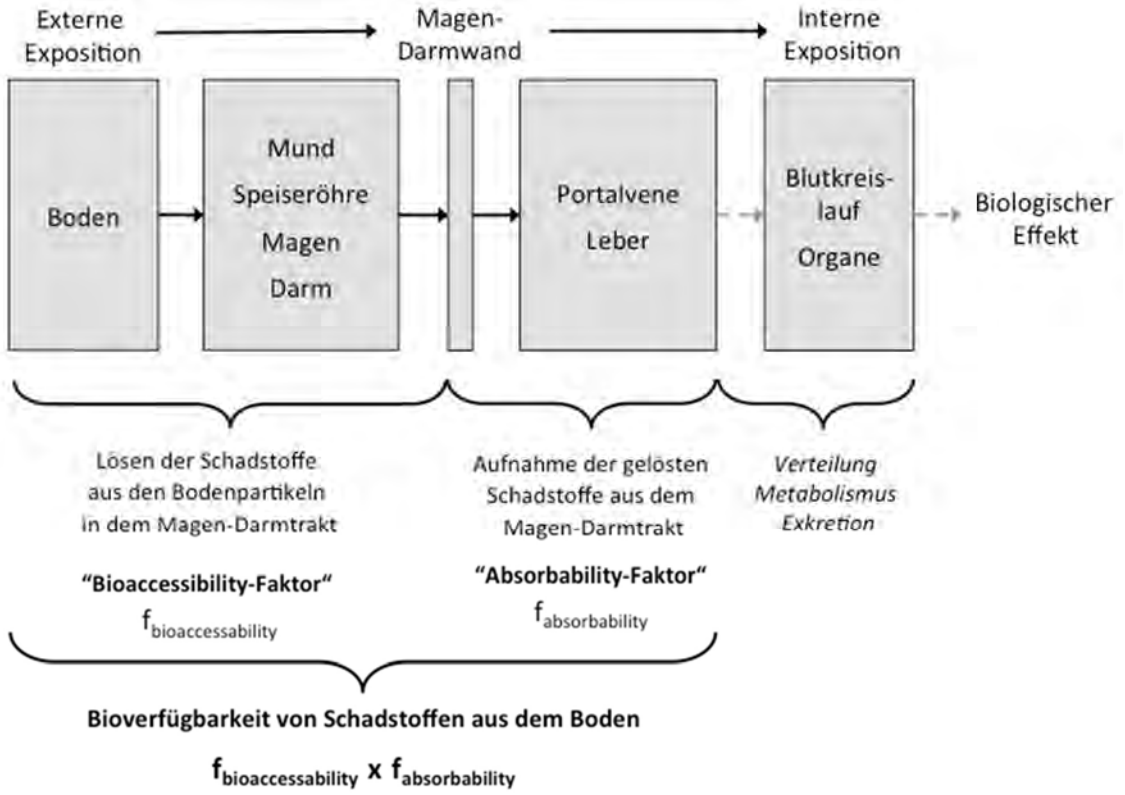
Die **Bioaccessibility** beschreibt die erste Phase, die die orale Bioverfügbarkeit von Schadstoffen aus dem Boden bestimmt. Sie bezeichnet den Anteil eines Schadstoffes, der sich an der Eintrittsstelle in den Körper von seiner Matrix (Boden, Staub) löst (USEPA 2007). Nach dem Verschlucken gelangen Schadstoffe, die an Boden- oder Staubpartikel gebunden sind über Mund und Speiseröhre zunächst in den Magen-Darm-Trakt. Dort werden sie mit Hilfe der Magen- und Darmsäfte von der Matrix gelöst und schaffen so die Voraussetzung für die Aufnahme des Schadstoffes in den Körper.

Diese zweite Phase wird durch die **Bioavailability** beschrieben (NRC 2003, S. citing Paustenbach et al., 1997; Ruby et al.,1999; USEPA "Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment" (USEPA 2007).. Nur von der Matrix gelöste Schadstoffe können in einem zweiten Schritt über die Blutgefässe der Magen- und Darmwand und die Portalvene der Leber in den Blutkreislauf aufgenommen/absorbiert werden. Diese Schadstoffe sind dann systemisch verfügbar, d.h. sie werden mit dem Blutstrom im Körper verteilt und können so die

verschiedenen Organe erreichen und schädigen. Schadstoffe, die nicht von der Matrix gelöst werden, werden vom Körper zusammen mit den Boden- oder Staubpartikel wieder ausgeschieden.

Abbildung 1-1: Vereinfachte schematische Darstellung zur Illustration der Bestimmung der oralen Bioverfügbarkeit von Schadstoffen nach Aufnahme über den Boden. In dieser vereinfachten Darstellung wird die Reduktion der Schadstoffkonznetration durch Abbauprozesse vernachlässigt.

(Quelle: basierend auf DEPA 2003)

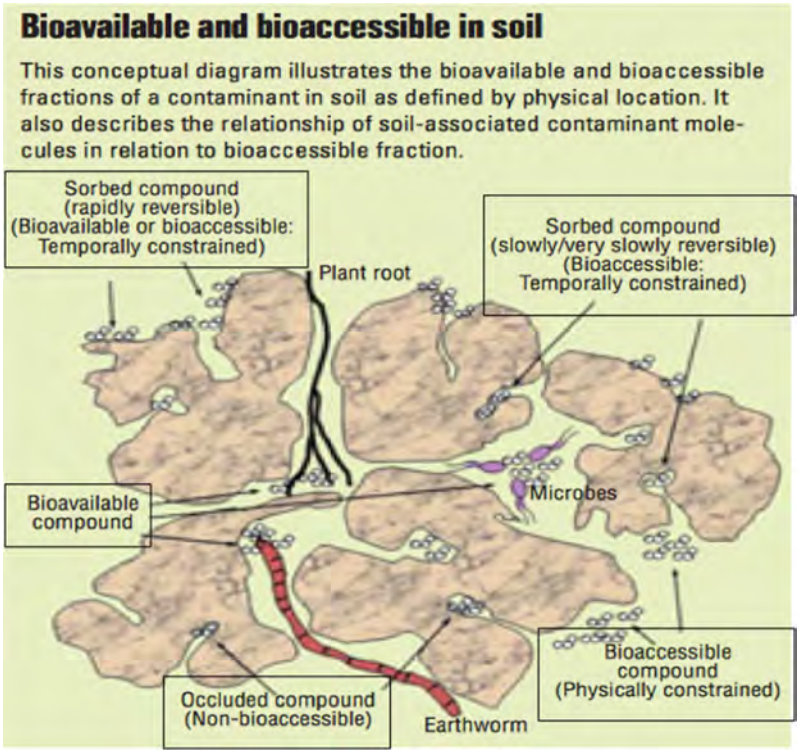


Wie hoch der Anteil der Schadstoffmenge aus dem Boden ist, der tatsächlich für eine Aufnahme über die Blutgefässe zur Verfügung steht (Bioaccessibility) hängt davon ab, wie stark ein Schadstoff an Bodenpartikel gebunden/absorbiert ist. Diese Bindung kann physikalischer oder chemischer Natur sein. Je nach Temperatur, pH-Wert oder Zusammensetzung des Bodens (z.B. Feuchtigkeit, organische Substanzgehalt, Gehalt an Mikroorganismen) kann die Stärke der Bindung variieren. Je stärker die Bindung umso geringer die Menge der Schadstoffsubstanz die systemisch verfügbar ist.

Abbildung 1-2 verdeutlicht die Zugänglichkeit der bodengebundenen Schadstoffe für Pflanzen und Regenwürmer. Das gleiche Prinzip lässt sich aber auf die Gefässwände des menschlichen Magen-Darmtraktes übertragen. Die limitierenden Prozesse zur Aufnahme von Schadstoffen aus dem Boden über Pflanzen oder Bodenorganismen (hier Regenwurm) sind konzeptionell auf die direkte Aufnahme von bodengebundenen Schadstoffen nach Verschlucken über den menschlichen Magen-Darmtrakt übertragbar.

Abbildung 1-2: Konzeptionelle Darstellung der Bioverfügbarkeit von bodengebundenen Schadstoffen am Beispiel eines Ökosystems.

(Quelle: Semple et al 2004, Fig.1)



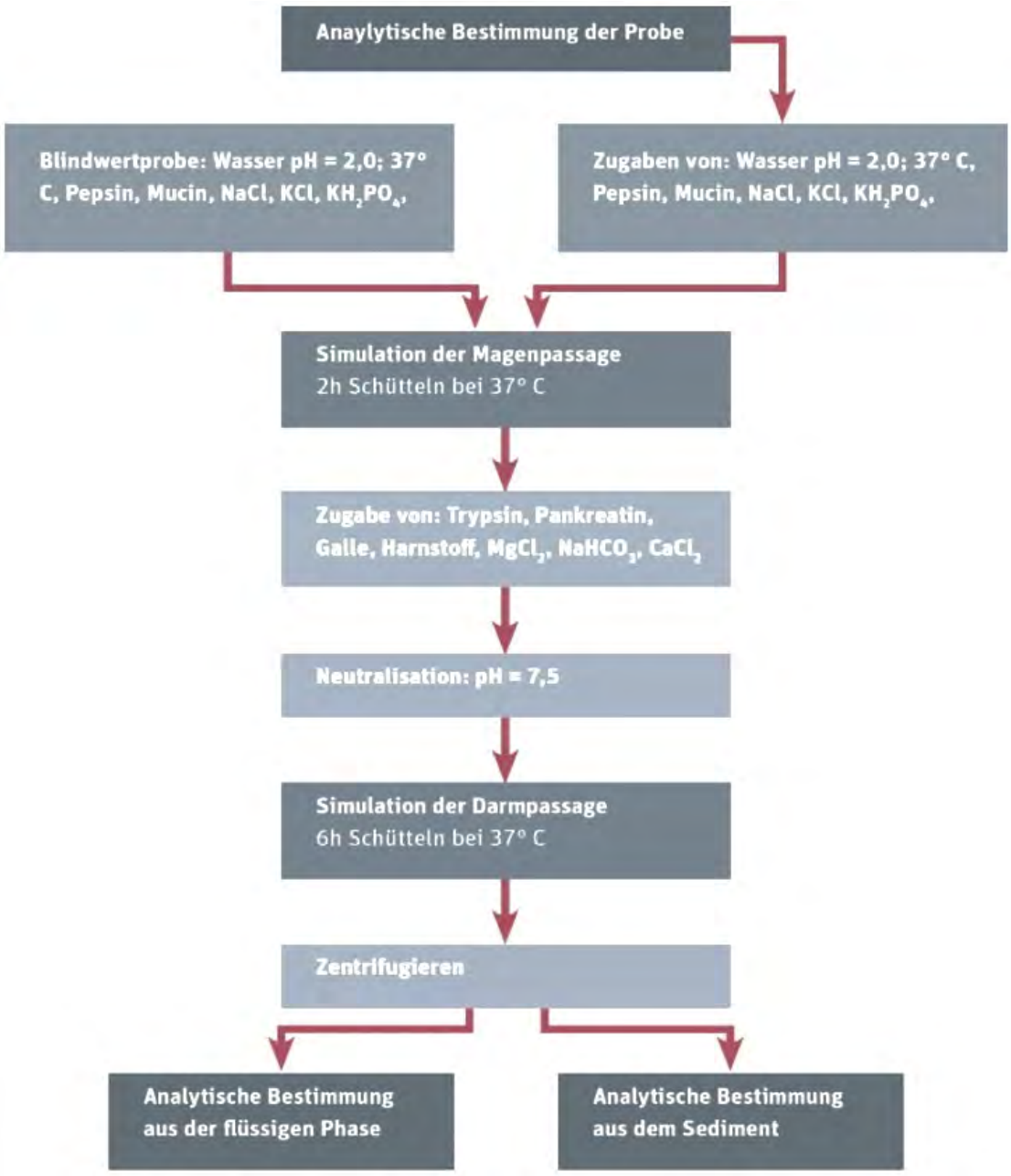
Zur **Abschätzung der "Bioaccessibility"** stehen verschiedene ***in vitro* Systeme** zur Verfügung, die Lösungsprozesse der Schadstoffe aus der Bodenmatrix während der Magen-und oder Darmpassage simulieren, z.B.:

- SBET – "Simplified Bioaccessibility Extraction Test" zur Simulation der Magenpassage
- PBET – "Physiollogically Based Extraction Test" zur Simulation der Magen-Darmpassage
- UBM – "Unified BARGE (BioAccessibility Research Group of Europe) Method" zur Simulation der Magen-Darmpassage nach harmonisierten PBET Test
- DIN EN 19738 – "Altlasten Resorptionsverfügbarkeit (Magen-Darm-Modell)" zur Simulation der Magen-Darmpassage (**siehe Abbildung 1-3**).

Abbildung 1-3: Schematische Darstellung eines *in vitro* Tests zur Bestimmung der "Bioaccessibility" von Schadstoffen aus dem Boden.

Altlasten Resorptionsverfügbarkeit von organischen und anorganischen Schadstoffen aus kontaminiertem Bodenmaterial – Flussdiagramm der „in vitro Elution" nach dem Magen-Darm-Modell DIN 19738.

(Quelle: Berghof 2014)



Generell ist die Messung der Bioaccessibility und/oder Bioavailability mit Hilfe von in vitro Systemen schwierig, weil die Komplexität der biochemischen und biologischen Prozesse im Magendarmtrakt oft unzureichend simuliert werden. Ausserdem sind die Daten aus verschiedenen Testsystemen i.d.R nicht direkt miteinander vergleichbar. Auch der Ansatz aus Kenntnis der Bioaccessibility die Bioavailability abzuleiten ist schwierig wie im nachfolgenden Abschnitt beschrieben wird.

1.2.9.4.2 Correlation between bioaccessibility and bioavailability

Several studies have attempted to compare bioaccessibility data with bioavailability data to understand if bioaccessibility could be used to predict relative bioavailability of contaminants in soil (e.g. Denys et al., 2012; Ruby et al., 1999; Schroder et al., 2003).

Gastrointestinal absorption of contaminants such as metals is a dynamic process involving dissolution and absorption. Since solubilization is usually required for absorption across membranes, poorly soluble forms of metals, with low bioaccessibility, may also have low bioavailability. In certain circumstances, if solubility is the major determinant of absorption at the portal of entry, bioaccessibility may be a predictor of bioavailability, as it is the case for lead (USEPA 2007, S.3).

It has been shown that the correlation between bioaccessibility and bioavailability strongly depends upon the interactions between dissolution and absorption kinetics. Correspondence or linear correlation between bioaccessibility and bioavailability has been reported from some studies but the limited data available (mostly lead, arsenic, cadmium and PAHs; Denys et al., 2012; Schroder et al., 2003) clearly demonstrate that the correlation is not obtained with all soils. For exemple, Denys et al. (2012) showed that bioaccessibility data obtained with the unified BARGE method are very good analogues of juvenile swine bioavailability measurements for As, Cd, and Pb. Furthermore the bioaccessibility of contaminants is highly variable even within the same soil type, source type and test. For most metals, no corresponding bioaccessibility and bioavailability data have been found (DEPA 2003, S. 61-66, 72).

Wragg and Cave (2003) reviewed some of the requirements in order to use bioaccessibility as a potential predictor of bioavailability: (i) the bioaccessibility extraction test must be based on physiologically relevant extraction test and should be validated against an animal or human study; (ii) consideration should be given to a wide range of metals and soil types; (iii) a reference soil material certified for total metal content should be used in the analyses; knowledge of the chemical speciation must be ascertained; etc. A correlation between in vitro bioaccessibility and in vivo bioavailability is necessary (i.e. the slope of the regression between bioaccessibility and bioavailability should be equal to 1), for both regulatory and scientific acceptance (Denys et al., 2012).

Wragg et al. (2011), based on the comparison of bioaccessibility data obtained with the UBM test against in vivo bioavailability on test soils, proposed a series of benchmark criteria that should be met by the in vitro and in vivo data and any subsequent mathematical regression relationship in order for the in vitro methodology to supply “fit for purpose data” for risk assessments:

1) The median repeatability on the bioavailability data should be better than 20% RSD;
2) The bioaccessibility repeatability (within-laboratory variability) should have a median value of 10% RSD and the bioaccessibility reproducibility (between-laboratory variability) a median value of 20% RSD;
3) Benchmark criteria related to the statistical parameters associated with linear regression fits to the relationship between in vivo relative bioavailability and in vitro relative bioaccessibilities[3] should be the following: *(i) the intercept is not significantly different from 0; (i) the slope should be between 0.8 and 1.2; and (iii) the r-square value (measure of the scatter around the line) should be greater than 0.6.*

These criteria were used by Denys et al. (2012) for the validation of lead, cadmium, arsenic and

[3] Relative bioaccessibility is defined as the ratio of the soil bioaccessibility to the reference matrix bioaccessibility, to allow a direct comparison with the relative bioavailability value (Denys et al., 2012).

antimony bioaccessibility UBM data against bioavailability measured in a juvenile swine model. Results indicated that the UBM produces bioaccessibility data that is a very good analogue of juvenile swine bioavailability measurements for lead, cadmium and arsenic.

1.2.9.4.3 Relative Bioavailability und 'relative absorption fraction' (RAF)-Konzept

Die Berechnung der oralen Bioverfügbarkeit als Produkt aus Bioaccessability-Faktoren und Bioabsorability-Faktoren wird häufig als wenig praktikabel eingestuft. Häufig findet deshalb das sog. RAF-Konzept Anwendung (NEPI 2000; NRC 2003 USEPA; 2007).

⇒ Auch das SCAHT wendet im Rahmen der vorliegenden Risikobeurteilung das **RAF-Konzept** an.

Im Wesentlichen beruht dieser Ansatz auf dem Vergleich der Bioverfügbarkeit von Schadstoffen aus dem Boden mit der Bioverfügbarkeit aus Nahrungsmitteln oder der Bioverfügbarkeit die in experimentellen Studien (in vivo-Fütterungsstudien und in vitro Studien) ermittelt wurden.

- Für den **Menschen** gibt es kaum Daten zur oralen Bioverfügbarkeit (RAFs) von Schadstoffen nach direkter Bodenaufnahme.
- Häufiger existieren ***in vivo* Daten** vor allem in Nagern, obwohl die USEPA mittlerweile die Untersuchung an jungen Schweinen empfiehlt **(USEPA 2007)**. Die in vivo Studien haben gezeigt, dass die Werte für die relative Bioverfügbarkeit von Schadstoffen aus dem Boden im Vergleich zur Verfügbarkeit aus der Nahrung stark schwanken je nach dem, mit welchen Böden die Studien durchgeführt wurden.
- Die Interpretation der Messung der Bioverfügbarkeit mit Hilfe von **in vitro Systemen** ist schwierig, weil die Komplexität der biochemischen und biologischen Prozesse im Magendarmtrakt oft unzureichend simuliert werden.

⇒ **Das SCAHT benutzt Daten aus in vitro Bioaccessibilitäts-Studien deshalb nur als Zusatzinformationen im Rahmen eines Weight-of-Evidence-Ansatzes**.

Box 6 beschreibt das **RAF-Konzept im Detail, der Mehrstufenansatz ist im Kapitel 1.1.2 näher beschrieben.**

BOX 6: RAF-Konzept: Relative bioavailability and 'relative absorption fraction' (RAF)

(Quelle: USEPA 2007, S.2-3; NRC 2003, S. 6-7; Ruby et al., 1999).

Absolute vs relative bioavailability

Bioavailability (BAv) expressed as a fraction (or percentage) of a dose that is absorbed and reaches the systemic circulation, is commonly referred to as absolute bioavailability (and can never be greater than 100%).

The term relative bioavailability refers to a comparison of absolute bioavailabilities, under two different exposure contexts - for example from a soil sample vs. food (therefore it can be greater than or less than 100%). For example, the absolute oral bioavailability of lead in soil ($^{Abs\ oral}BAv_{soil}$) is 30% (NRC 2003, p.71), and relative bioavailability of lead in soil compared to food is 60%. This is because 50% of lead that is bound to a food matrix is absorbed in absolute terms. But only 30% of lead that is bound to soil particles is absorbed in absolute terms. Therefore the relative absorption of lead in soil versus food is 30%: 50% = 60%.

The concept of relative bioavailability is important in human health risk assessment to understand the extent to which the absolute bioavailability of a metal increases or decreases in context with the exposure matrix (e.g., food vs. water vs. soil), or with the physical or chemical form(s) of the metal to which humans are exposed.

'Relative absorption fraction' (RAF)

Relative bioavailability is often referred to as the "relative absorption fraction" (RAF) (also termed the "relative absorption factor" or "relative bioavailability adjustment", RBA) which describes the ratio of the absorbed fraction of a substance from a particular exposure medium (e.g. soil) relative to the fraction absorbed from the dosing vehicle used in the toxicity study for that substance (e.g. a dietary study using food or water):

(Eq. 1) $$RAF = {}^{Abs\ oral}BAv_{soil} \ / \ {}^{Abs\ oral}BAv_{water\ and\ food}$$

(Eq. 2) $${}^{Abs\ oral}BAv_{soil} = RAF \times {}^{Abs\ oral}BAv_{water\ and\ food}$$

In the absence of data to the contrary, the bioavailability of a chemical should be assumed to be equal in soil, diet, and water, so that the default relative bioavailability factor i.e., RAF or RBA = 1.0 (100%). However, some cases may exist where sufficient data are available for a chemical to support development of 'medium-specific' default absorption factors for that chemical. The purpose of these medium-specific and chemical-specific default values is to increase the accuracy of exposure and risk calculations even when site-specific studies are not available (USEPA 2007, S.4). Default RAF values range typically from 0.5 to 1.0 (50-100%). For example, medium-specific values for metals are available for lead, cadmium and arsenic.

The paucity of absorption data, and the expense and difficulty associated with doing site-specific studies of relative bioavailability have led to extensive use of simplifying or default assumptions regarding chemical absorption in human health risk assessments. Regulatory agencies have not discouraged this and, as a practical matter, often specify the defaults they regard as acceptable. The most prominent default assumption imposed is this: relative bioavailability is assumed to be 100% unless there is compelling evidence to the contrary and a scientifically defensible adjustment factor can be derived (NRC 2003, p.63). Criteria as to what constitutes an acceptable scientific basis to choose a RAF other than 1.0 have not been clearly articulated by regulatory agencies. As a result, the burden of proof required to depart from a default assumption of 100% relative bioavailability is poorly defined. A default relative bioavailability assumption of 100% is often described as conservative.

To avoid overconservatism and account for more realistic exposures to soil pollutants, it is often advocated that bioavailability principles be included in risk and management-based approaches of contaminated soils for the derivation of risk-based, site-specific soil guidelines (e.g. Harmsen and Naidu, 2013; Kördel et al., 2013; Ng et al., 2015; Peijnenburg et al., 2007).

1.2.10 SCAHT tiered strategy to risk assessment

Das SCAHT hat einen Mehrstufenprozess (tiered approach) zur Abschätzung der absoluten oralen Bioverfügbarkeit aus dem Boden (Box 7) entwickelt, der sich in drei Stufen gliedert, die sich hinsichtlich der zur Verfügung stehenden Datenmenge und Datenqualität unterscheiden.

- Human toxicity data (e.g. derived from epidemiological surveys, case reports or occupational exposure data), if available, are preferred to in vivo data in experimental animals, since use of animal data as a proxy may not reflect the human situation and are associated with a greater uncertainty (interspecies differences in ADME characteristics, sensitivity, etc).

- In case there are no human toxicity studies available, experimental in vivo data in juvenile swine are preferred over rodent data. The juvenile swine model is considered the "gold standard" because the immature swine digestive system is physiologically similar, therefore more relevant and a better predictor of the human situation, in particular in the child.

- For Tier 2 assessments, following a weight-of-evidence approach, SCAHT does not disregard *in vitro* bioaccessibiilty (BAc) studies, but usees them to inform the overall assessment to better characterize the uncertainty.

TIER 1: Ideal case – data on absolute oral bioavailability from soil are available

***Abs oral*BAv_{soil}** **is known from human studies**

⇒ **no further data needed**

In a best case scenario in vivo soil ingestion studies are available from humans or experimental animals and the contaminant absolute oral bioavailability from soil value ($^{Abs\ oral}BAv_{soil}$) is available and there is no need for further data.

Within the remits of this evaluation this is only the case for lead, as outlined in the USEPA's IEUBK[4] Model for Lead in Children. An assumption in the model is that the absolute oral bioavailability of lead in soil ($^{Abs\ oral}BAv_{soil}$), at low intake rates, is 0.3 (30%) and the absolute oral bioavailability of soluble lead in water and food ($^{Abs\ oral}BAv_{water\ and\ food}$) is 0.5 (50%). This corresponds to a relative bioavailability of 0.6 (60%) for lead in soil ($^{Rel\ oral}BAv_{soil}$) compared to soluble lead in water or food ($^{Rel\ oral}BAv_{water\ and\ food}$).

TIER 2: Good case - data on absolute oral bioavailability from food are available

***Abs oral*BAv_{soil}** **is unknown but** ***Abs oral*BAv_{food}** **is known and default RAF is applied**

⇒ ***(Eq. 2)*** $^{Abs\ oral}BAv_{soil} = RAF \times {}^{Abs\ oral}BAv_{water\ and\ food}$

[4] Integrated Exposure Uptake Biokinetic Model (Hogan et al., 1998; USEPA 2007, S.4-5)

The contaminant absolute oral bioavailability from soil ($^{Abs\ oral}BAv_{soil}$) is not available from in vivo studies (humans or experimental animals) but can be estimated if human oral bioavailability data are available from dietary sources ($^{Abs\ oral}BAv_{water\ and\ food}$) using the "RAF" methodology:

To calculate/estimate $^{Abs\ oral}BAv_{soil}$, SCAHT uses a default RAF value between 50% and 100% depending on the data quality.

This is the case for most of the contaminants evaluated in this report (e.g. cadmium, arsenic, nickel, PCBs, PAHs, aliphatics). For metals (inorganics) other than lead, USEPA proposed a default RAF of 0.5 (50%) in soil compared to the water and food matrix.

TIER 3: Challenging case – extrapolation from *in vitro* bioaccessibility (BAc) studies needed

If there is evidence for a linear correlation between bioaccessibility and bioavailability based on biokinetic information

then $\boldsymbol{BAc_{in\ vitro}}$ ***is*** *used as a proxy for* $^{\boldsymbol{Abs\ oral}}\boldsymbol{BAv_{food}}$

and a default RAF is applied (RAF = 50% or 100% depending on the quality of the data base)

⇒ ***(Eq. 3)*** $^{Abs\ oral}BAv_{soil} = BAc_{in\ vitro} \times RAF$

In the case (i) absolute oral bioavailability from soil ($^{Abs\ oral}BAv_{soil}$) is not available from human or experimental animals studies, and (ii) oral bioavailability from water and/or food ($^{Abs\ oral}BAv_{water\ and\ food}$) is/are not available, *in vitro* bioaccessibility (BAc) studies could be used in certain cases as a predictor of relative absorption, provided that information on kinetics (i.e information on the dissolution and absorption processes) is available (see DEPA 2003, S.65). In such cases, preference is given to PBET or UBM tests over SBET because they are assumed to give more relevant physiological dissolution and absorption conditions for human health risk assessment. Equation 2 has to be modified as follows for the calculation: ***(Eq. 3)*** $^{Abs\ oral}BAv_{soil} = RAF \times BAc.$

⇒ **Das SCAHT versucht die limitierte orale Bioverfügbarkeit von Schadenstoffen nach direkter Bodenaufnahme zu berücksichtigen, in den es ein „realistic worst case"-Expositionsszenario für die humantoxikologische Risikobeurteilung entwickelt auf der Grundlage des in Kapitel 1.2.10.1.1. beschriebenen RAF-Konzeptes.**

⇒ **Zur Abschätzung der absoluten oralen Bioverfügbarkeit von Schadstoffen aus dem Boden ($^{Abs\ oral}BAv_{soil}$) geht das SCAHT schrittweise vor** (**siehe Box 7**). **In Tabelle 1.7 sind die vom SCAHT verwendeten Beurteilungswerte zusammengestellt. Die Verfügbarkeit und die Qualität der Studien zur Aufnahme von Schadstoffen bestimmen das Vorgehen.**

BOX 7: Entscheidungsbaum zur Riskobeurteilung von Schadenstoffen nach direkter Bodenaufnahme

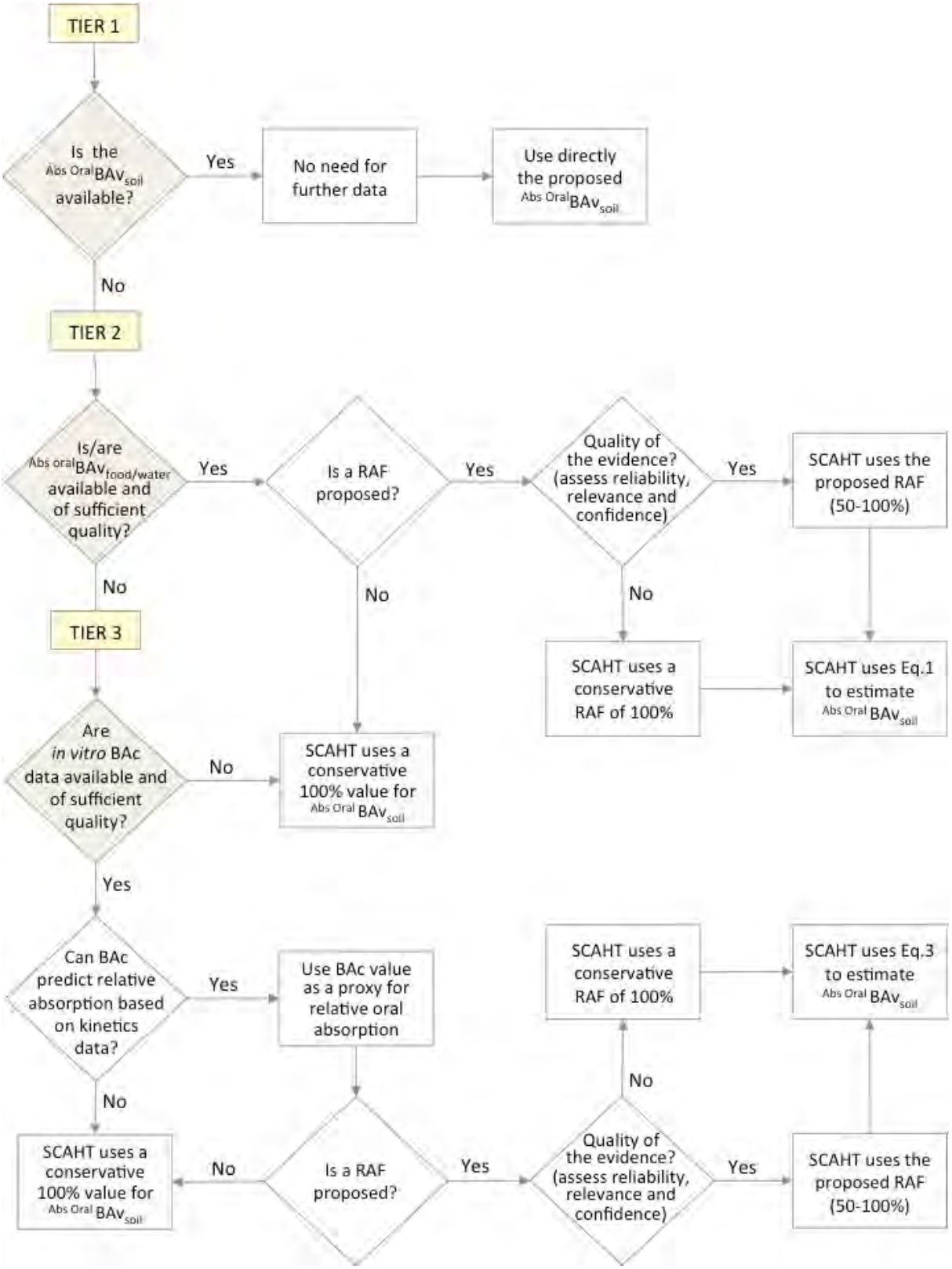


Tabelle 1-7: Zusammenstellung SCAHT verwendeter Beurteilungswerte.

Compound	Oral BAv from Food or Water	Relative Absorption Factor (RAF)	Absolute Oral BAv from Soil	Justification for RAF selection	References
Antimony	10%	100%	10%	Conservative approach to the RAF due to the lack of in vivo soil ingestion studies in animals and humans	NRC 2003; USEPA 2007
Arsenic	100%	50%	50%	Conservative approach to the RAF; USEPA (2012) estimated a collective RBA arithmetic mean of 31% (±16, SD, 5th-95th percentile range: 7-57%). RBA values used for HHRA were 42-80% for juvenile swine.	DEPA 2003; NRC 2003; USEPA 2012
Cadmium	10%	50%	5%	SCAHT uses the proposed RAF, based on relative soil absorption data from experimental animals.	Battelle & Exponent 2000; NRC 2003; Schilderman et al 1997; Schroder et al 2003.
Chromium (VI)	10%	100%	10%	Conservative approach to the RAF due to the lack of in vivo soil ingestion studies in animals and humans.	NEPI 2000; USEPA 2007
Copper	60%	100%	60%	Conservative approach to the RAF due to the lack of in vivo soil ingestion studies in animals and humans.	USEPA 2007
Lead	50%	60%	30%	Based on the USEPA IEUBK (Integrated Exposure and Uptake Biokinetic) Model	NRC 2003; USEPA 2007; Ruby et al 1999
Nickel	30%	50%	15%	Despite the poor quality of the in vivo soil ingestion databse, SCAHT uses the proposed RAF of 50%, which is strongly supported by consistent evidence from in vitro bioaccessibility studies.	de Miguel et al 2012; EU RAR 2008; Ljung et al 2007; NRC 2003; Rasmussen et al 2008; Saikat et al 2007;
Zinc	60%	100%	60%	Conservative approach to the RAF due to the lack of *in vivo* soil ingestion studies in experimental animals or humans.	USEPA 2007
Aliphatics C5-C10	100%	100%	100%	Proposed Relative Oral Bioavailability factors from soil for n-Hexane (C_6) and Nonane (C_9) of 0.91 (91%). SCAHT assumption is 100%.	NRC 2003
Aliphatics C11-C40	100%	100%	100%	Proposed Relative Oral Bioavailability factors from soil for Eicosane(C_{20}) of 0.91 (91%). SCAHT assumption is 100%.	NRC 2003
BTEX incl. Benzol	100%	100%	100%	Proposed RAF factors from soil for B, T, E, X of 1 (100%).	NRC 2003; MASS DEP 1992
NDL-PCBs	100%	50%	50%	NRC reports RAF of 0.5, supported by in vivo data in juvenile swine (5-90%); reported literature values in vivo in goats between 36-73%.	NRC 2003; Delannoy et al 2014a, 2014b; 2015
PAHs incl. BaP	100%	100% (S1) 50% (S2) 29% (S3)	100% (S1) 50% (S2) 29% (S3)	Three Scenarios are considered: (S1) SCAHT uses a conservative approach; (S2) RAF is based on the Magee rat study; (S3) RAF derivation based on expert judgment, reasoning not made explicit. S2 and S3 have been used by some US regional EPAs.	DEPA 2003; Magee et al 1996 ; NRC 2003

1.3 Zusammenfassung der wichtigsten Eckdaten zur Risikobeurteilung

Tabelle 1-8: SCAHT Standardannahmen zur Risikobeurteilung (1. Näherung)

Parameter	Wert
Expositionsdauer	Chronische Exposition
Expositionspfad	Oral
Alter des Kindes	1 - 3 Jahre
Gewicht des Kindes	12.5 kg
Bodenaufnahmemenge	250 mg/Tag (inklusive Hausstaub); Pica-Verhalten unberücksichtigt
Bioverfügbarkeit	Substanzspezifisch, wo Daten verfügbar sind.
Bioverfügbarkeit aus dem Boden ("Bioaccessibility")	Wird von Fall zu Fall als Zusatzinformation im Rahmen des Weight-of-evidence Ansatzes verwendet (siehe BOX 7).
Relative Adjustment Factor ("RAF")	Substanzspezifisch, wo Daten verfügbar sind .

1.4 Uncertainties

There are many uncertainties to the present assessment. In the following section, we describe the main identified sources of qualitative uncertainty that may impact on the overview assessment and conclusions drawn upon it. **Table 1-9** summarizes the impact of the individual sources of uncertainty on the overall outcome of the risk assessment. Not all of these uncertainties are equally relevant for individual risk assessments, e.g. some of these uncertainties appear to be more compound specific, such as ageing for organics or seasonal variations in soil organic matter content for inorganics.

Identified uncertainties can be split into:

- The estimation of bioavailability following ingestion of soil (section 1.4.1);

  Both environmental (e.g. phys-chem, pH, soil type, ageing) and physiological (e.g. biological factors: ADME, fasted vs non fasted state, homeostasis) conditions can influence a pollutant oral bioavailability from soil following ingestion. Similarly, the methodology used (e.g. in vivo study design, solubility of the test compound, sampling time) can have a large impact on the bioavailability data from the literature.

- The incidental exposure scenario constructed for the present assessment (section 1.4.2);

  The main parameters used to construct the incidental exposure scenario are reviewed in details in section 1.2.9. The main drivers are body weight, the amount of ingested soil and the duration of exposure.

1.4.1 Factors that may impact on the estimation of bioavailability from soil

Variability in relative bioavailability estimates may be due to several factors, including differences between animal species, the type of experimental methods used, a pollutant source, a pollutant concentration in the soil, and the dose used in the experiments, soil characteristics, the chemical speciation, etc. The following section describes in more details some of these contributing factors with their potential effect if they are not accounted for.

1.4.1.1 Environmental factors

- *Influence of chemical speciation (under-/over-estimation)*

  Ng et al. (2015) reported that in the case of lead, relative bioavailabilities ranking order found in various soil and soil-like materials obtained from juvenile swine dosing experiments were found to be: (i) in the low bioavailability range (RBA<25%) for lead oxide and lead sulfate; (ii) in the medium bioavailability range (RBA=25-75%) for lead phosphate and lead oxide; (iii) in the high bioavailability range (RBA>75%) for lead carbonate (see **Figure 1-4**).

- *Influence of particle size (under-/over-estimation)*

  Since a particle size of <250 µm is the most likely fraction ingested via hand-to-mouth activities by children (USEPA 2009), it is important that bioavailability be determined using this particle size fraction. Assessment of children and adult lead exposure following incidental ingestion in peri-urban contaminated soils indicated that soil particle size and bioaccessibility (inversed relationship between size particle and bioaccessibility with lead concentrations, see Figure 1-4) had a significant influence on the contribution of incidental soil ingestion to daily lead intake values (Juhasz et al., 2011). However Juhasz et al. noted that although the <250 µm particle size fraction is recommended for calculation of incidental soil ingestion, using this fraction has the potential to underestimate lead exposure due to the preferential adhesion to hands of smaller particles with elevated lead concentrations.

- *Influence of soil type and physico-chemistry (under-/over-estimation)*

  The nature of the mineral fraction (particulates, soluble, organically-bound) also plays a role (Alloway, 2004). Besides granulometry, soil pH, redox status, presence of inorganic and organic ligands, organic matter, soil microbiology can impact on the pollutant behaviour/fate, which can be more or less strongly bound to the soil, and thus more or less bioavailable for absorption. Garden top soils are assumed to have a higher total organic matter content (3-30% vs agricultural soils 1-10% and industrial sites <1%), which may contribute to reduce the mobility and therefore the absorption of soil pollutants if they are strongly adsorbed to soil particles. Metals sorb onto clays, and will thus be less bioavailable if the fraction of clay-sized material is high. Cations are more available at low pH, anions at higher pH. Calcium carbonate increase soil pH, and renders metals less bioavailable. Redox conditions can dissolve or precipitate oxides and sulphide, thus affecting the sorptive properties of a soil (Alloway, 2004).

- *Influence of soil ageing (overestimation)*

  Significant differences in oral bioavailability following singestion of soil are expected between freshly applied compounds at high concentrations, and aged residues present at low concentrations. At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures (Farrell and Reinhard, 1994; NEPI 2000, p.50). It has been shown, in particular for organic chemicals, that the bioaccessibility from soil will be reduced depending on soil ageing (NEPI 2000; Goon et al., 1991). The fractions of volatile organic chemicals (VOCs) that remain on the soil after several hours exposure to the atmosphere can be quite resistant to desorption/mobilization and stick to soil particles near the ground surface (NEPI 2000, p. 50).

1.4.1.2 Physiological and biological factors

- *Influence of inter- and intra-species variability on ADME (under-/over-estimation)*

  Bioavailability measurements in various biological tissues and organs can vary in any given study for the same species. For example, in a juvenile swine dosing experiment, Casteel et al (1997) measured a 28%, resp. 29% bioavailability in blood for two types of soils; the same measures in the liver tissues of the same animals gave a 43%, resp, 37% bioavailability for these soils. This makes averaging bioavailability more difficult.

- Susceptibility of children vs adults

  There is often limited amount of information available on the toxicity of inorganic or organic pollutants in children. Similarly, there is often insufficient information to determine whether the susceptibility of children would differ from that of adults. There is in general very little information available in which to assess whether the pharmacokinetic properties of pollutants would be different in children. In the absence of data to the contrary, it is likely that these organs/systems will also be sensitive targets in children. Therefore, this situation calls for a conservative approach to risk assessment.

1.4.1.3 Methodology

- *Influence of the solubility of the test compound in the study design (over-estimation)*

  Patinha et al (2012) raised the question of the validity of some human health risk

assessments because most animal toxicological studies are carried out with soluble forms of the contaminants, whereas many soil contaminants are or become embedded in the soil matrix and thus exhibit limited availability. Therefore these experimental in vivo studies tend overestimate the bioavailability from soil.

- *Lack of site-specific data (over-estimation)*

  The bioavailability may depend on the chemical speciation and the solubility of a pollutant as well as on site-specific soil chemistry. This indicates the need for site-specific evaluation of a soil pollutant bioavailability to avoid over- or underestimation of its actual bioavailability. In the absence of site-specific data, the bioavailability of a contaminant is assumed to be 100%. This conservative assumption could lead to unnecessary or expensive remediation options (Harmsen and Naidu, 2013; Kördel et al., 2013; Ng et al., 2015; Peijnenburg et al., 2007).

- *Analytical measurements of total pollutant content (over-estimation)*

  The determination of total pollutant content (disregarding any further chemical speciation e.g. organic vs inorganic [I, II] vs metallic [0] mercury) will lead to an over-estimation of risk (Luo et al., 2012; Kördel et al., 2013). Any assessment of contaminated sites should be based on the determination of mobile, soluble and potentially available fractions of pollutants in the soil or water compartments for uptake by plants, soil microflora and soil organisms as well as by humans (Harmsen and Naidu, 2013; Kördel et al., 2013; Peijnenburg et al., 2007).

- *Influence of the in vitro method used in bioaccessibility studies (under-/over-estimation)*

  Juhasz et al (2013) reported that lead bioaccessibility varied depending on (i) the in vitro methodology employed in the relative bioavailability leaching procedure; and (ii) the in vitro gastrointestinal assays providing more conservative lead bioaccessibility values compared to those determined using other types of assays (e.g. intestinal in vitro data) thus overestimating the bioavailability (see also Smith et al., 2011).

- *Influence of sampling time on the soil composition (under-/over-estimation)*

  Seasonal variations are known to impact on the soil organic matter contents, which in turn can change a pollutant soil bioaccessibility/bioavailability. Leinweber et al. (1994) has shown that these were reflected in significant differences in the carbon concentrations of organo-mineral particle-size fractions. The proportions of soil carbon associated with clay increased from 56% and 38% in April to 69% and 48% in October in the untreated and fertilized agricultural soils, respectively.

1.4.2 Assessment parameters used for the child incidental ingestion scenario

- *Influence of child physical characteristics (under-/over-estimation)*

  A time-weighted average body weight of 12.5 kg was used (similar to US EPA approach) for the selected age class 1-3 year old („toddlers“). Gender was not considered in the present assessment. Based on the WHO Child Growth Standards (http://www.who.int/childgrowth/standards/weight_for_age/en/), weight-for-age of 1-3 years old children in the 50th percentile population are: 8.9 kg (1yr), 11.5 kg (2 yr), 13.9 kg (3 yr) for girls, and 9.6 kg (1yr), 12.2 kg (2 yr), 14.3 kg (3 yr) for boys. A time weighted average based on WHO data would lead to 11.5 kg for girls and 12.1 kg for boys vs 12.5 kg according to the NHANES data. When considering the 50th percentile, this would lead only to a small difference in the calculation, e.g. in the case of lead $BMDL_{01}$ (NDT) of 0.5 µg/kg bw/day, a 12.5 kg child ingesting 250 mg contaminated soil (1000mg Pb/kg soil) would ingest 6.25 µg

lead/day, whereas a 11.5 kg child would ingest 5.75 µg lead/day. Taking an absolute oral bioavailability of lead from soil of 30%, this exposure would tranlsate in a clean up reference value of 83 mg vs 76 mg/kg, respectively. However the body weight range (P1-P99) is large, e.g. 8.7 to 15.5 kg for 2 years old girls, and 10.8 to 19.1 kg for 3 years old boys. This may represent a larger uncertainty.

- *Frequency and duration of exposure (over-estimation)*

  The exposure scenario is conservative as it assumes a chronic daily exposure over 365 days for a total duration of 3 years. For example, reduced outdoor activity during winter months is disregarded.

- *Amount of soil ingested (over-estimation)*

  An estimate of 250 mg daily ingestion of soil was selected (personnal communication US EPA), including housedust ingestion as well. For example, USEPA Exposure Factors Handbook 2011 recommends 200 mg/day for a realistic worse case scenario, but key studies reported 40-1000 mg intake. More recent estimates indicate average amount of 100 mg soil or even lower for use in health risk assessment. The proposed approach is therefore likely conservative.

Table 1-9: Summary of identified sources of qualitative uncertainty related to bioavailability estimates.

Sources of uncertainty	Direction
Influence of chemical speciation	*+/-*
Influence of particle size	*+/-*
Influence of soil type and physico-chemistry	*+/-*
Influence of soil ageing	*+*
Influence of inter- and intra-species variability	*+/-*
Influence of the solubility of the test compound in the study design	*+*
Lack of site-specific data	*+ [(a)]*
Analytical measurements of total pollutant content	*+*
Influence of the in vitro method used in bioaccessibility studies	*+/-*
Influence of sampling time on the soil composition	*+/-*
Influence of child physical characteristics	*+/-*
Frequency and duration of exposure	*+*
Amount of soil ingested	*+*

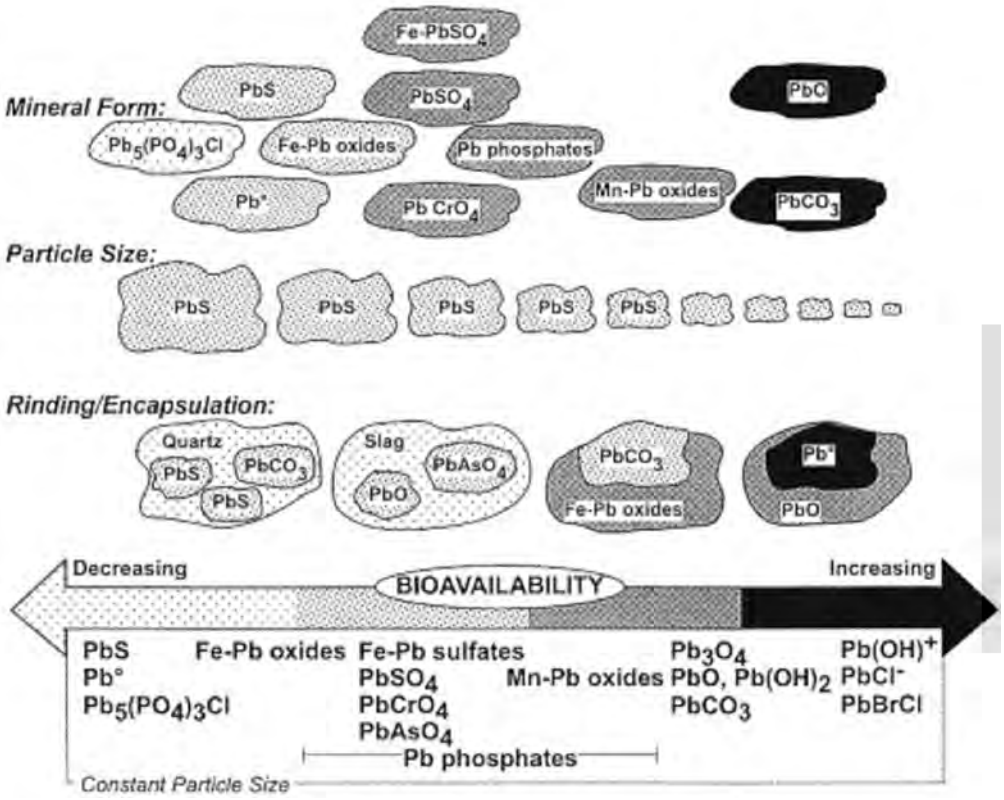
+: uncertainty with potential to cause over-estimation of exposure/risk.

-: uncertainty with potential to cause under-estimation of exposure/risk.

[(a)] conservatism would be applied, e.g. based on a worst case scenario rather than a realistic scenario to evaluate the risk.

Figure 1-4: Schematic of how different lead species, particle sizes, and morphologies affect lead bioavailability

(Quelle: Ruby et al., 1999)



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2 Kupfer

2.1 Datenblatt

Handlungsbedarf	Nein	Aktueller Sanierungswert von 1000 mg Cu/kg Boden kann beibehalten werden, sollte aber nicht erhöht werden, weil bereits eine Überversorgung mit Kupfer besteht.
Gefährdungspotential	Gering	Kupfer ist ein essentielles Spurenelement. Kupfer ist von geringer akuter und chronischer Toxizität.
Kanzerogen	Nein	Nur für Kupfer(II)8-hydroxyquinolin IARC Klassifizierung vorhanden: IARC Gruppe 3 (nicht klassifizierbar bezüglich Kanzerogenität für den Menschen.
Mutagen	Nein	
Reprotoxisch	Nein	Ja: in vivo bei hohen Dosen (27 - 120 mg/kg) Nein: Im Menschen gibt es keine Hinweise auf Reproduktionstoxizität
Neurotoxisch	Nein	
Andere	Ja	Akut: Gastrointestinaltrakt Chronisch: Leber
Gesundheitsbasierter Referenzwert		Tolerierbare tägliche Aufnahmemenge: 1.0 mg/Tag (Kinder 1 - 3 Jahre) Unter Berücksichtigung der Lebereffekte und der gastrointestinalen Effekte
Exposition		
Äussere Exposition Boden (250 mg)		1000 mg Cu/kg Boden = 250 µg Cu/250 mg Boden = 20 µg Cu/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 60% Bioavailability: 12 µg Cu/kg KG/Tag (KG: 12.5kg) = 150 µg /Tag = 3.5% der Kupferaufnahme über die Nahrung Bei 100% Bioavailability: 20 µg Cu/kg KG/Tag (KG: 12.5kg) = 250 µg /Tag = 5.8% der Kupferaufnahme über die Nahrung

Hintergrundexposition Nahrung, Wasser, Luft		Kupferbedarf: 0.5 - 1 mg/Tag (Kinder 1 - 3 Jahre) Tolerierbare tägliche Aufnahmemenge: 1.0 mg/Tag (Kinder 1 - 3 Jahre) Geschätzte Kupferaufnahme über die Nahrung: 4.3 mg/Tag (Kinder 1 - 3 Jahre)
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Unwahrscheinlich	Die geschätzte tägliche Kupferaufnahme durch die Nahrung überschreitet sowohl den Bedarf als auch die tolerierbare tägliche Aufnahmemenge. Die Aufnahme von Kupfer durch das Verschlucken von kontaminiertem Boden ist aber klein im Vergleich zur unvermeidbaren Hintergrundbelastung und stellt somit kein zusätzliches Gesundheitsrisiko dar. Generell stellt die Überschreitung der tolerierbaren Aufnahmemenge durch die Nahrung kein Gesundheitsrisiko dar, denn Kupfer ist von geringer Toxizität und der Körper kann den Kupferhaushalt auch bei Aufnahme hoher Kupfermengen im Gleichgewicht halten. Auch wenn man in einem „worst case“-Szenario von einer 100%igen Bioverfügbarkeit des Kupfers aus dem Boden ausgeht, besteht kein zusätzliches Gesundheitsrisiko, weil die Bandbreite der homöostatischen Regulation selbst dann nicht überschritten wird. Kupferbedarf : 0.5 - 1.0 mg/Tag (Kinder 1 - 3 Jahre) Tolerierbare Aufnahmemenge: 1.0 mg/Tag (Kinder 1 - 3 Jahre) Kupferaufnahme über die Nahrung: 4.3 mg/Tag (Schätzung für Kinder im Alter von 1 - 3 Jahren auf der Basis von 4-8-Jährigen, siehe Tabelle 2.3) Kupferaufnahme durch direkte Bodenaufnahme: 150 µg/Tag (60% Bioaccessibility) Grosse Bandbreite der Homöostase (bis zur Kupferaufnahme von 5.8 mg/Tag)
Grenzwert im Vergleich		USA: 3100-150; **CH: 1000**; A: 600; B: 400; NL & F: 190; S: 100; I: 120; CAN: 63 (mg/kg dm)
Datenlage	Zufriedenstellend	Es gibt keine Studien zur Bioverfügbarkeit von Kupfer aus dem Boden im Menschen oder Tier. Aufgrund der geringen Toxizität des Kupfers und der grossen Bandbreite der homöostatischen Regulation bestehen keine Unsicherheiten bezüglich der Risikobeurteilung.

2.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (AltlV)[1] festgelegte Sanierungswert für Kupfer in Höhe von 1000 mg Cu/kg Boden für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, kann beibehalten werden.

Kupfer ist ein essentielles Spurenelement, das neben Zink und Eisen als dritthäufigstes Element im Körper vorkommt. Kupfer fungiert primär als Cofaktor von vielen Metalloproteinen bzw. ist für deren Enzymfunktion notwendig.

Der Kupferbedarf von Kindern im Alter zwischen 1 und 7 Jahren wird auf 0.5-1.0 mg/Tag geschätzt. Die tolerierbare tägliche Aufnahmemenge (Tolerable Upper Intake Level, UL) für Kupfer steigt für Kinder mit zunehmendem Alter und beträgt zwischen 1-4 mg/Tag. Der UL für 1 bis 3-Jährige beträgt 1 mg/Tag und für 4 bis 6-Jährige beträgt er 2 mg/Tag. Die Kupferaufnahme über die Nahrung kann bei Kindern je nach Alter aber wesentlich höher liegen. So kann die Versorgung für Kinder ab dem 4. Lebensjahr bis zu 4.3 mg/Tag betragen. Deshalb bleibt rein rechnerisch gesehen kein grosser Spielraum für die zusätzliche Aufnahme von Kupfer.

Das Verschlucken von 250 mg Boden der mit 1000 mg Cu/kg Boden belastet ist, würde zu einer zusätzlichen externen Exposition von 250 µg Cu führen. Da es keine in vivo Studien zur oralen Bioverfügbarkeit von Kupfer aus dem Boden gibt, wendet das SCAHT einen konservativen Ansatz an und schätzt die absolute orale Bioverfügbarkeit aus dem Boden auf 60%. Damit würde die zusätzliche Belastung durch das Verschlucken von 250 mg Boden, der mit 1000 mg Cu/kg Boden belastet ist, auf 150 µg sinken.

Wie viel Kupfer tatsächlich vom Körper aufgenommen wird, ist homöostatisch reguliert und hängt vom Ernährungszustand ab. Bei normaler Ernährungsweise liegt die durchschnittliche Resorptionsrate im Bereich von 30-40%.

Das SCAHT geht davon aus, dass das zusätzliche Gesundheitsrisiko durch das Verschlucken von Boden gering ist. Aufgrund der publizierten Daten würde man ohnehin von einer Überversorgung der Kinder mit Kupfer ausgehen. Die zusätzliche Aufnahme von 60 µg Cu erscheint bei einem geschätzten Bedarf von 0.5-1 mg/Tag als wenig relevant für gesunde Kinder. Einerseits konnten verschiedene Studien zeigen, dass die Bandbreite der homöostatischen Regulation von Kupfer sehr gross ist d. h. dass der Körper eine grosse Toleranz gegenüber hohen Aufnahmemengen von Kupfer besitzt. So konnte gezeigt werden, dass bei einer Kupferaufnahme zwischen 0.8 und 5.5 mg/Tag der Kupfergehalt im Körper konstant bleibt (Turnland 1998 *in* SCF 2003, Seite 3, Paragraph 3). Andererseits ist die Toxizität von Kupfer gering. Akute Toxizität wird beim Menschen selten beobachtet und ist in der Regel auf eine Lebensmittel-/Trinkwasserkontamination durch kupferhaltige Aufbewahrungsgefässe zurückzuführen. In solchen Fällen kommt es zu gastrointestinalen Irritationen mit erhöhtem Speichelfluss, Bauchschmerzen, Brechreiz, Erbrechen und Durchfall. Der kritischste Endpunkt der chronischen Kupfertoxizität ist die Leber. Die chronische Exposition gegenüber Kupfer kann bei Kindern Durchfälle und akutes Leberversagen verursachen. Leberschäden bei Kindern sind aber auf solche Kinder beschränkt, die eine erbliche Prädisposition für eine erhöhte Kupfertoxizität haben.

Selbst unter der Annahme, dass Kinder gegenüber Kupferüberversorgung empfindlicher sind als Erwachsene, weil der Exkretionsmechanismus über die Galle seine volle Leistungsfähigkeit erst im

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

Laufe der ersten Lebensjahre entwickelt und für Säuglinge und Kleinkinder eine höhere Resorptionsrate als bei Erwachsenen angenommen wird, erscheint das zusätzliche Gesundheitsrisiko durch eine Kupferaufnahme über den Boden in Höhe von etwa 10% des geschätzten täglichen Bedarfs auch angesichts einer verminderten homöostatischen Regulation als wenig wahrscheinlich.

Nach Ansicht des SCAHT würde durch eine Reduktion des Sanierungswertes für Kupfer kein erheblicher Beitrag zur Risikominderung entstehen. Andererseits besteht aber nach Ansicht des SCAHT auch kein Grund, den Sanierungswert für Kupfer anzuheben, da bereits mit einer Überversorgung der Kinder durch die Nahrung zu rechnen ist.

2.3 Gefährdungspotential

Kupfer ist ein essentielles Spurenelement, das neben Zink und Eisen als dritthäufigstes Element im Körper vorkommt, vor allem in Form von komplexgebundenem-Cu^{2+}. Kupfer fungiert primär als Cofaktor von vielen Metalloproteinen (Cuproenzym), bzw. ist für deren Enzymfunktion notwendig (BFR 2004, Kapitel 15.2.2, Seite 281, Tabelle 41). Kupfer wird u. a. benötigt für das Wachstum, den körpereigenen Abwehrmechanismus, die Knochenstärke, die Reifung der roten und weissen Blutkörperchen, den Eisentransport und den Cholesterin- und Glukosemetabolismus (SCF 2003, Kapitel 2.1, Seite 2).

Die Toxizität des Kupfers variiert je nach chemischer Verbindung und ist u. a. abhängig vom Zink-, Eisen- und Molybdängehalt in der Nahrung.

- Für den Menschen ist Kupfer von geringer akuter Toxizität. Sie äussert sich vor allem in Form von lokalen gastrointestinalen Irritationen, Übelkeit, Erbrechen und Durchfällen (SCF 2003, Kapitel 3.2, Seite 6, BFR 2004, Kapitel 15.3.3.1, Seite 285, Paragraph 2). Akute Toxizität wird beim Menschen selten beobachtet und ist in der Regel auf eine Lebensmittel-/Trinkwasserkontamination durch kupferhaltige Aufbewahrungsgefässe zurückzuführen (SCF 2003, Kapitel 3.3.1, Seite 7).
- Als kritischsten Endpunkt der Toxizität im Menschen wird die Lebertoxizität nach chronischer Exposition betrachtet (SCF 2003, Kapitel 3.2, Seite 6). Bei chronisch überhöhter Exposition akkumuliert Kupfer in der Leber, die zunächst durch Komplexierung an Metallothionein oder das sog. Mitochondrocuprein längere Zeit geschützt zu sein scheint. Chronische Vergiftungserscheinungen sind insgesamt weniger markant und treten erst auf, wenn die Eliminationsfunktion der Leber für Kupfer überschritten wird. Bei einem Überangebot an Kupfer wird die biliäre Exkretion deutlich gesteigert (BFR 2004, Kapitel 15.3.3.1, Seite 285, Paragraph 3).
- Es gibt keine Hinweise auf Humankanzerogenität beim Menschen (SCF 2003, Kapitel 3.3.2.2, Seite 8, letzter Satz). Lediglich Kupfer(II) 8-hydroxyquinolin ist von der IARC (International Agency for Research on Cancer) als Gruppe 3 (nicht klassifizierbar bezüglich Kanzerogenität für den Menschen) eingestuft worden (SCF 2003, Kapitel 3.2.2, Seite 7, Paragraph 2). Das beruht aber auf der Tatsache, dass die vorhandenen in vivo Daten, die keine Hinweise auf Kanzerogenität im Tierversuch gaben, als nicht robust genug für eindeutige Klassierung eingestuft wurden (SCF 2003, Kapitel 3.2.2, Seite 7, Paragraph 1).
- Im Tierversuch bei hohen Dosen (27-120 mg/kg Körpergewicht (KG)/Tag) konnten Effekte auf Fortpflanzungsorgane (Gewicht/Histologie) sowie embryotoxische / fetotoxische Wirkungen festgestellt werden (SCF 2003, Kapitel 3.2.3, Seite 7). Beim Menschen gibt es keine Hinweise auf Reproduktionstoxizität (SCF 2003, Kapitel 3.3.3, Seite 9).

Akute Toxizität wird beim Menschen selten beobachtet und uneinheitlich beschrieben. So soll die versehentliche Aufnahme von 15-75 mg Kupfer gastrointestinale Störungen verursachen können. Eine Dosis von 25-75 mg führt zum Erbrechen. Andere Autoren berichten, dass Erbrechen und Magenbrennen als reversible Wirkungen bereits bei oralen Dosen von 10-15 mg beobachtet werden. Mit Trinkwasser aufgenommenes Kupfer führte bereits bei deutlich kleineren Dosen zu toxischen Wirkungen. Zwei Studien identifizierten die Schwelle für akute gastrointestinale Effekte von Kupfer in Wasser bei ca. 4.8 mg/Tag, basierend auf einer Konzentration von 3 mg Kupfer pro Liter Wasser und einer mittleren Wasseraufnahme von 1.6 Liter pro Tag. Nach einer weiteren Arbeit liegt die Schwelle zur akuten Toxizität von Kupfer in Trinkwasser bei etwa 6 mg pro Liter. Beim Menschen werden akute Vergiftungserscheinungen (Kuprismus) eher selten beobachtet, z. B. nach Verzehr von kontaminierten Lebensmitteln oder Getränken aus kupferhaltigen Behältnissen oder durch sonstige Aufnahme von Kupfersalzen (v.

a. Kupfersulfat, basisches Kupferacetat = Grünspan). Die Symptome umfassen verstärkten Speichelfluss, Magenschmerzen, Übelkeit, Erbrechen und blutig-wässrigen Durchfall. Bei höheren Dosen treten schwere bis schwerste Verlaufsformen auf, die zu Geschwürbildung, Hämorrhagien im Gastrointestinaltrakt, intravasaler Hämolyse, Hämoglobinurie, Hypotonie, Lebernekrose und Leberversagen sowie zu Nieren- und Kreislaufversagen, Kollaps, Koma und schliesslich zum Tod führen können. Die tödliche Dosis von Kupfersalzen (meist Kupfersulfat) soll bei ca. 200 mg/kg Körpergewicht liegen.

Der kritischste Endpunkt der chronischen Kupfertoxizität ist die Leber. Die chronische Exposition gegenüber Kupfer kann bei Kindern Durchfälle und akutes Leberversagen verursachen. Leberschäden bei Kindern sind aber auf solche Kinder beschränkt die eine erbliche Prädisposition für eine erhöhte Kupfertoxizität haben.

Bei chronisch überhöhter Exposition akkumuliert Kupfer in der Leber, die zunächst durch Komplexierung an Metallothionein oder das sog. Mitochondrocuprein längere Zeit geschützt zu sein scheint. Chronische Vergiftungserscheinungen sind insgesamt weniger markant und treten erst auf, wenn die Eliminationsfunktion der Leber für Kupfer überschritten wird. Es kann zu Leberparenchymschädigung, Hepatitis, Leberzirrhose und zu einer hämolytischen Krise kommen. Besonders empfindlich reagieren Säuglinge und Kleinkinder, bei denen es zu frühkindlicher Leberzirrhose kommen kann, wenn deren Nahrung mit saurem und über längere Zeit in Kupferinstallationen (Rohre, Boiler, Armaturen) abgestandenem Wasser ("Stagnationswasser") aus Hausbrunnen zubereitet worden war. Andere Faktoren, wie Virusinfektionen, Mangel anderer Spurenelemente, genetische Disposition bzw. angeborene Gallenwegs- und Stoffwechselanomalien, sind ebenfalls von Bedeutung. Eine hohe Kupferaufnahme kann neben anderen möglichen Faktoren zu der als "Indian Childhood Cirrhosis" (ICC) bekannt gewordenen Erkrankung führen und wird als Hauptauslöser für die Entstehung der "Idiopathic Copper Toxicosis" (ICT) angesehen.

Bei Patienten mit Morbus Wilson, einem seltenen autosomal-rezessiv vererbten Gendefekt, ist die Kupferhomöostase gestört. Die Inzidenz weltweit ist 1:30000 und führt zur toxischen Kupferakkumulation. Die klinischen Folgen dieser Kupferüberladung betreffen bei fehlender Behandlung insbesondere die Leber mit Zirrhose sowie das ZNS, darüber hinaus Augen, Blut und Nieren.

2.4 Gesundheitsbasierter Referenzwert

Die sichere Gesamtzufuhr „Tolerable Upper Intake Level (UL)“ wurde unter Berücksichtigung der Lebereffekte und gastrointestinalen Effekte, welche als die kritischsten toxikologischen Endpunkte gelten, abgeleitet. Es gibt Empfehlungen verschiedener Gremien, die in der Grössenordnung von 5-10 mg/Tag für Erwachsene liegen.

Die UL-Werte für Kinder wurden ausgehend von den Werten der Erwachsenen extrapoliert. Demnach ergibt sich für Kinder im Alter von 1-3 Jahren ein UL von 1 mg/Tag (SCF 2003, Kapitel 5.3, Seite 11; FNB 2001, Seite 251/797) (**Tabellen 2-1 und 2-2**).

Tabelle 2-1: Tolerable Upper Intake Level (UL) für Kupfer in mg pro Tag
(Quelle: SCF 2003, Kapitel 5.3, Seite 11)

Lebensjahre	Tolerable upper Intake level (UL) (mg/Tag)
<1	Nicht bestimmbar
1 - 3	1
4 - 6	2
7 - 10	3
11 - 14	4
15 - 17	4
Erwachsene	5
Schwangere/Stillende	Nicht bestimmbar

Tabelle 2-2: Tolerable Upper Intake Level (UL) für Kupfer in mg pro Tag
(Quelle: FNB 2001, Seite 251/797)

Lebensjahre	Tolerable upper Intake level (UL) (mg/Tag)
<1	Nicht bestimmbar
1 - 3	1
4 - 8	3
9 - 13	5
14 - 18	8
Erwachsene	10
Schwangere/Stillende	Nicht bestimmbar

2.5 Exposition

2.5.1 Äussere Exposition

Die Versorgung mit Kupfer übersteigt den Bedarf. Die angemessene Zufuhr und der Versorgungszustand können je nach Quelle stark schwanken (**Tabelle 2-3**). Eine einzelne Quelle, die Bedarf, Versorgung und zulässige sichere Gesamtzufuhr für Kinder in harmonisierten Altersgruppen auflistet, konnte nicht identifiziert werden. Die Interpretation der konsolidierten Daten aus verschiedenen Quellen (**Tabellen 2-3 und 2-4**) zur Aufnahme von Kupfer weist darauf hin, dass bei sonst gesunden Personen nicht mit einer unzureichenden Versorgung mit dem Spurenelement Kupfer zu rechnen ist (BfR 2004, Kapitel 15.1, Paragraph 1, Seite 279). Allgemein gilt in Europa, dass die geschätzte Versorgung mit Kupfer aus der Nahrung bei allen Altersgruppen mit Ausnahme der Säuglinge über dem Bedarf liegt.

Obwohl bei Säuglingen der tägliche Bedarf die Versorgung übersteigt, ist kein Kupfermangel zu erwarten. In Kombination mit dem bei der Geburt vorhandenen Kupferspeicher in der Leber und der bei Säuglingen höheren Absorptionsrate für Kupfer aus der Nahrung kann der Kupferbedarf in den ersten Lebensmonaten durch Muttermilch gedeckt werden (BfR 2004, Kapitel 15.2.3, Paragraph 1, seite 283).

2.5.1.1 Kupfer Bedarf

Der Verband der Deutschen, Österreichischen und Schweizer Gesellschaft für Ernährung (DACH) hat im Jahr 2000 den Bedarf von Kindern ab dem 7 Lebensjahr, Jugendlichen und Erwachsenen von 1.5-3.0 mg/Tag auf 1.0-1.5 mg/Tag reduziert (BfR 2004, Kapitel 15.2.1, Seite 281, Paragraph 2). Das SCF hat im Jahre 1992 ein Population Reference Intake (PRI) für Erwachsene von 1.1 mg/Tag festgelegt. USA und WHO benennen Bedarfswerte unter 1 mg/Tag bzw. beziffern den Durchschnittsbedarf von Erwachsenen mit 11 µg/kg Körpergewicht (BfR 2004, Kapitel 15.2.1, Seite 282, Paragraph 1). In den USA wurden für die tägliche Kupferzufuhr in Abhängigkeit vom Lebensalter Recommended Dietary Allowances (RDA) bzw. Adequate Intakes (AI) wie in **Tabelle 2-3**, Spalte USA festgelegt.

2.5.1.2 Kupfer Versorgung

- **Säuglinge**

  Der Kupfergehalt von Muttermilch ist nicht konstant, sondern fällt während der Stillzeit in den ersten sechs Monaten von 0.6 auf 0.2 mg pro Liter ab. Das voll gestillte Kind erhält täglich im Durchschnitt etwa 0.06 mg Kupfer pro kg Körpergewicht. Wegen der bei Geburt vorhandenen Kupferspeicher in der Leber und der hohen Absorptionsrate wird angenommen, dass der Kupferbedarf in den ersten Lebensmonaten allein durch Muttermilch gedeckt werden kann. Andere Autoren beschreiben unter der Annahme einer sezernierten Milchmenge von 750 ml/Tag und einer Bioverfügbarkeit von 50% für Stillende einen zusätzlichen Bedarf von 0.3 mg Kupfer/Tag (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 6).

- **Kinder**

  In Deutschland ist die Zufuhr von Kupfer mit der Nahrung in den letzten 10 Jahren angestiegen (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 1). Zu Kindern ab vier Lebensjahren und Jugendlichen in Deutschland liegen auf Basis von Erhebungen aus den Jahren 1985 - 1988 Medianwerte der täglichen Kupferzufuhr vor. Die Medianwerte betragen bei weiblichen Personen im Alter von 4 - 8 Jahren 1.4 mg/Tag bis 1.9 mg/Tag, das 97.5 Perzentil liegt bei 3.0 mg/Tag bis 3.7 mg/Tag. Für männliche Personen im Alter von 4 - 8 Jahren liegen die Werte bei 1.6 mg/Tag bis 2.3 mg/Tag (Median) und 3.2 mg/Tag bis 4.3 mg/Tag (97.5 Perzentil) (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 2).

⇒ **Das SCAHT konnte keine Daten zur Kupferversorgung der 1-3 Jährigen identifizieren und hat deshalb zur Abschätzung der Exposition das obere 97.5 Perzentil der 4-8-Jährigen verwendet. Das SCAHT begründet diesen konservativen Ansatz mit einer erhöhten Hand-zu-Mund-Aktivität von 1-3 Jährigen gegenüber 4-8 Jährigen.**

- **Erwachsene**

  Bei erwachsenen Frauen und Männern liegen die Werte bei 1.1 mg, bzw 1.2 mg (DACH, 2000). Andere Autoren geben Medianwerte der täglichen Aufnahme von Kupfer mit der Nahrung in Deutschland bei Erwachsenen mit 1.8 mg/Tag für Frauen bzw. 2.2 mg/Tag für Männer an, wobei die 97.5 Perzentilen 3.3 mg/Tag bzw. 4.0 mg/Tag betragen.

  Die mittlere Aufnahme von Kupfer mit der Nahrung bei Erwachsenen in verschiedenen europäischen Ländern wurde geschätzt in Bereichen von 1.0-2.3 mg/Tag für Männer und 0.9-1.8 mg/Tag für Frauen (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 3).

  Vegetarier zeigten mit einer Kupferaufnahme von ca. 2.1-3.9 mg/Tag eine höhere Aufnahme als Personen, welche sich nicht rein vegetarisch ernährten (1.0-1.5 mg/Tag) (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 4).

  Die WHO gibt die normale alimentäre Kupferaufnahme mit Werten von 0.94-2.2 mg/Tag an, für Kinder liegt sie häufig unter 1 mg/Tag (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 7).

  In den USA werden Medianwerte für die alimentäre Kupferaufnahme genannt, die für Männer im Bereich von 1.2 bis 1.6 mg/Tag und für Frauen von 1.0 bis 1.1 mg/Tag liegen. Personen, die kupferhaltige Nahrungsergänzungen (copper supplements) verzehren, nehmen im Mittel zusätzlich 0.3-0.5 mg/Tag auf (BfR 2004, Kapitel 15.2.3, Seite 283, Paragraph 8).

Tabelle 2-3: Schätzwerte für den Kupferbedarf und die Versorgung (Cu mg/Tag)
(Quelle: Bedarf: BfR 2004, Kapitel 15.2.2., Seite 281 Tabelle 41 und Seite 282, Paragraph 1; Versorgungszustand: BfR 2004, Kapitel 15.2.3., Seite 282 Tabelle 41 und Seite 282, Paragraph 1)

Alter	**Bedarf oder Versorgung**	**DACH (2000)/Andere Quellen**	**USA (FNB 2001)**	**WHO (1996, 1998)**	**SCF (1993)**
0-4 Monate	Bedarf Versorgung	0.2 - 0.6 $_{(DACH)}$ 60 µg kg KG/Tag	-	- -	- -
0-6 Monate	Bedarf Versorgung	- -	0.2 -	- -	- -
4-12 Monate	Bedarf Versorgung	0.6 - 0.7$_{(DACH)}$ -	- -	- -	- -
7-12 Monate	Bedarf Versorgung	- -	0.22 -	- -	- -
1-3 Jahre	Bedarf Versorgung	- -	0.34 -	- -	- -
1-7 Jahre	Bedarf Versorgung	**0.5 - 1.0$_{(DACH)}$** -	- -	- -	- -
4-8 Jahre	Bedarf Versorgung	- 1.4 - 1.9 (Median) (w_{Andere}) 3.0 - 3.7 (97.5 Percentil) (w_{Andere}) 1.6 - 2.3 (Median) (m_{Andere}) **3.2 - 4.3 (97.5 Percentil)** (m_{Andere})	0.44 -	- -	- -
7-15 Jahre	Bedarf Versorgung	1.0 - 1.5$_{(DACH)}$ -	- -	- -	- -
9-13 Jahre	Bedarf Versorgung	- -	0.70 -	- -	- -
14-18 Jahre	Bedarf Versorgung	- -	0.89 -	- -	- -
Jugendliche	Bedarf Versorgung	1.0 - 1.5$_{(DACH)}$ -	- -	- < 1.0	- -
Erwachsene	Bedarf Versorgung	1.0 - 1.5$_{(DACH)}$ 1.1 (w_{DACH}); 1.8 (Median) (w_{Andere}) 3.3 (97,5 Percentil) (w_{Andere}) 1.2 (m_{DACH}) 2.2 (Median) (m_{Andere}) 4.0 (97,5 Percentil (m_{Andere})	0.9 1.0 - 1.1 (Median) (w) 1.2 - 1.6 (Median) (m)	< 1.0 0.94 - 2.2	1.1 0.9 - 1.8 (w) 1.0 - 2.3 (m)
Schwangere	Bedarf Versorgung	1.0 -1.5$_{(DACH)}$ -	1.0 -	- -	- -
Stillende	Bedarf Versorgung	1.0 -1.5$_{(DACH)}$ -	1.0 -	- -	- -

Abkürzungen: DACH: Verband der deutschen, österreichischen und schweizerischen Gesellschaften für Ernährung; Andere: Zusätzliche Referenzen in BfR 2004 Dokument die sich nicht auf Angaben der DACH beziehen; SCF: Scientific Committee on Food of the European Commission; WHO: World Health Organization; m: männlich; w: weiblich.

Tabelle 2-4: Tägliche Kupferaufnahme (mg/Tag) aus Lebensmitteln in EU-Ländern
(Quelle: SCF 2013, Kapitel 2.7, Seite 5, Tabelle 1)

Land	Studientyp	n	Methode	Mittel	97.5%
Österreich[a]	Einzelperson	2488	24 h	2.0	4.2
Deutschland[b]	Einzelperson (m)	854	7 Tage Ernährungsprotokoll	2.2	4.0
	Einzelperson (w)	1134		1.8	3.3
UK[c]	Einzelperson (m)	1087	7 Tage gewichtete Lebensmittelvorräte	1.6	3.5
	Einzelperson (w)	1110		1.2	2.8
Italien[d]	Haushalt	2734	7 Tage Ernährungsprotokoll	1.4	2.8
Niederlande[e]	Einzelperson	5958	2 Tage Ernährungsprotokoll	1.1	1.2
Irland[f]	Einzelperson (m)	662	7 Tage geschätztes Ernährungsprotokoll	1.5	3.1
	Einzelperson (w)	717		1.2	2.7

[a] Elmadfa et al. (1998)
[b] Heseker et al. (1994) (VERA Study) - median values
[c] Gregory et al. (1990) - values are the mean with the median in parentheses
[d] Turrini (1996)
[e] Hulshof and Kruizinga (1999)
[f] IUNA (2001)

2.5.2 Innere Exposition

For copper, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

The absolute oral bioavailability of copper from soil is not directly available for humans. However, the copper absorption rate after oral exposure to food and/water is relatively well characterized in humans (section 2.5.2.1) and it is estimated to be 60% .

Therefore the Relative Oral Adjustment Factor (RAF) approach can be used to estimate the absolute oral bioavailability from soil. There are no in vivo soil ingestion studies for copper in humans (section 2.5.2.2) or in experimental animals (section 2.5.2.3). Given all these data gaps, SCAHT applies the US-EPA recommended upper default RAF-value of 100% (section 2.5.2.4).

In vitro studies which estimate the bioaccessbility of copper from soil and/or food and water are available. However, the relevance and reliability of these data is considered to be insufficient, to support the use of a RAF factor below 100% (section 2.5.2.5).

Therefore SCAHT applies a default RAF-value of 100%. This is in line with USEPA recommendations (USEPA 2007) for such situations.

2.5.2.1 Oral bioavailability from food and/or water from dietary studies

Kupfer wird vorwiegend aus dem Magen und oberen Dünndarm (Duodenum) aufgenommen. Die Resorptionsrate ist homeostatisch reguliert. Angaben zur Resorptionsrate schwanken zwischen 35-70% bzw. 20% und mehr als 50%. Bei normaler Ernährungsweise liegt die durchschnittliche Resorptionsrate im Bereich von 30-40% (SCF 2003, Kapitel 2.2, Seite 3, Paragraph 2). Proteine, Aminosäuren, Citrate oder Oxalate steigern die Resorption, während Faserstoffe, hohes Zink-, Calcium- oder Phosphatangebot sowie Phytate sie reduzieren (ATSDR 2004, p.70; EFSA 2009, p.9).

- Absorption of copper (mostly soluble salts, e.g copper sulphate) from various dietary sources has been found to vary between 25-60% (JECFA, 1982 in EFSA 2009, p.9). This in line with other human studies reviewed by ATSDR (2004, p.70) which reported that average

absorption efficiencies ranged from 24 to 60% in presumably healthy adults.

- In a series of six human dietary studies by Turnlund and colleagues (reviewed in Turnland et al., 1989) in which various age groups were fed with different diet types, it has been demonstrated that the average absorption of copper is ca. 30-40%, and that the rate of copper absorption varies inversely with copper intake and can be as low as 12% with very high copper intakes; from these studies, Turnland et al. (1989) estimated a theoretical maximum oral absorption of 63-67%.

⇒ **Based on these studies, SCAHT assumes a conservative oral bioavailability from the diet of 60% for its risk assesssment.**

2.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans or animals

No studies could be identified in the literature that investigated the oral absorption of copper in humans or experimental animals following soil ingestion. Therefore the absolute oral bioavailability of copper from soil is not directly available.

2.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

No studies could be identified in the literature that investigated the oral absorption of copper in experimental animals following soil ingestion.

2.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of copper from soil compared to food or water, is to use the Relative Oral Adjustment Factor (RAF) approach proposed by the USEPA, as outlined in the methodology section (TIER 2 approach).

- A RAF default medium-specific value of 0.5 (50%) has been proposed for inorganics, and could theoretically be used for copper (NRC 2003, Table 2.1 pp.69-70). However, given the lack of *in vivo* soil ingestion studies, either in humans or in experimental animals, this default value could not be applied.

⇒ **Therefore SCAHT uses a more conservative approach and a RAF-value of 100% is used, which is in line with USEPA recommendations (USEPA 2007) for such situations.**

⇒ This decision is further supported by a qualitative comparison with other metals which suggests that copper is in the higher range of the bioaccessibility values. However, in vitro data are very limited and kinetics information is lacking, so bioaccessibility information cannot be used here to predict the bioavailability of copper. This lack of data further supports a more conservative approach to the use of RAF. For information purposes, in vitro bioaccessibility studies are summarized in section 2.5.2.4.

⇒ **In conclusion, considering a maximal dietary oral bioavailability of 60% in humans and a RAF of 100% to account for the higher uncertainty of the database, SCAHT applies a conservative absolute oral bioavailability from soil of 60% for its risk assessment**.

2.5.2.5 Summary of the in vitro bioaccessibility information

Die Bioverfügbarkeit von Kupfer aus dem Boden (= “bioaccessibility“) ist wie bei anderen Metallen abhängig von seiner chemischen Form, der Partikelgrösse und der physikalisch-chemischen Eigenschaften des Bodens. Boden-pH-Wert, löslicher Gehalt organischer Substanzen, Metall-Oxid-Gehalt, Tongehalt und -art, die Anwesenheit organischer und anorganischer Liganden, und die Konkurrenz durch andere Metallionen haben einen wesentlichen Einfluss auf die Mobilität des Kupfers. Insbesondere erwartet man, dass der Hauptteil des Kupfers (40-74%) an den organischen, Fe-Mn-Oxid und Carbonat-Fraktionen der meisten Böden gebunden ist (Ma und Rao 1997 *in* ATSDR 2004 Kapitel 6.3.1.3, Seite 149, erster Absatz). Im Gegensatz zu anderen Metallen wird die Verteilung von Kupfer im Boden weit weniger durch Änderungen der pH-Werte bestimmt (ATSDR 2004, Kapitel 6.3.1.3, S. 146, letzter Absatz).

- Die Bioverfügbarkeit von Kupfer für den Menschen aus Böden in Familiengärten kann gemäss einer in vitro Bioaccessability studie von Poggio et al. (2009) zu 24% berechnet werden. Die Daten basierend auf einer PBET Studie. Zur Berechnung der Bioverfügbarkeit wurden die in der Studie angegebenen Werte zur „human bioaccessible 1st phase und 2nd phase“ addiert und mit dem Pseudototal verglichen: 9 + 4 mg/kg von 54 mg/kg = 24%).
- Im Gegensatz dazu hat De Miguel et al (2012) in einer in vitro Bioaccessabilitystudie (PBET) die Verfügbarkeit von Kupfer auf Spielplätze mit einen Mittelwert von 61% (SD: 38-84%) beschrieben (siehe **Tabelle 2-5**).

Table 2-5: Overview of selected Cu bioaccessibility values for urbans soils published in the literature (1998-2012)

(Quelle: De Miguel et al. 2012, S.682-683, Tabelle 4)

Type of phase in the *in vitro* model	Mean	Range or (SD)	Type of soil	Reference
gastric	46	(±8.9)	Playground	De Miguel et al. 2012
gastric	44	39-57	Urban (Torino)	Madrid et al. 2008
gastric	32	(±10)	Urban	Rasmussen et al. 2008
gastric	20	13-24	Urban (Seville)	Madrid et al. 2008
gastric	17	(±19)	Urban	Luo et al. 2012
gastric+intestinal	61	(±22.5)	Playground	De Miguel et al. 2012

2.6 Risikoabschätzung

Die Risikobewertung des derzeitigen Sanierungswerts für Kupfer in Familiengärten in Höhe von 1000 mg/kg Boden durch das SCAHT basiert auf einem vom SCF festgesetzten UL von 1 - 4 mg/Tag für Kinder verschiedener Altersklassen.

- Das SCAHT schliesst sich der Argumentation des SCF an, wonach in der EU die mittlere Kupferaufnahme von Erwachsenen und Kindern ab 4 Jahren (**Tabellen 2-3** und **2-4**) unterhalb der in Tabelle 2.1 und 2.2 genannten ULs liegt.
- Die 97.5-Percentile der Gesamtkupferaufnahme liegen für alle Altersgruppen aber nahe bei den genannten ULs, was nach Meinung des SCF keinen Anlass zur Besorgnis gibt (SCF 2003, Kapitel 6, Seite 11). Allerdings bleibt rein rechnerisch gesehen auch kein grosser Spielraum für die zusätzliche Aufnahme von Kupfer.

Für Kleinkinder im Alter von 1 - 3 Jahren, die im Rahmen dieser Risikobeurteilung standardmässig betrachtet werden, liegt der UL bei 1 mg/Tag (**Tabellen 2-1 und 2-2**). Allerdings liegen für diese Altersklasse keine Angaben zur Versorgung mit Kupfer vor (**Tabellen 2-3 und 2-4**), so dass die Argumentation des SCF für Kinder im Alter von 1 - 3 Jahren nicht explizit verifiziert werden kann. Zwar wird angenommen, dass Kinder gegenüber Kupferüberversorgung empfindlicher sind als Erwachsene, weil der Exkretionsmechanismus über die Galle seine volle Leistungsfähigkeit erst im Laufe der ersten Lebensjahre entwickelt, aber es liegen keine Berichte zu einer stärkeren Empfindlichkeit der Altersgruppe von 1 - 3 Jahren im Vergleich zur Altersgruppe von 4 - 8 Jahren vor.

Das Verschlucken von 250 mg Boden der mit 1000 mg Cu/kg Boden belastet ist, würde zu einer zusätzlichen externen Exposition von 250 µg Kupfer führen. Die Bioverfügbarkeit von Kupfer aus dem Boden nach direkter Aufnahme durch den Menschen gemäss SCAHT ist 60%. Damit würde die zusätzliche Belastung durch das Verschlucken von 250 mg Boden der mit 1000 mg Cu/kg Boden belastet ist auf 150 µg sinken. Wie viel Kupfer tatsächlich aus dem Magen-Darm-Trakt in den Körper aufgenommen wird, ist homeostatisch reguliert und hängt vom Ernährungszustand ab. Bei normaler Ernährungsweise liegt die durchschnittliche Resorptionsrate im Bereich von 30 - 40%.

Das SCAHT geht davon aus, dass das dadurch bedingte zusätzliche Gesundheitsrisiko relativ gering ist.

- Aufgrund der publizierten Daten zum Kupferbedarf und der Kupferversorgung würde man ohnehin eher von einer Überversorgung der Kinder mit Kupfer ausgehen (**Tabelle 2-3**). Die Aufnahme von geschätzten 150 µg Kupfer über den Boden entspricht etwa 15 - 30% des von dem DACH geschätzten Bedarf an Kupfer für Kinder aller Altersklassen (DACH 2000) und scheint wenig relevant für gesunde Kinder. Für Säuglinge geht man wenn überhaupt von einer Unterversorgung mit Kupfer über die Nahrung aus, die durch Kupferspeicher in der Leber ausgeglichen werden kann.
- Es ist anzunehmen, dass diese Zusatzbelastung aufgrund der grossen Bandbreite der homöostatischen Regulation von Kupfer keine negativen Folgen für die Gesundheit hat, weil der Kupfergehalt über einen breiten Bereich im Gleichgewicht gehalten werden kann. Bei einer Kupferaufnahme zwischen 0.8 und 5.5 mg/Tag bleibt der Kupfergehalt im Körper konstant (Turnland 1998 *in* SCF 2003, Seite 3, Paragraph 3). Andere Studien zeigen, dass sich der Kupfergehalt im Körper infolge einer Verzehnfachung des Kupfergehalts in der Nahrung lediglich verdoppelte (Turnland 1991 *in* SCF 2003, Seite 3, Paragraph 3).
- Ausserdem ist die Toxizität von Kupfer gering. Akute Toxizität wird je nach Quelle ab einer Aufnahme von 5 - 10 mg Kupfer beschrieben (BfR 2004, Kapitel 15.3.3.1). Auch chronische Kupferintoxikationen beim Menschen sind selten. Am ehesten betroffen scheinen Bevölkerungsgruppen, welche einer überhöhten Kupferkonzentration im Trinkwasser

ausgesetzt sind, die Kupfergefässe z. B. zum Kochen und Aufbewahren von Milch benutzen und Personen mit hereditärer Disposition. Insbesondere betroffen können Säuglinge sein, deren Nahrung unter Verwendung von "weichem" und "saurem" (pH < 6,0) über Kupferinstallationen zugeleiteten Leitungswasser (z. B. aus Hausbrunnen) hergestellt wird.

Nach Ansicht des SCAHT kann deshalb der derzeitige Sanierungswerts von Kupfer im Boden von Familiengärten in Höhe von 1000 mg/kg Boden beibehalten werden. Andererseits besteht aber nach Ansicht des SCAHT auch kein Grund den Sanierungswert für Kupfer anzuheben, da bereits mit einer Überversorgung der Kinder durch die Nahrung zu rechnen ist.

2.7 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften in Europa, USA und Kanada (z.B. Carlon 2007; Provoost et al, 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden (siehe **Anhang 1**).

Der Schweizer Sanierungswert erscheint hoch im internationalen Vergleich.

USA: 3100-150; **CH: 1000**; A: 600; B: 400; NL & F: 190; S: 100; I: 120; CAN: 63 (mg /kg dm).

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3 Cadmium

3.1 Datenblatt

Handlungsbedarf	Nein	Aktueller Sanierungswert von 20 mg Cd/kg Boden kann beibehalten werden. Da die Cadmiumaufnahme durch das Verschlucken von Boden den zulässigen gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) nur zu <6% ausschöpft (unter der Annahme einer 5% orale Bioverfügbarkeit aus dem Boden aber die geschätzte Aufnahme über die Nahrung den gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) z. T. deutlich überschreitet.
Gefährdungspotential	Hoch	Die inhalative Toxizität ist höher als die orale Toxizität. Cadmium akkumuliert im Körper: Biologische Halbwertszeit 10 - 30 Jahre. Niere am empfindlichsten (Filtrationsrate sinkt).
Kanzerogen	Ja	IARC: Krebserzeugend beim Menschen (nach inhalativer Exposition hoher Dosen am Arbeitsplatz)
Mutagen	Ja	
Reprotoxisch	Ja	
Neurotoxisch	Ja	
Andere	Ja	Niere am empfindlichsten (Filtrationsrate sinkt).
Gesundheitsbasierter Referenzwert		PTWI: 2.5 µg Cd/kg KG/Woche = 0.36 µg Cd/kg KG/Tag (KG: 12.5kg) Unter Berücksichtigung der Nierenschäden
Exposition		
Äussere Exposition Boden (250 mg)		20 mg Cd/kg Boden = 5 µg Cd/250 mg Boden = 0.4 µg Cd/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 50% orale Bioverfügbarkeit aus dem Boden: 0.2 µg Cd/kg KG/Tag (KG: 12.5kg) **Bei 5%** orale Bioverfügbarkeit aus dem Boden **0.02 µg Cd/kg KG/Tag (KG: 12.5kg)**
Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte mittlere Cadmiumaufnahme über die Nahrung: 2.56 – 3-46 µg Cd/kg KG/Woche = 0.37 – 0.49 µg Cd/kg KG/Tag Max. Werte: 5.49 µg Cd/kg KG/Woche = 0.78 µg Cd/kg KG/Tag

Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Unwahrscheinlich	Die geschätzte Aufnahmemenge alleine über die Nahrung überschreitet bereits den gesundheitsbasierten Referenzwert. Die geschätzte Cadmiumaufnahme durch direkte Bodenaufnahme ist klein im Vergleich zur Cadmiumaufnahme über die Nahrung und klein im Vergleich zum gesundheitsbasierten Referenzwert (<6%). Ein zusätzliches Gesundheitsrisiko durch das Verschlucken von kontaminiertem Boden ist unwahrscheinlich (unter der Annahme einer limitierten Bioverfügbarkeit des Cadmiums aus dem Boden von 5%). Deshalb können Massnahmen zur Reduktion der Cadmiumaufnahme über die Nahrung einen wesentlicheren Beitrag zur Minimierung des Gesundheitsrisikos darstellen als die Sanierung kontaminierter Böden. Geht man dagegen in einem „worst case“ – Szenario von einer 100% Bioverfügbarkeit des Cadmiums aus dem Boden aus, besteht ein zusätzliches Gesundheitsrisiko. Gesundheitsbasierter Referenzwert (PTWI): 0.36 µg Cd/kg KG/Tag Cadmiumaufnahme über die Nahrung: 0.37 – 0.49 µg Cd/kg KG/Tag (max: 0.78) Cadmiumaufnahme durch direkte Bodenaufnahme: 0.02 µg Cd/kg KG/Tag
Grenzwert im Vergleich		USA: 80; CH: 20; D & F: 20; NL: 12; A & CAN: 10; UK: 8; B: 6; S: 0.4 (mg/kg dm)
Datenlage	Ausreichend	

3.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten)[1] festgelegte Sanierungswert für Cadmium für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 20 mg Cd/kg Boden sollte gemäss dem ALARA-Prinzip reduziert werden, da bereits die Aufnahme über die Nahrung den gesundheitlich unbedenklichen Schwellenwert überschreitet.

Cadmium hat keine bekannte biologische Funktion, sondern ahmt andere zweiwertige Metalle nach, die wesentlich für verschiedene biologische Funktionen sind. Durch die Störung der Kalzium-, Zink- oder Eisen-Homöostase können grundlegende zelluläre Funktionen gestört werden. Das Gefährdungspotenial von Cadmium ist abhängig davon, in welcher chemischen Verbindung es vorliegt (wobei die zweiwertige Form des Cadmiums am relevantesten ist) und ob die Aufnahme inhalativ oder oral erfolgt. Als empfindlichstes Zielorgan gegenüber oral aufgenommenem Cadmium gilt die Niere. Eine Exposition über einen längeren Zeitraum oder gegenüber hohen Dosen schädigt die Tubuli, was schliesslich die glomuläre Filtrationsrate beeinflusst und zum Nierenversagen führen kann. Cadmium kann auch direkt oder indirekt über die Störung der Nierenfunktion zur Knochendemineralisation führen. Die IARC hat Cadmium auf der Grundlage von inhalativen Expositionsstudien am Arbeitsplatz als krebserzeugend beim Menschen (Gruppe 1) eingestuft. Neuere Daten zur Cadmium-Exposition der Allgemeinbevölkerung deuten ebenfalls auf ein erhöhtes Krebsrisiko (Lunge, Endometrium, Blase und Brust) hin.

Für Nichtraucher stellen Lebensmittel die grösste Quelle für Cadmiumbelastungen der Allgemeinbevölkerung dar. Die mittlere ernährungsbedingte Cadmium-Aufnahme Erwachsener in Europa wurde auf 2.3 µg/kg Körpergewicht (KG) und Woche geschätzt (Bereich 1.89 bis 2.96 µg). Bei stärker belasteten Konsumenten wird die durchschnittliche Belastung auf 3 µg/kg KG und Woche geschätzt (Bereich 2.54 - 3.91 µg). Kinder sind im Mittel fast 60% stärker belastet als Erwachsene, weil sie pro kg KG mehr Nahrung aufnehmen und sich die Zusammensetzung der Nahrung von der Erwachsener unterscheidet (mehr Milch und Milchprodukte). Die Maximalbelastung kann bis zu 5.49 µg/kg KG und Woche betragen und ist damit vergleichbar mit der Belastung von Vegetariern.

Der Provisional Tolerable Weekly Intake (PTWI) für Cadmium stellt die vorläufig duldbare wöchentliche Aufnahmemenge dar und wurde 2012 von der EFSA auf 2.5 µg/kg KG und Woche (entspricht 0.36 µg/kg KG/Tag) festgelegt. Tatsächlich überschreitet die geschätzte Aufnahmemenge für Cadmium aus Lebensmitteln für Kinder und Erwachsene bereits den PTWI (und zwar je nach Schätzung um mehr als 100%) und es bleibt aus toxikologischer Sicht kein Spielraum für eine zusätzliche Cadmiumaufnahme.

Die intestinale Resorptionsrate ist allgemein relativ niedrig (3 - 5%), kann aber je nach individuellem, aktuellen Nährstoffprofil von 1 - 10 % variieren. Hohe orale Absorptionsraten findet man aufgrund von Eisenmangel vor allem bei Frauen in gebärfähigem Alter. Bei Kindern ist die Absorptionsrate gegenüber Erwachsenen ebenfalls erhöht. Cadmium wird in der Niere und der Leber gespeichert und hat eine lange biologische Halbwertszeit von 10 - 30 Jahren.

Das Verschlucken von 250 mg Boden, der mit 20 mg Cd/kg Boden belastet ist, würde zu einer zusätzlichen externen Exposition von 5 µg Cd führen, die sich unter Berücksichtigung der

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

Bioverfügbarkeit des Cadmiums reduziert.

Es wird geschätzt, dass die orale Bioverfügbarkeit von Cadmium für den Menschen durch direkte Aufnahme über Böden um 50% niedriger ist als die Bioverfügbarkeit von löslichen Cadmiumverbindungen aus der Nahrung (Battelle and Exponent 2000). Da die maximale Absorptionsrate für Cadmium aus der Nahrung 10% beträgt, berechnet sich die orale Bioverfügbarkeit von Cadmium für den Menschen durch direkte Aufnahme über den Boden zu 5%. Unter diesen Annahmen reduziert sich die zusätzliche Belastung durch das Verschlucken von 250 mg Boden, der mit 20 mg Cd/kg Boden belastet ist, auf 0.25 µg Cd/Tag. Bei einem 12.5 kg schweren Kind bedeutet dies eine Aufnahme von 0.021 µg Cd/kg KG/Tag, womit der PTWI von 0.36 µg/kg KG/Tag zu <6% ausgeschöpft ist. Dieser Aufnahmepfad stellt somit keinen Hauptexpositionspfad dar. Die USEPA berichtet sogar, dass die orale Verfügbarkeit von Cadmium aus dem Wasser 5% beträgt und nimmt an, dass die Verfügbarkeit aus der Nahrung nur 2.5% beträgt. Unter diesen Annahmen würde sich der Beitrag des Cadmiums aus dem Boden halbieren.

Der in der Fremd- und Inhaltsstoffeverordnung festgelegte Grenzwert für Cadmium von 3.0 µg/l in Trinkwasser und natürlichen Mineralwässern (FIV 2014) führt unter der Annahme einer 10% Bioverfügbarkeit des Cadmiums aus dem Wasser und einem täglichen Konsum von einem Liter Wasser zu einer Exposition von 0.3 µg Cd/Tag. Diese Exposition liegt in der gleichen Grössenordnung wie die durch das Verschlucken kontaminierter Böden (0.25 µg Cd/Tag) im oben genannten Fallbeispiel.

Wenn bereits die Aufnahme über die Nahrung den gesundheitlich unbedenklichen Schwellenwert für Cadmium überschreitet, sollte standardmässig für die Festlegung des Sanierungswerts von Cadmium im Boden von Familiengärten das ALARA-Prinzip zur Anwendung kommen.

Da allerdings die Cadmiumaufnahme durch das Verschlucken von Boden den zulässigen gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) nur zu <6% ausschöpft, aber die geschätzte Aufnahme über die Nahrung den gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) z. T. deutlich überschreitet, könnten Massnahmen zur Reduktion der Cadmiumaufnahme über Lebensmittel einen wesentlicheren Beitrag zur Risikominimierung darstellen als die Reduktion des Sanierungswertes für Böden.

Andererseits liegt der Sanierungswert für Cadmium in Böden von Familiengärten mit 20 mg/kg Boden TR um einen Faktor 168 bis 39 über den von der NABO (NAtionale BOdenbeobachtung) gemessenen Werten in der Schweiz. Nach Meinung des SCAHT sollte deshalb geprüft werden, ob der aktuelle Prüfwert für Cadmium in der Schweiz von 10 mg/kg Boden als möglicher neuer Sanierungswert festgelegt werden könnte, um einen Teilbeitrag zur Risikominimierung darzustellen.

3.3 Gefährdungspotential

Cadmium (Cd) ist ein Element, das natürlicherweise in der Erdkruste vorkommt. Als reines Schwermetall liegt Cadmium in der Natur nicht vor. Das zweiwertige Cadmium überwiegt in Umwelt und biologischen Organismen. In der Regel tritt Cadmium als Cd^{2+} gebunden in Form von Cadmiumoxid, Cadmiumchlorid, Cadmiumsulfat oder Cadmiumsulfit auf. Die verschiedenen Verbindungen, die ineinander übergehen können, unterscheiden sich in ihrer Löslichkeit. Häufig bilden Cadmiumverbindungen mit Zink-, Blei- und Kupferverbindungen Komplexe. Im Wasser liegt Cadmium überwiegend als freies Ion vor, während es in Nahrungsmitteln meistens in Komplexen gebunden vorkommt. Als Komplexbildner dienen dabei verschiedene Liganden, wie Proteine oder Metallothionein.

- Cadmium hat keine bekannte biologische Funktion, sondern ahmt andere zweiwertige Metalle nach, die wesentlich für verschiedene biologische Funktionen sind. Durch die Störung der Kalzium-, Zink- oder Eisen-Homöostase können grundlegende zelluläre Funktionen gestört werden.

- Im Körper hat Cadmium eine lange biologische Halbwertszeit von 10 - 30 Jahren. Aufgrund der schlechten zellulären Exportsysteme verweilt es lange in den Geweben, wie dem Darm, der Leber und den Nieren. Nephrotoxizität, Osteoporose, Neurotoxizität, Kanzerogenität und Genotoxizität, Teratogenität und endokrine und reproduktive Wirkungen sind die Folge erhöhter Cadmiumexposition.

- Das Gefährdungspotenzial von Cadmium ist abhängig davon, in welcher Verbindung es vorliegt und ob die Aufnahme oral oder inhalativ erfolgt, u. a. weil die Bioverfügbarkeit durch Einatmen mit 5 - 50% deutlich höher ist als die orale Bioverfügbarkeit (1 - 10%) (ATSDR 2012, Kapitel 1.4, Seite 4).

- Als empfindlichstes Zielorgan gegenüber oral aufgenommenem Cadmium gilt die Niere. Eine Exposition über einen längeren Zeitraum oder gegenüber hohen Dosen schädigt die Tubuli, was schliesslich die glomuläre Filtrationsrate beeinflusst und zum Nierenversagen führen kann.

- Cadmium kann auch direkt oder indirekt über die Störung der Nierenfunktion zur Knochendemineralisation führen. Cadmium konkurriert im Darm mit dem Calcium um die Bindungsstellen am Ca-bindenden Protein in der Darmmukosa. Zusätzlich blockiert Cadmium die Neusynthese von Calcitriol in den Nierentubuluszellen. Calcitriol ist notwendig, um die Synthese des calciumbindenden Proteins in der Darmmukosazelle zu aktivieren. Letztendlich bewirkt Cadmium eine verminderte Rückresorption des Calciums in Darm und Niere sowie die erhöhte Ausscheidung mit dem Harn, was eine Calciumfreisetzung aus den Knochen und damit dessen Abbau zur Folge hat.

- Nach inhalativer Exposition kann Cadmium Krebs verursachen. Eine kanzerogene Wirkung wird vor allem bei hohen Expositionen am Arbeitsplatz beobachtet. Die IARC hat Cadmium auf der Grundlage von inhalativen Expositionsstudien am Arbeitsplatz als krebserzeugend beim Menschen (Gruppe 1) eingestuft. Darüber hinaus gibt es Daten zur Cadmium-Exposition der Allgemeinbevölkerung, die ebenfalls auf ein erhöhtes Krebsrisiko (Lunge, Endometrium, Blase und Brust) hindeuten.

Industriell kommt Cadmium aufgrund seiner Toxizität eine zurückgehende Bedeutung zu. Die grössten industriellen Einsatzbereiche für Cadmium stellen aktuell die Stahlindustrie und – noch expandierend – die Galvanik dar.

3.4 Gesundheitsbasierter Referenzwert

Der Provisional Tolerable Weekly Intake (PTWI) für Cadmium stellt die vorläufig duldbare wöchentliche Aufnahmemenge nach dem heutigen Kenntnisstand dar. Der PTWI für Cadmium lag zunächst bei 7 µg/kg Körpergewicht (KG) und Woche (JECFA 2009,) und wurde 2009 vom CONTAM-Panel der EFSA auf 2.5 µg/kg KG reduziert. Das entspricht einer täglichen Aufnahme von 0.36 µg/kg KG/Tag (EFSA 2009, Zusammenfassung, Seite 2 Vorletzter Paragraph – Seite 3 erster Paragraph).

Der PTWI wurde im Rahmen epidemiologischer Studien abgeleitet. Bei Ableitung des PTWI wurde die Funktionsstörung der Nierentubuli als der kritischste toxikologische Endpunkt betrachtet (EFSA 2009, Seite 9, Paragraph 3). Als Biomarker für die tubuläre Dysfunktion aufgrund der Anreicherung des Cadmiums in der Niere diente der Gehalt an Beta-2-Microglobulin (B2M) bezogen auf die mit dem Harn ausgeschiedene Kreatininmenge. Kreatinin ist ein wichtiger Nierenretentionsparameter, dessen Erhöhung auf eine eingeschränkte Nierenfunktion hindeutet.

Die Ableitung des PTWI erfolgte stufenweise.

⇒ In einem ersten Schritt konnte nach der Bestimmung der Dosis-Wirkungsbeziehung zwischen dem Harngehalt an B2M und dem Cadmiumgehalt im Harn die kritische Cadmiumkonzentration im Urin, die zu Nierenschäden führt, indirekt durch die Messung des B2M bestimmt werden. Sie wurde im Rahmen eines $BMDL_5$ mit 4 µg Cd/g Kreatinin bestimmt. Unter Berücksichtigung eines zusätzlichen substanzspezifischen Sicherheitsfaktors von 3.9, der die Unterschiede der Cadmiumausscheidung in den einzelnen Studien berücksichtigte, wurde eine sichere Dosis von 1 µg Cd/g Kreatinin festgelegt.

⇒ In einem zweiten Schritt wurde die ernährungsbedingte Aufnahme an Cadmium modelliert, so dass bei Personen im Alter von 50 Jahren mit 95%-iger Sicherheit der kritische Cadmiumgehalt von 1 µg Cd/g Kreatinin nicht überschritten wird. Daraus ergab sich der PTWI von 2.5 µg/kg Körpergewicht/Woche.

3.5 Exposition

3.5.1 Äussere Exposition

Für Nichtraucher stellen Lebensmittel bei weitem die grösste Quelle für Cadmiumbelastungen der Allgemeinbevölkerung dar (EFSA 2009, Kapitel 4.6, Seite 18/139). Die Hauptnahrungsmittel, die zur Cadmiumexposition beitragen, sind Getreide und Gemüse. Der Cadmiumgehalt in Kulturpflanzen hängt von der Aufnahme aus dem Boden ab. Die Pflanzen Aufnahmerate wird hauptsächlich durch die Art der chemischen Verbindung, der physikalisch-chemischen Eigenschaften des Bodens und der Pflanzenspezies beeinflusst. Fleisch und Fisch enthalten normalerweise weniger Cadmium. Innereien wie Leber und vor allem Niere sind stärker belastet, weil sie Cadmium speichern. Die Allgemeinbevölkerung (Nichtraucher) nimmt weniger als 10% des Gesamtcadmiums durch Einatmen schwach belasteter Luft, Hausstaub oder Trinkwasser auf (EFSA 2009, Kapitel 4.6, Seite 19/139). Berufsbedingt sind vor allem Arbeiter in der metallverarbeitenden Industrie Cadmiumdämpfen ausgesetzt. Cadmium hat einen geringen Dampfdruck, kann aber in der Luft als Schwebpartikel aus Gischt, Industrieemissionen, Verbrennung fossiler Brennstoffe oder der Bodenerosion vorkommen. In Prozessen, die bei extrem hohen Temperaturen ablaufen (z. B. in der Eisen- und Stahlindustrie), kann sich Cadmium verflüchtigen und als Dampf abgegeben werden. Die dermale Exposition ist nicht relevant (ATSDR 2012, Kapitel 1.4, Seite 4).

Die Gesamtexposition gegenüber Cadmium wurde 2009 von der EFSA (EFSA 2009, Kapitel 7.5, Seite 53-54/139, Tabelle 30) abgeschätzt und ist in **Tabelle 3-1** aufgelistet. Die ernährungsbedingte Exposition wurde 2012 erneut von der EFSA abgeschätzt und ist in **Tabelle 3-2** aufgelistet (EFSA 2012, Kapitel 3.2, Tabelle 11, Seite 17).

- Die mittlere ernährungsbedingte Cadmium-Aufnahme Erwachsener in Europa wurde auf 2.3 µg/kg Körpergewicht und Woche geschätzt (Bereich 1.89-2.96 µg). Bei stärker belasteten Konsumenten wird die durchschnittliche Belastung auf 3 µg/kg KG und Woche geschätzt (Bereich 2.54-3.91 µg). Personen die stärker belastete Lebensmittel aus Anbauflächen in Industriegebieten verzehren, sind im Durchschnitt mit 5.4 µg/kg Körpergewicht und Woche belastet (Bereich 3.3-5.8 µg). Bei Vegetariern liegt die geschätzte ernährungsbedingte Exposition mit 5.47 µg/kg KG und Woche fast 2.5-fach höher als bei Nichtvegetariern (EFSA 2009).

- Kinder sind im Mittel fast 60% stärker belastet als Erwachsene, weil sie pro kg KG mehr Nahrung aufnehmen und sich die Zusammensetzung der Nahrung von der Erwachsener unterscheidet (mehr Milch und Milchprodukte). Die Maximalbelastung kann bis zu 5.49 µg/kg KG und Woche betragen und ist damit vergleichbar mit der Belastung von Vegetariern. Allerdings kann bei Kindern die zusätzliche Belastung durch die Cadmiumaufnahme über den Hausstaub mit 0.607 µg/kg KG und Woche eine weitere wichtige Expositionsquelle darstellen (EFSA 2009, Kapitel 7.5, Tabelle 30, Seite 54).

⇒ Die neueren Schätzungen der EFSA von 2012 zur Cadmiumaufnahme über die Nahrung (Tabelle 3.2) liegen in der gleichen Grössenordnung wie die bereits 2009 publizierten Werte und zeigen die gleiche Tendenz. Kinder, und hier besonders Kleinkinder im Alter von 1 - 3 Jahren, sind deutlich stärker belastet als Erwachsene. Die mittlere Exposition von durchschnittlich belasteten Kleinkindern im Alter von 1-3 Jahren liegt bei 4.85 µg/kg KG und Woche, das 95-Perzentil liegt im Mittel mit 8.19 deutlich höher.

⇒ Aus **Tabelle 3-1** und **Tabelle 3-2** wird ersichtlich, dass die mittlere Exposition von Kindern den PTWI von 2.5 µg/kg KG/Woche bereits um das 2 bis 3-fache überschreiten kann.

⇒ Das CONTAM-Gremium beurteilt das individuelle Risiko für Nierenschäden in ganz Europa als sehr niedrig, fordert aber trotzdem, dass die Belastung durch Cadmium auf Bevölkerungsebene reduziert werden sollte (EFSA 2009, Zusammenfassung, Seite 3).

Tabelle 3-1: Schätzungen zur durchschnittlichen wöchentlichen Cadmiumexposition erwachsener Europäer über verschiedene Expositionspfade.

(EFSA 2009, Kapitel 7.5, Tabelle 30, Seite.54)

Source		Pathway	Range of calculated or reported exposures [µg/kg b.w. per week]	
			Adults	Children
Dietary exposure	Food mean current opinion	Oral	1.89-2.96	2.56-3.46
	Food high current opinion		2.54-3.91	5.49
	Food in industrial areas	Oral	3.3-5.8[a)]	4.6[a)]
	Extreme diets current opinion	Oral	2.87-4.64	
	Vegetarians	Oral	5.47	
Non-Dietary Exposure	House dust	Oral	0.076	0.607
	Air	Inhalation	0.0024	0.0033 [b)]
	Smoking	inhalation	0.35-0.70	-

[a)] estimated using a factor of 1.86 times average exposure derived from (Vromman *et al.*, 2008)

[b)] assuming a daily inhalation volume of 7 m³ and a body weight of 15 kg

Tabelle 3-2: Schätzungen zur durchschnittlichen wöchentlichen Cadmiumaufnahme über die Nahrung in µg/kg KG.
(EFSA 2012, Kapitel 3.2, Tabelle 11, Seite 17)

Age group	N	Mean			P95		
		LB	MB	UB	LB	MB	UB
Infants	876	1.97	2.74	3.50	4.97	6.56	8.42
Toddlers	1,597	3.80	4.85	5.90	6.76	8.19	9.84
Other children	8,468	3.23	3.96	4.69	5.55	6.58	7.66
Adolescents	6,329	1.87	2.20	2.54	3.66	4.17	4.70
Adults	30,788	1.41	1.70	1.98	2.72	3.09	3.50
Elderly	4,056	1.30	1.56	1.82	2.47	2.82	3.18
Very elderly	1,614	1.38	1.63	1.89	2.56	2.87	3.21
Adjusted average[8]		**1.68**	**2.04**	**2.39**	**3.17**	**3.66**	**4.18**

3.5.2 Innere Exposition

For cadmium, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

The absolute oral bioavailability of cadmium from soil is not directly available for humans. However, the cadmium absorption rate after oral exposure to food/water is relatively well characterized and it is estimated to be maximum 10% in humans (section 3.5.2.1).

Therefore the Relative Oral Adjustment Factor (RAF) approach can be used to estimate the absolute oral bioavailability from soil (section 3.5.2.4). For cadmium, US EPA recommended a RAF-value of 50%. No information on soil ingestion in humans is available for cadmium (section 3.5.2.2), but there

are some *in vivo* soil ingestion studies available in experimental animals, which demonstrated *mean relative bioavailabilities of 43-63%* compared with food (section 3.5.2.3). These data, in particularly in the juvenile swine, are considered sufficiently relevant and reliable to support the use of the proposed medium specific default RAF value of 50%.

In vitro bioaccessbility studies for cadmium from soil and/or food and water are available (section 3.5.2.5). Based on limited kinetic information that showed a correlation between bioaccessibility and bioavailability in the swine model, this would support further the chosen RAF value of 50%.

3.5.2.1 Oral bioavailability from food and/or water from dietary studies

Die intestinale Resorptionsrate aus der Nahrung variiert je nach individuellem, aktuellen Nährstoffprofil, Alter und Geschlecht zwischen 1 bis 10% (ATSDR 2012; EFSA 2009, Zusammenfassung, Seite 3). Hohe Absorptionsraten findet man aufgrund von Eisenmangel (vor allem bei Frauen im gebärfähigen Alter) und Kalziummangel. Hohe Zinkwerte beeinflussen ebenfalls die Absorption, Verteilung oder Eliminierung von Cadmium. Bei Kindern ist die Absorptionsrate gegenüber Erwachsenen ebenfalls erhöht.

Similarly, experimental animal studies have shown digestive absorption rates varying between 0.5 and 12% (on average 2%) depending on the animal species and the chemical form of cadmium; the higher values have been reported for monkeys and large animals compared to rodents. In small animals, absorption in the range of 1 to 2% is commonly reported (EU RAR 2008, p.182). According to USEPA (2007), bioavailability of cadmium in water is greater than that of Cd in food by a factor 2, i.e. 5% vs 2.5%, respectively.

⇒ **SCAHT geht von, einer oralen Bioverfügbarkeit aus der Nahrung/Wasser von 10% aus.**

3.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

No studies could be identified in the literature that investigated the oral absorption of cadmium in humans following soil ingestion. Therefore the absolute oral bioavailability of cadmium from soil is not directly available for humans.

3.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

Several *in vivo* soil ingestion studies in experimental animals are available from the literature; they suggest mean relative oral bioavailability from soil in the range 43-63%:

- Schilderman et al. (1997) assessed differences in bioavailability of an artificial soil spiked with cadmium chloride versus Cd chloride in saline in the male rat following oral administration. Relative bioavailability, calculated on the basis of blood Cd levels for the Cd-soil group as compared to the Cd-saline group, appeared to be 43%.
- Schroder et al. (2003) evaluated relative bioavailable cadmium measured from dosing trials using male juvenile swine for ten contaminated soils from hazardous waste sites. Animals were fed twice daily with Cd chloride for two weeks to mimic childhood cadmium ingestion that is likely to occur between meals while children are in a fasted or semifasted state. *In vivo* relative bioavailable Cd ranged from 10.4 to 116% with a mean of 63.4%. Comparable data were found by Denys et al. (2012)

3.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of cadmium from soil compared to food or water, is to use the Relative Oral Adjustment Factor (RAF) approach proposed by the USEPA, as outlined in the methodology section (TIER 2 approach).

- A RAF default medium-specific value of 0.5 (50%) has been proposed for cadmium (NRC 2003, Table 2.1 pp.69-70; USEPA 2007). The proposed RAF of 50% is well supported by key studies of Schildermann et al (1997) and Schroder et al (2003). A RAF of 33% was used by the US Oklahoma State Department of Environmental Quality based on in vivo soil ingestion rat studies (NRC 2003, p. 86-87, table 2-4).

⇒ **Allerdings wird die orale Bioverfügbarkeit von Cadmium für den Menschen aus Böden allgemein mindestens 50% niedriger angenommen als die Bioverfügbarkeit von löslichen Cadmiumverbindungen in der Nahrung (Battelle and Exponent 2000, Kapitel „Design of Previous In Vivo Studies", Seite 3.5).**

⇒ **Das SCAHT nimmt eine absolute orale Bioverfügbarkeit aus dem Boden für Cadmium von 5% an, basierend auf einer maximalen intestinalen dietätischen Resorptionsrate von 10% und auf einer RAF von 50%.**

3.5.2.5 Summary of the in vitro bioaccessibility information

The major factors governing cadmium mobility and bioaccessibility in soils are: speciation; pH; presence of organic and inorganic ligands, and competition from other metal ions; soluble organic matter content; hydrous metal oxide content; clay content and type. Retention (sorption) processes due to solid/water interface reactions decrease cadmium solubility and migration; cadmium generally form stable, insoluble complexes with inorganic and organic soil constituents, which are moderatly mobile, but transport processes through colloid formation may increase their solubility and mobility (ATSDR 2012; EFSA 2009; SAEFL 2003).

Several in vitro studies were identifed in the literature, however none relate specifically to garden soils. The reported range of bioaccessibility values is broad:

- Schroder et al. (2003) evaluated bioaccessible cadmium determined by an in vitro gastrointestinal (IVG) method. Mean in vitro bioaccessibility values for cadmium were 63% (range: 21-96%) for the gastric phase, and 39% (range: 15-55%) for the intestinal phase.
- A few studies used the Unified BARGE[2] Method. Pelfrêne et al (2011) assessed cadmium human bioaccessibility in 36 smelter-contaminated agricultural and urban topsoils in northern France; they reported mean values of cadmium bioaccessible fraction of 82% (range 61-100%) and 45% (range: 24-62%) of the pseudototal Cd concentration during the gastric phase and gastrointestinal phase, respectively. Xia et al (2016) evaluated seven different types of soil spiked with cadmium and aged for one year. They found that bioaccessibility of cadmium ranged from 72 ± 4.3 to 99 ± 0.8% in the gastric phase and 6.2 ± 0.3 to 45 ± 2.7% in the intestinal phase.
- Denys et al (2012) showed that there was good correlations between bioaccessibility data as produced with the UBM test compared with bioavailability measurements for cadmium in the juvenile swine model. Values were comparable to those reported by Schroder et al. (2003).
- Other *in vitro* studies have been summarized by the Danish EPA (DEPA 2003, Appendix).

[2] BioAccessibility Research Group of Europe (BARGE)

3.6 Risikoabschätzung

Das RIVM (Dutch National Institute for Public Health and the Environment) hat in einem Worst-Case-Szenario die Cadmiumexposition durch das Verschlucken von Staub und Böden für Kinder abgeschätzt (EFSA 2009, Kapitel 7.4, Seite 54, Paragraph 4). Dabei ging man davon aus, dass Kinder 100 mg Staub/Tag aufnehmen. Die Cadmiumkonzentration wurde auf 13 mg Cd/kg Staub festgelegt, was dem höchsten publizierten geometrischen Mittelwert entspricht, der in einem australischen Industriegebiet gemessen wurde. Die Bioverfügbarkeit wurde mit 100% angenommen. Unter diesen Bedingungen ergibt sich für ein 15 kg schweres Kind die Exposition von 0.607 µg/kg Körpergewicht pro Woche. Das entspricht einer 8.5%-igen Auslastung des 2009 gültigen PTWI von 7 µg/kg Körpergewicht pro Woche. Die EFSA folgert daraus, dass das „Hand in den Mund Verhalten" von Kindern in Gebieten mit hoher Umweltverschmutzung durch die Industrie eine erhebliche Cadmiumquelle darstellt, aber immer noch keinen Hauptexpositionspfad (EFSA 2009, Kapitel 7.4, Seite 54, Paragraph 5).

Das SCAHT-Szenario zur Abschätzung der Cadmiumbelastung aus Staub und Böden geht von einer höheren Aufnahmemenge für Boden und Staub (250 mg/Tag vs. 100 mg/Tag), einer höheren Kontamination des Bodens (20 mg Cd/kg Boden vs. 13 mg Cd/kg Boden), aber einer deutlich niedrigeren Bioverfügbarkeit (5% vs. 100%) für Cadmium aus dem Boden aus. Ausserdem orientiert sich die Risikoabschätzung an dem 2012 von der EFSA festgelegten niedrigeren PTWI für Cadmium von 2.5 µg/kg Körpergewicht pro Woche. Auch in diesem Szenario stellt das Verschlucken von Staub und Boden mit einer Auslastung von <6% keinen Hauptexpositionspfad dar.

Das Verschlucken von 250 mg Boden, der mit 20 mg Cd/kg Boden belastet ist, würde zu einer zusätzlichen externen Exposition von 5 µg Cd führen, die sich unter Berücksichtigung der Bioverfügbarkeit des Cadmiums reduziert. Die maximale Absorptionsrate für Cadmium aus der Nahrung wird mit 10% angegeben. Die orale Bioverfügbarkeit von Cadmium für den Menschen durch direkte Aufnahme über den Boden wird mindestens 50% niedriger eingeschätzt als die Bioverfügbarkeit von löslichen Cadmiumverbindungen in der Nahrung (Battelle and Exponent 2000, Seite 3.5, Abschnitt „Design of Previous In Vivo Studies). Demzufolge schätzt das SCAHT die absolute orale Bioverfügbarkeit aus dem Boden auf 5% (50% von 10%). Unter diesen Annahmen reduziert sich die zusätzliche Belastung durch das Verschlucken von 250 mg Boden, der mit 20 mg Cd/kg Boden belastet ist, auf 0.25 µg Cd/Tag. Bei einem 12.5 kg schweren Kind bedeutet dies eine Aufnahme von 0.02 µg Cd/kg KG/Tag, womit der PTWI von 0.36 µg/kg KG/Tag zu <6% ausgeschöpft ist. Diese Aufnahmepad stellt somit keinen Hauptexpositionspfad dar.

⇒ Da aber bereits die Aufnahme über die Nahrung den gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) überschreitet, sollte für die Festlegung des Sanierungswerts von Cadmium im Boden von Familiengärten das ALARA-Prinzip zur Anwendung kommen.

Bei der Risiko-Nutzenanalyse einer möglichen Reduktion des Sanierungswerts sollte das zu erwartende Ausmass der Risikominimierung berücksichtigt werden.

⇒ Da die Cadmiumaufnahme durch das Verschlucken von Boden den zulässigen gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) nur zu <6% ausschöpft und die geschätzte Aufnahme über die Nahrung den gesundheitlich unbedenklichen Schwellenwert für Cadmium (PTWI) z. T. deutlich überschreitet, könnten Massnahmen zur Reduktion der Cadmiumaufnahme über Lebensmittel einen wesentlicheren Beitrag zur Risikominimierung darstellen.

⇒ Zum anderen wurde der PTWI mit dem Ziel festgelegt, den Cadmiumgehalt pro Gramm Kreatinin im Urin bei 95% der Bevölkerung im Alter von 50 Jahren unter 1 µg Cd/g Kreatinin zu halten. Cadmium akkumuliert im Köper. Bei der Geburt ist der Cadmiumgehalt null, dann steigt er bis zum Alter von 50 an, bevor er wieder sinkt. Angesichts der Tatsache, dass die zusätzliche Aufnahme von Cadmium durch das Verschlucken von belasteten Böden den PTWI nur zu einem geringen Grad ausschöpft und zudem zeitlich eng auf die orale Phase der Kleinkinder begrenzt ist, scheint der Beitrag zur Erreichung des maximalen Cadmiumgehalts pro Gramm Kreatinin im Alter von 50 Jahren noch geringer.

Die EFSA gibt die Hintergrundbelastung in Oberböden mit 0.01 bis 2.7 mg/kg an. Die mittlere Cadmiumkonzentration in kultivierten Böden liegt in Europa bei 0.5 mg/kg (EFSA 2009, Kapitel 4.3, Seite 17). In der Schweiz wurden von 1985 bis 2004 in 5-Jahresabständen die Cadmiumgehalte in 105 Böden (Landwirtschaft, Wald und Wiesen) gemessen (BAFU 2014). In 54 Standorten konnten Cadmiumkonzentrationen im Bereich von 0.119 bis 0.511 mg Cd / kg Boden Trockenrückstand (TR) gemessen werden. Allerdings konnte im Verlauf der Zeit keine signifikante Veränderung der Cadmiumgehalte in den Böden festgestellt werden.

⇒ Somit liegt der Sanierungswert für Cadmium in Böden von Familiengärten von 20 mg/kg Boden TR um einen Faktor 2000 bis 7.4 über der von der EFSA angegebenen Hintergrundbelastung und um einen Faktor 168 bis 39 über den von der NABU gemessenen Werten in der Schweiz. Inwiefern dies Rückschlüsse auf die technische Umsetzung einer Sanierung zur Erreichung von Werten unter 20 mg Cd/kg Boden zulässt, ist nicht Gegenstand dieser Betrachtung.

3.7 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften in Europa, USA und Kanada (z.B. Carlon 2007; Provoost et al, 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden (siehe **Anhang 1**).

USA: 80; **CH: 20;** D & F: 20; NL: 12; A & CAN: 10; UK: 8; B: 6; S: 0.4 (mg /kg dm)

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4 Zink

4.1 Datenblatt

Handlungsbedarf	Nein	Aktueller Sanierungswert von 2000 mg Zn/kg Boden kann beibehalten werden. Rein rechnerisch kann aus humantoxikologischer Sicht der aktuelle Sanierungswert, um etwa einen Faktor 10 auf maximal 21600 mg angehoben werden.
Gefährdungspotential	Gering	Zink ist ein essentielles Spurenelement. Zink ist von geringer akuter und chronischer Toxizität. Die Beeinflussung des Kupferhaushalts ist der kritischste toxikologische Effekt.
Kanzerogen	Nein	Bedeutung der Prostatakarzinome in epidemiologischen Studien bislang unklar.
Mutagen	Nein	
Reprotoxisch	Nein	
Neurotoxisch	Nein	
Andere	Ja	Am kritischsten ist die Beeinflussung des Kupferhaushalts (bei Mengen von >9 mg/Tag über der tolerierbaren täglichen Aufnahmemenge). Ansonsten gastrointestinale Irritationen, Erbrechen, Übelkeit, Diarhö.
Gesundheitsbasierter Referenzwert		Tolerierbare tägliche Aufnahmemenge: 7.0 mg/Tag (Kinder 1 - 3 Jahre) Unter Berücksichtigung der Störung des Kupferstoffwechsels
Exposition		
Äussere Exposition Boden (250 mg)		2000 mg Zn/kg Boden = 500 µg Zn/250 mg Boden => 40 µg Zn/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 100% Bioavailability: 40 µg Zn kg KG/Tag (KG: 12.5kg) = 500 µg /Tag => 11.6% der Zinkaufnahme über die Nahrung Bei 60% Bioavailability: 24 µg Zn/kg KG/Tag (KG: 12.5kg) = 300 µg /Tag => 7.0% der Zinkaufnahme über die Nahrung

Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte tatsächliche Zinkaufnahme über die Nahrung: 4.3 mg/Tag (Kinder 1 - 3 Jahre)
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Unwahrscheinlich	Die geschätzte tägliche Zinkaufnahme durch die Nahrung überschreitet zwar den Bedarf, aber nicht die tolerierbare tägliche Aufnahmemenge. Die Aufnahme von Zink durch das Verschlucken von kontaminiertem Boden ist klein im Vergleich zur unvermeidbaren Hintergrundbelastung (>2%). Auch die kombinierte Aufnahme von Zink aus der Nahrung und dem Boden überschreitet die tolerierbare Aufnahmemenge nicht. Ein Gesundheitsrisiko ist unwahrscheinlich. Auch wenn man in einem „worst case"–Szenario von einer 100% Bioverfügbarkeit des Zinks aus dem Boden ausgeht, besteht kein zusätzliches Gesundheitsrisiko, weil die tolerierbare tägliche Aufnahmemenge selbst dann nicht überschritten wird. Zinkbedarf : 3.6 mg/Tag (Kinder 1 - 3 Jahre) Tolerierbare Aufnahmemenge: 7.0 mg/Tag (Kinder 1 - 3 Jahre) Zinkaufnahme über die Nahrung: 4.3 mg/Tag (Kinder 1 - 3 Jahre) Zinkaufnahme durch direkte Bodenaufnahme: 250 µg/Tag (50% Bioaccessibility)
Grenzwert im Vergleich		USA: 23000; F: 9000; CZ: 2500; CH: 2000; B: 1000; NL: 720; S: 350; CAN: 200; I: 150; (mg/kg dm)
Datenlage	Zufriedenstellend	Es gibt keine Studien zur Bioverfügbarkeit von Zink aus dem Boden im Menschen oder Tier. Aufgrund der geringen Toxizität des Zinks und der grossen Bandbreite der homöostatischen Regulation bestehen keine Unsicherheiten bezüglich der Risikobeurteilung.

4.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (AltlV)[1] festgelegte Sanierungswert für Zink für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 2000 mg Zn/kg Boden kann beibehalten werden. Rein rechnerisch könnte aus humantoxikologischer Sicht der aktuelle Sanierungswert, um etwa einen Faktor 10 auf maximal 21600 mg angehoben werden.

Zink ist ein essentielles Spurenelement für den Stoffwechsel, das als Bestandteil von über 300 Enzymen strukturelle, regulatorische oder katalytische Funktionen besitzt. Zink ist unerlässlich für das Wachstum, die Entwicklung, die testikuläre Reifung, die Wundheilung und die Immunkompetenz.

Zink ist von geringer Toxizität für den Menschen. Der kritischste Endpunkt der Zinktoxizität ist die Beeinflussung des Kupferhaushalts bei stark erhöhten Zinkzufuhren. Allerdings ist die Relevanz hinsichtlich langfristiger Auswirkungen auf die Kupfer-Homöostase ungeklärt.

Der Zinkbedarf für Kinder im Alter von 1 bis <3 Jahren wurde von der EFSA in 2014 auf 3.6 mg/Tag, für Kinder von 4 bis 6 Jahren auf 4.6 mg/Tag und für 7 bis 10-Jährige auf 6.2 mg/Tag geschätzt**.** Die Hauptexpositionsquelle für Zink im Alltag sind die Nahrung, Nahrungsergänzungsmittel und das Trinkwasser.

Die durchschnittliche Zinkaufnahme aus der Nahrung für Kinder aller Altersklassen liegt über dem geschätzten Bedarf, aber unterhalb der tolerierbaren Höchstmenge. Auch durch das zusätzliche Verschlucken von mit 2000 mg Zn/kg Boden kontaminiertem Boden würde die tolerierbare Höchstmenge nicht überschritten.

Das Verschlucken von 250 mg Boden, der mit 2000 mg Zn/kg Boden belastet ist, würde zu einer zusätzlichen externen Exposition von 500 µg Zn führen, die sich unter Berücksichtigung der Bioverfügbarkeit des Zink reduziert. Für Zink gibt es keine in vivo Studien, zur oralen Bioverfügbarkeit nach direkter Aufnahme durch den Menschen über den Boden. Das SCAHT geht von der konservativen Annahme einer oralen Bioverfügbarkeit des Zink aus dem Boden von 60% aus. Unter diesen Bedingungen reduziert sich die Belastung durch das Verschlucken von 250 mg Boden, der mit 2000 mg Zn/kg Boden belastet ist, auf 300 µg.

Wie viel Zink tatsächlich vom Körper aufgenommen wird, ist homeostatisch reguliert und hängt vom Ernährungszustand ab, wobei Kupfer und Zink um die Aufnahme konkurrieren. Bei normaler Ernährungsweise liegt die durchschnittliche Resorptionsrate im Bereich von 15-60%.

Das SCAHT geht davon aus, dass ein zusätzliches Gesundheitsrisiko durch das Verschlucken von mit 2000 mg Zn/kg Boden kontaminiertem Boden unwahrscheinlich ist, weil die tolerierbare Höchstmenge für Zink auch unter Berücksichtigung der Zinkaufnahme über die Nahrung nicht überschritten wird.

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

4.3 Gefährdungspotential

Zink ist ein essentielles Spurenelement für den Stoffwechsel, das in seinen Verbindungen in der Oxidationsstufe Zn^{2+} vorliegt. Es ist Bestandteil von über 300 Enzymen, in denen es strukturelle, regulatorische oder katalytische Funktionen besitzt. Zink ist unerlässlich für das Wachstum, die Entwicklung, die testikuläre Reifung, die Wundheilung und die Immunkompetenz (SCF 2003, Kapitel 2.1., Seite 2).

Nach längerem Verzehr von Zinksupplementen in Bereichen von 50 - 300 mg/Tag wurden verschiedene Veränderungen beobachtet. Diese schliessen Hypocuprämie, eine erniedrigte Aktivität der Superoxid Dismutase (und als Folge erhöhten oxidativen Stress) und des Ceruloplasmins (Kupferspeicher und Eisentransporter), einen veränderten Lipoprotein-Cholesterinmetabolismus, Leukopenie, Neutropenie, Anämie und eine Beeinträchtigung der Immunfunktion ein. Viele der Veränderungen werden in ähnlicher Weise bei Kupfermangel beobachtet, jedoch sind die Veränderungen für einen solchen Mangel nicht spezifisch und die klinische Relevanz mancher Veränderungen unklar (SCF 2003, Kapitel 3.3.2, Seite 7).

- Der kritischste Endpunkt der Zinktoxizität ist die Beeinflussung des Kupferhaushalts. Bei Zinkzufuhren, die ungefähr 9 mg/Tag oder mehr über den vom SCF empfohlenen Zufuhrmengen liegen, kann die Kupferbilanz zumindest kurzzeitig beeinflusst werden, allerdings ist die Relevanz hinsichtlich langfristiger Auswirkungen auf die Kupfer-Homöostase ungeklärt (SCF, 2003).

- Eine der am häufigsten beobachteten Auswirkungen erhöhter Zinkzufuhren ist die erniedrigte Aktivität der erythrozytären Superoxid Dismutase (und als Folge erhöhter oxidativer Stress). Sie ist allerdings mit keinen negativen Wirkungen verbunden und kann nicht als Indikator eines erniedrigten Kupferstatus herangezogen werden. Die physiologische Relevanz dieser Beobachtung bleibt unklar (SCF 2003, Kapitel 3.3.3.2, Seite 8 letzter Paragraph).

- Die Datenlage bezüglich der Auswirkungen erhöhter Zinkzufuhren (40 - 160 mg/Tag) auf den Lipoprotein- und Cholesterinmetabolismus ist uneinheitlich. Nur vereinzelt wurden negative Auswirkungen beobachtet (SCF 2003, Kapitel 3.3.3.3, Seite 9).

- Langanhaltende erhöhte Zinkzufuhren verursachten Anämien und Veränderungen bei roten und weissen Blutzellen (wobei die Symptome auf einen induzierten Kupfermangel hinweisen). Einzelfallberichte mit Auftreten von Hypocuprämie, Anämie (Blutmangel/ Hämoglobinmangel), Leuko- und Neutropenie (Leukozytenmangel/Immunabwehr geschwächt) bei Zufuhren von 150 mg/Tag liegen vor. Zusätzlich wurden bei Zinkgaben von 50 mg/Tag erniedrigte Hämatokritwerte (erniedrigter Anteil der Erythrozyten in Blut) beobachtet. Jedoch kommt der SCF unter Würdigung weiterer Studien, die keine negativen Effekte beobachteten, zu dem Schluss, dass bei Zufuhrmengen unter 60 mg/Tag keine einheitlichen Ergebnisse über negative Wirkungen auf Parameter des Blutbilds vorliegen (SCF 2003, Kapitel 3.3.3.3, Seite 9; BfR 2004 Kapitel 13.3.1, Seite 255 -256).

- Als weitere negative Wirkungen erhöhter Zinkzufuhren wurde eine Beeinträchtigung der Immunabwehr beobachtet (300 mg über 6 Wochen); bei Zufuhr von 53 mg über 90 Tage eine erhöhte Aktivität der knochenspezifischen alkalischen Phosphatase (Dephosporylierung von Proteinen). Diabetiker wiesen bei Zufuhr von 50 mg/Tag Zink (28 Tage) erhöhte Hämoglobin A1C-Werte auf, wobei die klinische Bedeutung dieser Erhöhung unklar bleibt (SCF 2003, Kapitel 3.3.3.6, Seite 10; BfR 2004 Kapitel 13.3.1, Seite 256, Paragraph 2).

- In einer epidemiologischen Untersuchung zur Assoziation von Zinksupplementation und dem Auftreten fortgeschrittener Prostatakarzinome konnte bei Zufuhren bis zu 100 mg/Tag kein erhöhtes relatives Risiko (RR) gegenüber der Kontrollgruppe (Non-User) beobachtet werden. Die zusätzliche Zinkzufuhr von mehr als 100 mg/Tag war aber mit einem erhöhten relativen Risiko (RR = 2.29; 95% Konfidenz-Intervall = 1.06 – 4.95) assoziiert. Bei Untersuchungen zur Dauer der Supplementierung wurde (ohne Differenzierung nach supplementierten Zinkmengen) ein erhöhtes Risiko nach mehr als 10-jähriger Supplementierung beobachtet (RR = 2.37; 95% Konfidenz-Intervall = 1.42 – 3.95). Die Bedeutung dieser epidemiologischen Untersuchung bleibt unklar, weil die Autoren eine Verfälschung der Ergebnisse durch "restliche Störfaktoren" ("residual confounding") nicht ausschliessen konnten (BfR 2004, Kapitel 13.3.1, Seite 256, Paragraph 3).

4.4 Gesundheitsbasierter Referenzwert

Aufgrund der vom SCF evaluierten Toxizitätsdaten (vergleiche Kapitel 2.2) wurde ein NOAEL von 50 mg/Tag abgeleitet, der darauf gründet, dass hier keine unerwünschten Auswirkungen auf eine Reihe relevanter Parameter des Kupferstoffwechsels als dem kritischsten Endpunkt der Zinktoxizität beobachtet wurden. Der SCF hat, basierend auf einem NOAEL von 50 mg/Tag und Anwendung eines Unsicherheitsfaktors von 2, für Erwachsene ein Tolerable Upper Intake Level (UL) von 25 mg/Tag abgeleitet. Die Höhe des Unsicherheitsfaktors wird mit geringen Probandenzahlen und kurzen Studiendauern begründet (SCF 2003, Kapitel 5.1 und 5.3, Seite 11). Auf der Grundlage des Tolerable UL für Erwachsene wurden seitens des SCF ULs für Kinder und Jugendliche extrapoliert (**Tabelle 4-1**).

Tabelle 4-1: Tolerable Upper Intake Level (UL) für Zink
(SCF, 2003, Kapitel 5, Seite 11)

Lebensjahre	**(UL_{SCF}) (mg/Tag)**
<1	Nicht bestimmbar
1 - 3	7
4 - 6	10
7 - 10	13
11 - 14	18
15 - 17	22
Erwachsene	25
Schwangere und Stillende	25

Als mögliche Risikogruppen für eine Überversorgung mit Zink werden Personen, die an Hämochromatose (erhöhte Eisenaufnahme) leiden und Diabetiker eingestuft. Für diese Personengruppen konnte aufgrund unzureichender Daten keine sichere Gesamtzufuhr abgeleitet werden (BfR 2004, Kapitel 13.4, Seite 257, Paragraph 3).

4.5 Exposition

4.5.1 Äussere Exposition

Der Zinkbedarf für Kinder im Alter von 1 bis <3 Jahren wurde wie in **Tabelle 4-2** angegeben von der EFSA in 2014 auf 3.6 mg/Tag, für Kinder von 4 bis 6 Jahren auf 4.6 und für 7 – 10-Jährige auf 6.2 mg/Tag geschätzt (EFSA 2014, Tabelle 12, Seite 34).

Tabelle 4-2: Täglicher Zinkbedarf (mg/Tag)
(EFSA 2014, Kapitel 6.3.2, Tabelle 12, Seite 34)

Age	Average Requirement (mg/day)	Population Reference Intake (mg/day)
7–11 months	2.4	2.9
1–3 years	3.6	4.3
4–6 years	4.6	5.5
7–10 years	6.2	7.4
11–14 years	8.9	10.7
15–17 years (M)	11.8	14.2
15–17 years (F)	9.9	11.9

M, males; F, females.

Die Hauptexpositionsquelle für Zink im Alltag sind die Nahrung, Nahrungsergänzungsmittel und das Trinkwasser. Die durchschnittliche Zinkaufnahme aus der Nahrung für Kinder verschiedener Altersklassen ist in **Tabelle 4-3** aufgelistet. Ein Vergleich mit den Werten in Tabelle 4.2 zeigt, dass für Kinder aller Altersklassen die geschätzte Aufnahme über dem geschätzten Bedarf liegt.

Tabelle 4-3: Tägliche Zinkzufuhr (mg/Tag)
(EFSA 2014, Kapitel 6.3.2, Tabelle 12, Seite 34)

	Level of phytate intake (mg/day)	Population Reference Intake (mg/day)
Age		
7–11 months		2.9
1–3 years		4.3
4–6 years		5.5
7–10 years		7.4
11–14 years		9.4
15–17 years (M)		12.5
15–17 years (F)		10.4
≥ 18 years (M)	300	9.4
	600	11.7
	900	14.0
	1 200	16.3
≥ 18 years (F)	300	7.5
	600	9.3
	900	11.0
	1 200	12.7
Pregnancy		+ 1.6
Lactation		+ 2.9

M, males; F, females.

4.5.2 Innere Exposition

For zinc, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

The absolute oral bioavailability of zinc from soil is not directly available for humans. However, the zinc absorption rate after oral exposure to food/water is relatively well characterized in humans and it is estimated to be 60% as a conservative estimate (section 4.5.2.1).

Therefore the Relative Oral Adjustment Factor (RAF) approach can be used to estimate the absolute oral bioavailability from soil. For zinc there are no *in vivo* soil ingestion studies in humans 4.5.2.2) or experimental animals (section 4.5.2.3). Therefore, given the quality of the available data, SCAHT applies the USEPA (2007) recommended upper default RAF-value of 100% (section 4.5.2.4).

In vitro studies which estimate the bioaccessbility of zinc from soil and/or food and water are available. However, the relevance and reliability of these data is considered to be insufficient, to support the use of a RAF factor below 100% (section 4.5.2.5).

Therefore SCAHT applies a default RAF-value of 100%. This is in line with USEPA recommendations (USEPA 2007) for such situations.

4.5.2.1 Oral bioavailability from food and/or water from dietary studies

Zink wird aus dem Jejunum (Teil des Dünndarms) durch einen Carrier-vermittelten Transportprozess und passive Diffusion (bei hohen Zn-Gehalten) absorbiert. Die Resorptionsrate ist homöostatisch reguliert. Kupfer, Kalzium, Eisen und Phytate vermindern die Zn-Absorption und bestimmte Aminosäuren erhöhen die Zn-Absorption. Je nach Ernährungszustand kann die Absorptionsrate zwischen 15 und 60% schwanken (SCF 2003, Kapitel 2.2, Seite 3, Paragraph 1). Es gibt keinen spezifischen Zinkspeicher im Körper (SCF 2003, Kapitel 2.2, Seite 3, Paragraph 1). Der Zinkgehalt in Geweben und die Aktivität der Zn-gesteuerten Prozesse kann über einen breiten Bereich der diätischen Zinkaufnahme (2.8 mg/kg KG - 40 mg/kg KG) (King 2000, Seite 1360S, rechte Spalte, Paragraph 2) im Gleichgewicht gehalten werden. Bei erhöhter Zinkaufnahme wird die Absorption erniedrigt und die Ausscheidung über den Darm mehrfach gesteigert. Reichen diese Mechanismen nicht aus, wird Zn zusätzlich über die Haare abgeben.

⇒ **SCAHT uses a conservative oral bioavailability from food/water of 60 % in its risk assessment approach.**

4.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

Data on absolute or relative bioavailability of zinc from soil in humans or experimental animals are not available.

4.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

Data on absolute or relative bioavailability of zinc from soil in experimental animals are not available.

4.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of zinc from soil compared to food or water, is to use the Relative Oral Absorption Factor (RAF) approach proposed by the USEPA, as outlined in the Methodology section. A RAF default medium-specific value of 0.5 (50%) has been proposed for inorganics, and could theoretically be used for copper (NRC 2003, Table 2.1 pp.69-70).

- However, no *in vivo soil ingestion* studies either in humans or in experimental animals could be located in the literature. Therefore no information on relative absorption of zinc in soil is

available. This make the use of the RAF more difficult. In such a case, a RAF of 1.0 (100%) would be recommended (USEPA 2007).

- A qualitative comparison with other metals suggests that zinc is in the medium range of the bioaccessibility values. However, *in vitro* data are limited and kinetics information is lacking, so bioaccessibility information cannot be used here to predict the bioavailability of zinc. This lack of information would support a more conservative approach to the use of RAF. This lack of data further supports a more conservative approach to the use of RAF. For information purposes, in vitro bioaccessibility studies are summarized in section 4.5.2.5.

⇒ **Therefore SCAHT uses a more conservative approach and a RAF-value of 100% is used, which is in line with USEPA recommendations (USEPA 2007) for such situations**

⇒ **In conclusion, considering a maximal dietary oral bioavailability of 60% for zinc in humans and a RAF of 100% to account for the higher uncertainty of the database, SCAHT applies a conservative absolute oral bioavailability from soil of 60% for its risk assessment**.

4.5.2.5 Summary of the in vitro bioaccessibility information

Die **Bioverfügbarkeit von Zink aus dem Boden** (= "bioaccessibility") ist wie bei anderen Metallen abhängig von seiner chemischen Form, der Partikelgrösse und der physikalisch-chemischen Eigenschaften des Bodens. Boden-pH-Wert, löslicher Gehalt organischer Substanzen, Metall-Oxid-Gehalt, Tongehalt und -art, die Anwesenheit organischer Liganden, und die Konkurrenz durch andere Metallionen haben einen wesentlichen Einfluss auf die Mobilität des Zinks.

Zinc ions are strongly adsorbed to soils at pH 5 or greater and are expected to have low mobility in most soils. Zinc binds strongly to clay, organic matter and many organic ligands, depending on the site-specific soil characteristics. Accumulation tends to be higher in soils of higher organic matter content, due to increased metal binding capacity, with a smaller dependency of soil pH than for other metals. Acidic soils and sandy soils with a low organic content have a reduced capacity for zinc absorption (ATSDR 2005).

A few *in vitro* bioaccessiblity studies are available in the literature.

- De Miguel et al (2012) reviewed several studies for zinc-contaminated urban and playground soils (siehe **Tabelle 4-4**).

Tabelle 4-4: Overview of selected Zn bioaccessibility values for urbans soils published in the literature (1998-2012)

(Source: De Miguel et al. 2012, page 682-683, Table 4)

Type of phase in the *in vitro* model	Mean	Range or (SD)	Type of soil	Reference
gastric	55	(32-83)	Urban (Seville)	Madrid et al. 2008
gastric	47	(±14)	Playground	De Miguel et al. 2012
gastric	47	(17-85)	Urban	Roussel et al. 2010
gastric	40	34-43	Urban (Torino)	Madrid et al. 2008
gastric	29	(±16)	Urban	Rasmussen et al. 2008
gastric+intestinal	46	(±12)	Playground	De Miguel et al. 2012
gastric+intestinal	23	(8-47)	Urban	Roussel et al. 2010
gastric+intestinal	21	(±6.1)	Urban	Poggio et al. 2009

4.6 Risikoabschätzung

Die Risikobewertung des derzeitigen Sanierungswerts für Zink (Zn) in Familiengärten in Höhe von 2000 mg/kg Boden durch das SCAHT basiert auf einer vom SCF festgesetzten sicheren Höchstaufnahme (UL-Wert) von 25 mg/Tag und den daraus abgeleiteten ULs von 7-22 mg/Tag für Kinder verschiedener Altersklassen.

Ein Vergleich der ULs für Zn mit den von der EFSA geschätzten täglichen Aufnahmemengen (siehe **Tabelle 4-5**) zeigt, dass die Zinkzufuhr über die Nahrung die empfohlenen Höchstgrenzen in keiner Altersklasse überschreitet.

Das Verschlucken von 250 mg Boden, der mit 2000 mg Zn/kg Boden belastet ist, würde zu einer zusätzlichen externen Exposition von 500 µg Zn führen, die sich unter Berücksichtigung der Bioverfügbarkeit des Zink reduziert. Für Zink gibt es keine *in vivo* Studien, die über oralen Bioverfügbarkeit nach direkter Aufnahme durch den Menschen über den Boden informieren. Deshalb, wendet SCAHT einen konservativen Anstaz zu RAF Abschätzung. **Das SCAHT benutzt für seine Risikoabschätzung eine absolute orale Bioverfügbarkeit aus dem Boden von 60%**.

⇒ Unter diesen Bedingungen reduziert sich die Belastung durch das Verschlucken von 250 mg Boden, der mit 2000 mg Zn/kg Boden belastet ist, auf 300 µg/Tag.

⇒ Damit liegt die Gesamtbelastung der Zinkzufuhr über Nahrung und Boden für ein 1 bis 3-jähriges Kind mit 4.55 mg/Tag (4.3 mg/Tag laut **Tabelle 4-5** plus 0.3 mg/Tag aus dem Boden) immer noch deutlich unter der zulässigen Höchstdosis (7 mg/Tag; **Tabelle 4-1**) und das SCAHT geht davon aus, dass ein zusätzliches Gesundheitsrisiko durch das Verschlucken von kontaminiertem Boden unwahrscheinlich ist.

⇒ Der in der Schweizer Altlasten-Verordnung (AltlV) festgelegte Sanierungswert für Zink für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 2000 mg Zn/kg Boden kann beibehalten werden.

⇒ Rein rechnerisch besteht aus humantoxikologischer Sicht ein grosser Spielraum zur Erhöhung des bestehenden Sanierungswertes. Geht man bei 1-3 jährigen Kindern von einer zulässigen täglichen Höchstzufuhr von 7 mg/Tag aus und einer Hintergrundbelastung durch die Nahrung in Höhe von 4.3 mg/Tag, könnten zusätzlich 2.7 mg Zn/Tag aufgenommen werden. Unter der Annahme einer 60% oralen Bioverfügbarkeit von Zn nach direkter Bodenaufnahme würde das Verschlucken von 250 mg Boden der mit etwa 21600 mg Zn/kg Boden kontaminiert ist, wahrscheinlich kein Gesundheitsrisiko darstellen. Der bestehende Grenzwert von 2000 mg Zn/kg Boden könnte also um den Faktor 10 auf 21600 mg Zn/kg Boden angehoben werden. **Selbst bei der Annnahme einer 100% oralen Bioverfügbarkeit von Zink nach direkter Bodenaufnahme, könnte der Bestehende Grenzwert noch um etwa den Faktor 5 angehoben werden**. Ob dies aus Gründen des Umwelt- und Gewässerschutzes vertretbar ist, muss evaluiert werden.

Wie viel Zink tatsächlich vom Körper aufgenommen wird, ist homeostatisch reguliert und hängt vom Ernährungszustand ab, wobei Kupfer und Zink um die Aufnahme konkurrieren. Die Resorptionsrate von Zink liegt im Bereich von 15 - 60% (SCF 2003, Kapitel 2.2, Seite 3, Paragraph 1).

Tabelle 4-5: Vergleich der Tolerable Upper Intake Level (UL) für Zink mit der täglichen Aufnahmemenge über die Nahrung und kontaminierten Boden.

Lebensjahre	(UL_{SCF}) (mg/Tag)	Zn-Zufuhr Nahrung (mg/Tag) (EFSA 2014)	Zn-Zufuhr Boden (mg/Tag) (SCAHT-Schätzung)
<1	-	2.9	-
1 - 3	7	4.3	0.250
4 - 6	10	5.5	-
7 - 10	13	7.4	-
11 - 14	18	9.4	-
15 - 17	22	12.5	-
Erwachsene	25	-	-
Schwangere Stillende	25	-	-

Es ist anzunehmen, dass auch eine höhere Zusatzbelastung aufgrund der grossen Bandbreite der homöostatischen Regulation von Zink keine negativen Folgen für die Gesundheit hat, weil der Zinkgehalt in Geweben und die Aktivität der Zn-gesteuerten Prozesse über einen breiten Bereich der diätischen Zinkaufnahme (2.8 mg/kg KG – 40 mg/kg KG) im Gleichgewicht gehalten werden kann (King et al., 2000).

- Ausserdem ist die Toxizität von Zink gering. Chronische und subchronische Toxizität von Zink wurde bei Erwachsenen nach längerem Verzehr von Zinksupplementen in Bereichen von 50 - 300 mg/Tag beobachtet. Solche Aufnahmemengen werden bei Kindern durch die Aufnahme kontaminierter Böden bei weitem nicht erreicht.

- Viele bei einer Zinküberversorgung beobachteten Veränderungen (Hypocuprämie, Leukopenie, Neutropenie, Anämie, beeinträchtigte Immunfunktion, erniedrigte Aktivität der Superoxid Dismutase und des Ceruloplasmins, Veränderungen im Lipoprotein-und Cholesterinmetabolismus) werden in ähnlicher Weise auch bei Kupfermangel beobachtet. Die Veränderungen sind allerdings nicht spezifisch für einen Kupfermangel und die klinische Relevanz mancher Zn-induzierter Veränderungen bleibt, wie im Kapitel 2.2 beschrieben, unklar.

⇒ Der kritischste Endpunkt der Zinktoxizität ist die Beeinflussung des Kupferhaushalts. Bei Zinkzufuhren, die ungefähr 9 mg/Tag oder mehr über den vom SCF empfohlenen Zufuhrmengen liegen, kann die Kupferbilanz zumindest kurzzeitig beeinflusst werden, allerdings ist die Relevanz hinsichtlich langfristiger Auswirkungen auf die Kupfer-Homöostase ungeklärt. **Die zusätzliche Belastung mit** 300 µg **Zink durch das Verschlucken von Boden scheint vor diesem Hintergrund wenig relevant**.

4.7 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften in Europa, USA und Kanada (z.B. Carlon 2007; Provoost et al 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden (siehe **Anhang 1**).

USA: 23000; F: 9000; CZ: 2500; **CH: 2000**; B: 1000; NL: 720; S: 350; CAN: 200; I: 150; (mg /kg dm)

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5 PAK

5.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 100 mg PAK-16 und 10 mg BaP/kg Boden sollte gemäss dem ALARA-Prinzip überprüft werden. Um den von der EFSA empfohlenen Mindest-MOE für kanzerogene Effekte von >10000 zu erreichen müssten die Werte auf etwa 2.2 bzw. 0.3 mg/kg Boden für PAH-16 und BaP reduziert werden. Die Liste der zu überprüfenden PAK-16 sollte um folgende PAKs erweitert werden: • Dibenzo(a,l)pyren (CAS-191-30-0) • Benzo(c)fluoren (CAS 205-12-9) • Benzo[e]pyren (CAS 192-97-2) • Benzo[j]fluoranthen (CAS-205-82-3) Begründung: • Laut IARC sind Dibenzo(a,l)pyren und Dibenz(a,h)anthracen stärker kanzerogen als BaP. Während Dibenz(a,h)anthracen in der PAH-8 Liste bereits erfasst ist, wird Dibenzo(a,l)pyren (CAS-191-30-0) in der PAH-16 Liste nicht erfasst. • Das WHO/FAO Joint Expert Committee on Food Additives (JECFA) identifizierte zudem Benzo(c)fluoren (CAS 205-12-9) als prioritäre Substanz, weil es nach oraler Exposition in hohem Masse (stärker als Benzo(a)pyren) zur Bildung von Lungentumoren beiträgt. • Zudem erachtet das deutsche Bundesinstitut für Risikobewertung BfR die offiziell von der EU als karzinogen eingestuften Benzo[e]pyren (CAS 192-97-2) und Benzo[j]fluoranthen (CAS-205-82-3) als kritisch.
Gefährdungspotential	Hoch	Kanzerogenität ist am kritischsten.

Kanzerogen	Ja	Lungen- und Hautkrebs nach inhalativer Exposition und Hautkrebs nach dermaler Exposition am Arbeitsplatz. Krebs des Magen-Darm-Trakts und der Atmungswege nach oraler Exposition im Tierversuch.
Mutagen	Ja	z.B. BaP und Chrysen
Reprotoxisch	Ja	z.B. BaP
Neurotoxisch	Nein	
Andere	Ja	Immuntoxizität, Lebertoxizität, Nierentoxizität. Nicht neoplastische Läsionen werden bei der Risikobeurteilung vernachlässigt, weil die Schwellenwerte über denen für kanzerogene Effekte liegen.
Gesundheitsbasierter Referenzwert		Kein Schwellenwert für genotoxische Kanzerogene. Oraler $BMDL_{10}$ für kanzerogene Effekte: BaP: 0.07 mg BaP/kg KG/Tag ; PAH-8: 0.49 mg PAH-8/kg KG/Tag Dermaler DMEL (10^{-5} – 10^{-6} Krebsrisiko): BaP, PAH-6, PAH-16: 0.004 -30 ng BaP, PAH-6, PAH-16/kg KG/Tag
Exposition		
Äussere Exposition Boden (250 mg)		BaP: 10 mg BaP/kg Boden = 2.5 µg BaP/250 mg Boden = 0.2 µg BaP/kg KG/Tag (KG: 12.5kg) PAH-16: 100 mg PAH-16/kg Boden = 25 µg PAH-16/250 mg Boden = 2 µg PAH-16/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Szenarioplanning (S1, S2, S3) (S1) 100% absolute orale Bioverfügbarkeit aus dem Boden (based on USEPA upper default RAF-value): BaP: 0.2 µg BaP/kg KG/Tag (KG: 12.5kg) PAH-16: 2 µg PAH-16/kg KG/Tag (KG: 12.5kg) (S2) 50% absolute orale Bioverfügbarkeit aus dem Boden (based on US Michigan State DEQ lower RAF-value of 50%, however no justification was provided by the State Agency): BaP: 0.1 µg BaP/kg KG/Tag (KG: 12.5kg) PAH-16: 1 µg PAH-16/kg KG/Tag (KG: 12.5kg)

		(S3) 29% absolute orale Bioverfügbarkeit aus dem Boden (based on US Massachussetts State DEP lower RAF-value of 29%, based on a rat study; juvenile swine is the gold standard): BaP: 0.058 µg BaP/kg KG/Tag (KG: 12.5kg) PAH-16: 0.58 µg PAH-16/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Mittlere PAH-Aufnahme über die Nahrung: BaP: 3.9 ng BaP/kg KG/Tag PAH-8: 28.8 ng PAH-8/kg KG/Tag
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Möglich	Die geschätzte PAH-Aufnahmemenge über die Nahrung liegt unterhalb des jeweiligen gesundheitsbasierten Referenzwertes. Die geschätzte PAH-Aufnahme durch direkte Bodenaufnahme ist klein im Vergleich zu den gesundheitsbasierten Referenzwerten, aber gross im Vergleich zur PAH-Aufnahme über die Nahrung (µg versus ng). Da bereits die gesundheitsbasierten Referenzwerte risikobehaftet sind und die MOE mit <500 wesentlich kleiner ist als die von der EFSA vorgeschlagene MOE von 10000 für kanzerogenen Effekte, sollte eine Reduktion der Sanierungswerte in Betracht gezogen werden. Gesundheitsbasierter Referenzwert (Oraler $BMDL_{10}$ für kanzerogene Effekte): BaP: 0.07 mg/kg KG/Tag PAH-8: 0.49 mg /kg KG/Tag PAH-Aufnahme über die Nahrung: BaP: 3.9 ng BaP/kg KG/Tag PAH-8: 28.8 ng PAH-8/kg KG/Tag PAH-Aufnahme durch direkte Bodenaufnahme: BaP: 0.2 µg BaP/kg KG/Tag (KG: 12.5kg) PAH-16: 2 µg PAH-16/kg KG/Tag (KG: 12.5kg)
Grenzwert im Vergleich		Summenparameter für PAHs

		CZ: 280 (Σ12); CH: 100 (ΣEPA16); A: 50 (nicht spezifiziert); NL: 40 (Σ10); D: 10 (ΣEPA16); I: 10 (Σ10); S: 0.3 (Σ7 kanzerogene PAKs) und 20 (Σ9 nicht kanzerogene PAKs) (mg/kg dm) B(a)P: CH: 10; CZ: 2; A: 5; D: 4 &; CAN: 0.7; E: 0.2; I: 0.1; USA: 0.022-0.2 (mg/kg dm)
Datenlage	Zufriendenstellend	Es gibt keine Studien zur Bioverfügbarkeit von PAK aus dem Boden im Menschen, aber es gibt mehrere Tierstudien. Epidemiologische Daten zur kanzerogenen Wirkung von PAHs nach oraler Exposition sind nicht schlüssig. Daten zu Mischungstoxizitäten von PAH-Kongeneren und/oder in Kombination mit Dioxinen, Furanen und PCBs sind kaum zu erfassen.

5.2 Zusammenfassung

The Swiss Contaminated Sites Ordinance (CSO)[1] clean up values of 100 mg polycyclic aromatic hydrocarbons (PAH-16)[2]/kg soil and 10 mg benzo[a]pyrene (BaP)/kg soil for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly, should be "As Low As Reasonably Achievable" in line with the ALARA-principle for genotoxic carcinogens for which no risk free threshold level can be set. To satisfy the European Food Safety Authority (EFSA) recommended minimum-Margin of Exposure (MOE) for carcinogens of > 10000, PAH-16 and BaP soil clean up values should be reduced to 2.2 bzw. 0.3 mg/kg soil respectively. The SCAHT would recommend to keep monitoring the existing PAH-16 to allow comparison with historical data but to expand the list to cover the highly potent dibenzo(a,l)pyrene, benzo[c]fluorene, benzo[e]pyrene and benzo[j]fluoranthene.

Consumers and workers are exposed to complex mixtures of probably up to several hundred PAH congeners in combination with dioxins, furans and PCBs and other substances in either occupational or environmental situations. Therefore, it is difficult to ascertain the toxicity of a single PAH component or a given mixture of PAHs.

The most critical health effect of PAHs in humans is carcinogenicity. Other non-neoplastic effects including reprotoxicity, immunotoxicity and liver and kidney toxicity have been described, but based on comparisons of dietary intakes with "No Observed Effect Levels" (NOELs) for various endpoints non-neoplastic effects were not considered to be of concern. It is assumed that thresholds for non-neoplastic effects will be clearly higher than the range of "Derived Minimal Effect Levels" (DMELs) for neoplastic lesions and therefore the SCAHT risk assessment focuses on the carcinogenic hazard from PAHs.

Evidence that mixtures of PAHs are carcinogenic to humans is primarily derived from occupational studies of workers following inhalation and dermal exposure. The majority of the epidemiological data associated airborne PAH exposures with increased lung cancer risk. In addition, exposed workers, particularly at coke ovens and aluminium smelters, have shown excess bladder cancer for which a relationship to PAH exposure was highly suggestive. Skin cancer has been reported to be positively associated with dermal but not with inhalation PAH exposure. There are few epidemiological studies investigating directly the possible association between dietary PAH intake and cancer, which are inconclusive, but there is strong evidence from experimental animal studies.

Following oral administration of pure BaP or PAH mixtures, induction of local and systemic tumours has been noted in rats and mice. In rats treatment-related tumours were found in the gastrointestinal tract and liver and mice studies revealed tumours in the gastrointestinal tract, liver, and respiratory tract. Inhalation of PAH or BaP caused lung tumours in rats and mice and respiratory tract tumours in hamsters. BaP is also a potent experimental skin carcinogen. It produced skin tumours after dermal application in mice, rats, rabbits, and guinea pigs. Mixtures of PAHs that include BaP such as coal tar were also found to be dermal carcinogens in experimental animals.

For genotoxic carcinogens like PAHs a threshold for tumorigenic activity cannot be set. Instead, EFSA established in 2008 benchmark doses which are associated with a 10% extra risk for carcinogenicity

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

[2] Those are the 16 PAHs originally defined by US EPA as most relevant for environmental risk assessment (see **Table 5-1**).

after dietary exposure. These are 0.07 and 0.49 mg/kg bw/day for BaP and PAH-8. The German Federal Institute for Risk Assessment (BfR) developed DMELs for an additional cancer risk of 10^{-5} to 10^{-6} for PAH-8 in the range of 0.004 – 30 ng/kg bw/day.

For adult non-smokers exposure to PAH occurs mainly by ingestion of food and by inhalation of air but for small children exposure via ingestion of dust and soil can become a major exposure pathway. EFSA estimated that the overall average dietary exposure in the EU für BaP is 3.9 ng/kg bw per day and for PAH-8 it is 28.8 ng/kg bw/day (assuming a bw of 60 kg) (no data are available for PAH-16). In contrast, a child that ingests 250 mg of soil that is contaminated with 100 mg PAH-16/kg soil or 10 mg BaP/kg soil would be exposed to 2 µg PAH-16/kg bw/day or 0.2 µg BaP/kg bw/day assuming a body weight of 12.5 kg and an absolute oral bioavailability of PAHs in soil of 100%.

⇒ The combined oral exposure from food and soil does not exceed the Benchmark Dose Level - 10% ($BMDL_{10}$) for oral toxicity. However, calculating margins of exposure (MOEs) by dividing the lowest $BMDL_{10}$ values by the combined oral exposure from food and soil to PAHs results in MOE well below 500. According to EFSA a MOE below 10000 indicates a potential concern for consumer health and a possible need for risk management action.

Therefore the SCAHT recommends reconsidering the existing threshold values for BaP and PAH-16.

- The fact that the overall oral background exposure does not exceed the EFSA-derived oral $BMDL_{10}$ indicates a low additional health risk but under the discussed soil ingestion scenario soil ingestion creates a massive additional exposure compared to the dietary background exposure.
- Furthermore, the EFSA-derived $BMDL_{10}$-level is not risk free but already associated with a 10% increase in cancer risk above background level. With respect to carcinogenicity children have to be considered a particularly sensitive sub-population both, in terms of an inherent greater sensitivity and their longer remaining life-span which is increasing the statistical risk for the development of cancer following exposure towards PAHs.
- Moreover, inhalation of resuspended soil particles is discussed in the scientific literature as an additional exposure pathway for PAHs, which has not been considered in the 1st tier SCAHT risk assessment.
- The DMELs for dermal toxicity are several orders of magnitude lower compared to $BMDLs_{10}$ for oral toxicity but again dermal toxicity of PAH has not been the focus of this 1st tier risk assessment.

The SCAHT also recommends reviewing whether or not the existing list of PAH-16 in the Swiss CSO is most appropriate to meet the risk management goals and recommends to expand the list to cover the highly potent dibenzo(a,l)pyrene, benzo[c]fluorene, benzo[e]pyrene and benzo[j]fluoranthene.

- The International Agency for Research on Cancer (IARC) argues that a few PAHs seem to be more potent carcinogens than BaP. Of particular concern is dibenzo(a,l)pyrene which seems to be more than ten times more potent than BaP in rats. IRAC recommended that this potent polycyclic aromatic hydrocarbon compound should be measured routinely in the workplace and the environment.
- The WHO/FAO Joint Expert Committee on Food Additives (JECFA) also identified an additional substance, benzo[c]fluorene, as a priority substance because it may contribute significantly to the formation of lung tumours after oral exposure to coal tar based on a much higher number of adducts than BaP.
- The BfR argues that for consumer protection the focus should be on those PAH-8 which are explicitly known and legally classified as genotoxic carcinogens in Annex VI to Reg. No.

1272/2008 (CLP regulation). The BfR considers benzo[e]pyrene (CAS 192-97-2) and benzo[j]fluoranthene (CAS-205-82-3) as critical for human health. The EU classifies both compounds as carcinogens.

The SCAHT would recommend to keep monitoring the existing PAH-16 to allow comparison with historical data but to expand the list to cover dibenzo(a,l)pyren (CAS-191-30-0), benzo(c)fluoren (CAS 205-12-9), benzo[e]pyren (CAS 192-97-2), benzo[j]fluoranthen (CAS-205-82-3).

5.3 Gefährdungspotential

5.3.1 Introduction: development of USEPA-16 list

In a recent publication, Keith (2015) reviewed the historical, regulatory and scientific context which led to the development of the USEPA 16 PAH-list (USEPA PAH-16) in 1976. detailing where, when, how, and (very importantly) why each of the 16 PAHs Priority Pollutants were selected as representative compounds to regulate. PAH selection was as follows:

- **Acenaphthene**, **naphthalene**, and **fluoranthene** (3): selected based on the original “list of 65 toxic pollutants" in the 'EPA 1976 Consent Decree';
- **Benzo(a)anthracene**, **benzo(a)pyrene**, **benzo(b)fluoranthene**, **benzo(k)fluoranthene**, **chrysene**, **dibenzo(a,h)anthracene**, and **indeno(1,2,3-c,d)pyrene** (7): selected because an analytical standard was available and each met some or all priority selection criteria[3];
- **Acenaphthalene**, **fluorene**, and **phenanthrene** (3): selected based on a 1975 USEPA interim report which highlighted a potential carcinogenicitiy through water supplies;
- **Anthracene** (1): selected because it is a common PAH obtained from coal tar and frequently used as a chemical intermediate for dyes and other fine chemicals;
- **Benzo(ghi)perylene** (1): selected because it is a representative of a 6-membered ring PAH;
- **Pyrene** (1): selected because it is a common PAH obtained from coal tar, is produced under a wide range of combustion conditions and is used as a chemical intermediate for dyes, etc.

5.3.2 Grouping of PAH congeners for risk assessment

Consumers and workers are exposed to complex mixtures of probably up to several hundred PAH congeners (Deutschland 2010, chapter B. 1.4, page 34, paragraph 1). The challenge for risk assessment is that PAH congeners and mixtures vary widely in the level of their carcinogenic potential (IARC 2010, second paragraph, page 31) and their abundance in the environment. Therefore the evaluation of human cancer risk attributable to PAH mixtures largely depends on the individual PAHs measured in environmental and biological samples.

For a sound risk assessment the most toxic and most abundant PAHs for a given exposure scenario should be selected, and therefore the selection could vary depending on the protection goal (general population, workers, environment) and the expsoure scenario. **Table 5-1** and **Table 5-2** list some groupings of PAHs used in regulatory risk assessment. However, please note that for the above mentioned reasons the grouping of PAHs is not harmonised.

- The Swiss Contaminated Sites Ordinance (CSO)[1] includes 16 PAHs. Those are the 16 PAHs originally defined by US EPA as priority pollutants (USEPA PAH-16). BaP is part of the USEPA PAH-16 but the CSO also sets a separate reference value for BaP which is most frequently used as a lead compound for toxicity testing of PAH mixtures. Using BaP as a lead compound allows the comparison of studies with otherwise different PAH mixtures.
- The German proposal for use restriction of PAHs in consumer products to the European

[3] Selection/prioritization criteria for multiple potential representative compounds were (Keith LH, 2015): (i) Consideration of the frequency of occurrence; (ii) Consideration of manufactured quantities; and (iii) consideration of absolute commercial availability so that an analytical reference material/standard could be used to confirm a GC-MS identification".

Commission focuses on PAH-8 (BfR PAH-8) which are explicitly known and legally classified as genotoxic carcinogens in Annex VI to Reg. No. 1272/2008 (CLP regulation).

- EFSA also uses a slightly different list of eight PAHs (EFSA PAH-8)[4] either individually or in a combination to assess the carcinogenic potency of PAHs in food. However, EFSA argues that EFSA PAH-8 is not providing much added value compared to a short list of four PAHs (EFSA PAH-4) (EFSA 2008, chapter: conclusions, page 97, last paragraph).

Table 5-1: Different groups of PAHs commonly referred to in the regulatory context.

PAH-Group	Description	Full list of most relevant 18 PAHs for regulatory risk assessment
USEPA PAH-16 (CH CSO PAH-16)	The 16 PAHs listed in Annex 3, chapter 2 of the Swiss Contaminated Sites Ordinance (CSO), (same as USEPA PAH-16). – acenaphthene – acenaphthylene – anthracene – benz[a]anthracene – benzo[a]pyrene (BaP) – benzo[b]fluoranthene – benzo[ghi]perylene – benzo[k]fluoranthene – chrysene – dibenzo[ah]anthracene – fluoranthene – fluorene – indeno[1,2,3-cd]pyrene – naphthalene – phenanthrene – pyrene	acenaphthene acenaphthylene anthracene benz[a]anthracene benzo[a]pyrene (BaP) benzo[b]fluoranthene benzo[ghi]perylene benzo[k]fluoranthene chrysene dibenzo[ah]anthracene fluoranthene fluorene indeno[1,2,3-cd]pyrene naphthalene phenanthrene pyrene benzo[e]pyrene benzo[j]fluoranthene
PAH-6	**The six legally classified carcinogens as defined by EU which are also listed in the USEPA-PAH-16.** – benz[a]anthracene – benzo[a]pyrene (BaP) – benzo[b]fluoranthene – benzo[k]fluoranthene – chrysene – dibenzo[ah]anthracene	
PAH-2	– benzo[a]pyrene (BaP) – chrysene	

[4] The lists of PAH-8 defined by EFSA and BfR are not identical. EFSA PAH-8 includes benzo[a]pyrene, benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[ghi]perylene, chrysene, dibenz[a,h]anthracene, indeno[1,2,3-cd]pyrene. In the BfR PAH-8 list benzo[ghi]perylene and indeno[1,2,3-cd]pyrene are replaced by benzo[e]pyrene and benzo[j]fluoranthene (see also tables 5-1 and 5-2).

PAH-Group	Description	Full list of most relevant 18 PAHs for regulatory risk assessment
BfR PAH-8 (EU PAH-8)	The eight legally classified carcinogens as defined by EU. EU PAH-8 = BfR PAH-8 = PAH-6 + benzo[e]pyren + benzo[j]fluoranthene – benz[a]anthracene, – benzo[a]pyrene (BaP) – benzo[b]fluoranthene – benzo[k]fluoranthene – chrysene – dibenz[a,h]anthracene – **benzo[e]pyren** – **benzo[j]fluoranthene**	
EFSA PAH-8	The eight PAHs considered by EFSA as relevant for consumer exposure. EFSA PAH-8 = BfR PAH-8 but benzo[e]pyrene and benzo[j]fluoranthenere are replaced with benzo[ghi]perylene and indeno[1,2,3-cd]pyrene. – benz[a]anthracene – benzo[a]pyrene (BaP) – benzo[b]fluoranthene – benzo[k]fluoranthene – **benzo[ghi]perylene** – chrysene – dibenz[a,h]anthracene – **indeno[1,2,3-cd]pyrene**	
EFSA PAH-4	The four PAHs considered by EFSA as most relevant for consumer exposure. Based on the outcome of a tiered assessment, EFSA argued that EFSA PAH-8 do not provide additional value over EFSA PAH-4 (see also table 5-3): – benz[a]anthracene – benzo[a]pyrene (BaP) – benzo[b]fluoranthene – chrysene	

Table 5-2: List of most relevant PAHs under regulatory scrutinity (EC, 2011; HSA 2009; EFSA 2008; BfR 2010)

List of PAHs Common name	US EPA & CH CSO Annex 3, chapter 2 (PAH-16)	EFSA (PAH-16)	EFSA (PAH-8)	EFSA (PAH-4)	BfR (PAH-8)	Health Australia (PAH-17)	JECFA FAO/WHO (PAH-15)	SFC (PAH-15)
acenaphthene	x					x		
acenaphthylene	x					x		
anthracene	x					x		
benz[a]anthracene	x	x	x	x	x	x	x	x
benzo[a]pyrene	x	x	x	x	x	x	x	x
benzo[e]pyrene					x	x		
benzo[b]fluoranthene	x	x	x	x	x	x	x	x
benzo(c)fluorene		x						
benzo[g,h,i]perylene	x	x	x			x	x	x
benzo[j]fluoranthene		x			x	x	x	x
benzo[k]fluoranthene	x	x	x		x	x	x	x
chrysene	x	x	x	x	x	x	x	x
cyclopenta[cd]pyrene		x					x	x
dibenz[a,h]anthracene	x	x	x		x	x	x	x
dibenzo[a,e]pyrene		x					x	x
dibenzo[a,h]pyrene		x					x	x
dibenzo[a,i]-pyrene		x					x	x
dibenzo[a,l]pyrene		x					x	x
fluoranthene	x					x		
fluorene	x					x		
indeno[1,2,3-c,d]pyrene	x	x	x			x	x	x
naphtalene	x							
phenanthrene	x					x		
pyrene	x					x		
5-methylchrysene		x					x	x

5.3.3 Health effects

The most critical health effect of PAHs in humans is carcinogenicity. Other effects have been described as well. For example BaP and chrysene are classified for mutagenicity and BaP also for toxicity to reproduction.

⇒ However, non-neoplastic[1] effects have not been considered in this risk assessments because it is assumed that thresholds for non-neoplastic effects will be clearly higher than the range of DMELs for neoplastic lesions[2] (see also Deutschland 2010, page 52 for a similar approach). The following section will therefore focus on the carcinogenic hazard from PAHs.

Exposure of humans to PAHs is often characterised by a mixture of PAHs congeners, dioxins, furans and PCBs and other substances in either occupational or environmental situations.

⇒ Therefore, it is difficult to ascertain the carcinogenicity of a single PAH component or a given mixture of PAHs as presumably amplification of carcinogenicity may have occurred through the presence of other carcinogenic substances in the mixtures. In addition, PAH levels are not quantified in most reports and confounding factors such as smoking may have contributed to the effects but are not adequately considered (Deutschland 2010, chapter B.5.8.4, pages 74-79).

5.3.3.1 Human carcinogenicity

- Evidence that mixtures of PAHs are carcinogenic to humans is primarily derived from occupational studies of workers following inhalation and dermal exposure.
- The majority of the epidemiological data associated airborne PAH exposures with increased lung cancer risk. In addition, exposed workers, particularly at coke ovens and aluminium smelters, have shown excess bladder cancer for which a relationship to PAH exposure was highly suggestive.

  Skin cancer has been reported to be positively associated with dermal, but not with inhalation PAH exposure. No data were located regarding cancer in humans following inhalation of individual PAH compounds.
- There are few epidemiological studies investigating directly the possible association between dietary PAH intake and cancer (IARC 2010, page 32, 2nd paragraph). IARC reviewed the epidemiological studies that suggest a possible association between consumption of PAHs in foods and increased risks of colorectal adenoma and pancreatic cancer and concluded that these epidemiological studies were too limited to be considered conclusive (IARC 2010, page 32, 2nd paragraph; Straif 2005). Although no adequate long-term studies are available to assess the human health risk from oral exposure to single PAHs or PAH mixtures (Deutschland 2010, chapter B.5.8.4, page 74, last paragraph – page 75, first paragraph) there is strong evidence from experimental animal studies as outlined in the chapter below.

5.3.3.2 In vivo carcinogenicity

- *In vivo* oral carcinogenicity

  Following oral administration of pure BaP or PAH mixtures induction of local and systemic tumours has been noted in rats and mice. In rats treatment-related tumours were found in the gastrointestinal tract and liver and mice studies revealed tumours in the gastrointestinal tract,

[1] Tumors are also called neoplasms. Non-neoplastic lesions refer to toxicological effects other than cancer.

liver and respiratory tract.

Three long-term studies of recent date are considered as the most adequate studies for the derivation of reference values/DMEL(s) for the oral route of exposure: A study in rats treated by gavage with BaP (Kroese et al 2001) and two feeding studies in mice, one comparing pure BaP with two coal tar mixtures (Culp et al., 1998) and a similar meta study with BaP and a PAH-rich manufactured gas plant residue (Schneider et al., 2002). For a detailed list of oral carcinogenicity studies please refer to Deutschland 2010, chapter B.5.8.1, pages 57-63.

- *In vivo* inhalation carcinogenicity

  Inhalation of PAH or BaP caused lung tumours in rats and mice and respiratory tract tumours in hamsters.

  In reviews, reference to carcinogenic effects of PAH-containing mixtures or pure BaP by the inhalation route was limited to a small number of studies which were evaluated as adequate animal cancer data and were selected for further estimations. Regarding the possible use for calculating cancer risk values and for derivation of DMELs for the inhalation route of exposure the most relevant studies are presented in Deutschland 2010, chapter B.5.8.2, pages 64 -68.

- *In vivo* dermal carcinogenicity

  BaP is a potent experimental skin carcinogen and is often used as a positive control in bioassays on other substances. BaP produced skin tumours after dermal application in mice, rats, rabbits, and guinea pigs. Mixtures of PAHs that include BaP such as coal tar were also found to be dermal carcinogens in experimental animals (Deutschland 2010, chapter B.5.8.3, pages 69, paragraph 3).

  The majority of carcinogenicity studies in laboratory animals to examine tumour formation following exposure to BaP and various PAHs were conducted as skin painting studies. In addition, a number of chronic animal studies used dermal application of condensates containing various PAH compounds. Tested condensates were obtained from tobacco smoking, diesel and gasoline engine exhaust, carbon blacks, coal tar and coal gasification derived products, etc. In various strains of mice the ability of the PAHs to induce benign and malignant skin tumours after repeated exposure to comparatively low doses (< 100 µg/kg bw/day) was demonstrated. Although many studies were not conducted according to current EU or OECD guidelines, they clearly indicate that PAHs induce skin tumours (Deutschland 2010, chapter B.5.8.3, pages 69-73).

5.4 Gesundheitsbasierter Referenzwert

The PAH-16 referred to in the Swiss CSO include PAH-6 which are known genotoxic carcinogens. Even if it is acknowledged that the potential mechanisms of chemical carcinogenesis are certainly more complex, in general the central paradigm of the risk assessment of genotoxic carcinogens, i. e. that a threshold for tumorigenic activity cannot be set, is still generally accepted and applied in the characterisation of the potential risk caused by genotoxic carcinogens.

Therefore, no health-based guidance value can be set that is without any hazardous effect to human health (Deutschland 2010, chapter B.5.11, page 90, first paragraph). Instead health-based guidance values that are associated with a small additional human health risk can be derived from toxicology data, and can bear different names depending on the regulatory context, such as DMELs[2] under REACH Regulation or BMDLs, which are typically referred to by EFSA.

- DMEL values are risk-based exposure limits for which no reference risks exist. Therefore it is left to the manufacturers and distributors themselves to decide what risk of disease they intend to consider acceptable for the exposed individuals and to take as basis for establishment of DMEL values. BfR considered in its risk characterisation different risk levels (one additional cancer finding in 100’000 and 1'000'000).

5.4.1 $BMDL_{10}$ for oral toxicity (EFSA 2008)

In 2008 EFSA established health based reference values for dietary exposure to BaP, PAH-2, PAH-4 and PAH-8 (**Table 5-3**). Benchmark doses which are associated with a 10% extra risk for carcinogenicity were derived from a 2-year carcinogenicity study on coal tar mixtures in rats (Culp 1998). This study was considered to be the most adequate for dose-response modelling. To derive the $BMDL_{10}$ any carcinogenic endpoint was considered relevant for calculations. The results are indicated in table 5.3 below (EFSA 2008, chapter 9, page 90, table 33, column BMDL).

Table 5-3: EFSA-derived $BMDL_{10}$ values for oral toxicity of BaP, PAH-2, PAH-4 and PAH-8.
(EFSA 2008, chapter 9, page 90, table 33, column BMDL).

Group	Compounds	$BMDL_{10}$ (mg/kg bw/day)
BaP	BaP	0.07
PAH-2	BaP Chrysene	0.17
PAH-4	BaP benz[a]anthracene, benzo[b]fluoranthene, chrysene	0.34
PAH-8	BaP benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[ghi]perylene, chrysene, dibenz[a,h]anthracene, indeno[1,2,3-cd]pyrene	0.49

[2] For a more details on the definition of DNEL and DMEL in the REACH context please refer to: http://www.dguv.de/ifa/Gefahrstoffdatenbanken/GESTIS-DNEL-Datenbank/Was-sind-DNELs/index.jsp

5.4.2 DMELs for dermal toxicity (BfR 2010)

In June 2010, Germany submitted a proposal for use restriction of PAHs in consumer products to the European Commission. An integral part of this restriction dossier is a risk assessment on PAHs in consumer products which was performed by the BfR. The risk assessment focuses on the carcinogenic potential after dermal exposure. The PAHs evaluated included BaP, 16 US EPA PAHs and the six carcinogenic PAHs in this group of US EPA PAK-16 (see also table 5.1) (BfR 2010, chapter 2, page 2, last paragraph).

DMELs were calculated from animal studies using serveral different approaches which combined different dose descriptors (T25[3], BMD_{10}[4] and $BMDL_{10}$[5]) with different assessment factor approaches ('Large Assessment Factor' which is the REACH guidance terminology for a MOE-approach and 'Linearised' approach) and considering different risk levels (one additional cancer finding in 100'000 and 1'000'000).

⇒ The comparison on the outcome of the linearied approach and the MOE approach of the guidance shows that the resulting DMEL (for PAH-8) is principally the same (ECHA 2012b in Appendix 8-7) and the DMEL results ranges as indicated in **Table 5-4** were obtained (Deutschland 2010, page 97, BfR 2010, chapter 3.2.4, Seite 6).

Instead of taking the most sensitive DMEL from a single study forward to quantitative risk characterisation, BfR used the whole range of DMELs. The boundaries of these ranges roughly represent the results from the most (lower boundaries) and least (upper boundaries) sensitive studies, respectively.

Table 5-4: Derived DMEL values for dermal toxicity of BaP, PAH-6, PAH-16.
(Deutschland 2010, page 97, BfR 2010, chapter 3.2.4, Seite 6).

Risk Assessment Approach	DMEL (ng/kg bw/d)
Large Assessment Factor / MOE-approach	0.1 – 30
Linearised approach, 10^{-5} risk level	0.03 – 10
Linearised approach, 10^{-6} risk level	0.004 – 1

⇒ The $BMDLs_{10}$ for oral toxicity (**Table 5-3**) and DMELs for dermal toxicity (**Table 5-4**) are different by several orders of magnitude. Different toxicokinetics for the different exposure routes might contribute the differences as well as the selection of studies considered relevant for the risk assessment.

[3] T25: Chronic dose rate that will give 25% of the animals' tumours at a specific tissue site after correction for spontaneous incidence, within the standard life time of that species. It is a value calculated from a single observed dose-response and based upon the assumption of a linear dose-response relationship over the entire dose-range.

[4] BMD_{10}: Benchmark-dose representing a 10% tumour response upon lifetime exposure. This response value is derived by fitting quantitative information available from all dose levels using a multistage model.

[5] $BMDL_{10}$: Lower 95% confidence dose of BMD10. The use of the $BMDL_{10}$ rather than the BMD_{10} is recommended if one wants to reflect the uncertainties and statistical errors in the available cancer dose-response data.

5.5 Exposition

5.5.1 Äussere Exposition

In principle, consumer exposure to PAH-contaminated articles may occur along all three major exposure routes, i. e. via dermal or oral uptake or by inhalation.

- **Table 5-5** shows a comparison of the estimated total personal PAH intake from food, drinking water and inhalation (EC 2002, chapter 2.3.3, Page 23, table 2.3.4) based on available PAH concentrations in drinking water and in urban atmosphere as measured in the 1990s in European countries (NB: details are given in the Annex of EC 2002):

Table 5-5: Estimate of daily exposure to PAHs by different routes (ng/person)
(EC 2002, chapter 2.3.3, Page 23, table 2.3.4 and EFSA 2008, chapter 7.4.1, page 63, table 22)

Table 2.3.4 Estimate of the mean daily intake by different routes for an adult non-smoker (ng/person)

PAH	Food [a]	Drinking water [b]	Air [c]
Anthracene	<30-640		20
Phenanthrene	<330-4510		400
Fluoranthene	600-1660	2-200	100
Pyrene	600-1090	0.2-200	100
Benz[a]anthracene	<20-410	0.2-10	20
Chrysene	200-1530	200 [d]	20
Benzo[*b*]fluoranthene	5-360	0.1-2	20
Benzo[*j*]fluoranthene	<30	0.02-0.2	
Benzo[*k*]fluoranthene	40-140	0.02-2	20
Benzo[*b*+*j*+*k*]fluoranthene	<70-1100		60
Benzo[*a*]pyrene (BaP)	50-290	0.2-2	20
Benzo[*e*]pyrene	200		20
Benzo[*ghi*]perylene	120-360	0.2-2	20
Indeno[1,2,3-*cd*]pyrene	<20-460	0.2-2	20
Dibenz[*a*,*h*]anthracene	<10-80		2

[a] Range of mean values (from table 2.3.1).

[b] Range from the orders of magnitude of concentration (see the Annex, table 1.3.7), assuming ingestion of 2 L/day.

[c] From the order of magnitude of concentration (see the Annex, table 1.3.7), assuming a ventilation rate of 20 m^3/day. Occupational exposure is excluded.

[d] CHR + TRI.

⇒ For non-smokers, exposure to PAH occurs mainly by ingestion of food (2'325 – 12'860 ng/person or 33 - 184 ng/kg bw assuming a bw of 70 kg) and by inhalation of air (842 ng/person or 12 ng/kg bw assuming a bw of 70 kg). Contribution from drinking water was estimated at 203 - 620 ng/ person or 3 - 9 ng/kg bw assuming a bw of 70 kg (EC 2002, chapter 2.3.3, Page 23, table 2.3.4) (table 5.4).

Other, possible minor, exposure routes are ingestion of dust and soil, ingestion of drinking water, dermal absorption from soil and water and the use of PAH-contaminated products (such as preparations containing coal-tar) (EC 2002, chapter 1, Page 6, paragraph 2).

- More recent dietary exposure estimates from EFSA for BaP, and PAH-2, PAH-4 and PAH-8 in the EU (EFSA 2008, chapter 7.2.1, page 59 -61) are presented in **Table 5-6** below. It was concluded that the overall average dietary exposure across European countries for which data are available is 235 ng/day (3.9 ng/kg bw per day assuming a body weight of 60 kg) for BaP (range: 185 - 255 ng/day) and 1'729 ng/day (28.8 ng/kg bw per day assuming a body weight of 60 kg) for PAH-8 (range: 1'415 – 2'136 ng/day). The resulting median of the "high exposures" across Europe is 389 ng/day (6.5 ng/kg bw per day assuming a body weight of 60 kg) for BaP alone (range 231 - 709 ng/day) and 3078 ng/day (51.3 ng/kg bw per day assuming a body weight of 60 kg) for the sum of PAH-8 (range 1'693 – 6'568 ng/day).

Table 5-6: Estimate of median and high EU dietary exposure to different PAHs (ng/kg bw/day)
(Collated from EFSA 2008, chapter 9, Page 90, table 33 and 34)

Selected PAH	Median EU estimated mean dietary exposure (ng/kg bw/day)	Median EU estimated 97.5%ile dietary expsoure (ng/kg bw/day)
BaP	3.9	6.5
PAH-2	10.7	18.0
PAH-4	19.5	34.5
PAH-8	28.8	51.3

- A UK survey (see **Table 5-7** below) estimated the PAH-19 intake by schoolchildren and toddlers of seven age groups and identified that in general exposure of 1.5 – 2.5 year old children is 2.4-fold higher than for adults (EC 2002, chapter 2.3.1, Page 20, paragraph 1).

⇒ On a per kg body weight basis, the daily intake of BaP as well as that of all PAH decreases with increasing age. The youngest age group (1.5 - 2.5 years) had the highest exposure, about 2.4-fold higher than adults (EC 2002, chapter 2.3.1, Page 21, table 2.3.2).

1.5 - 2.5 year old toddlers had an average intake of BaP of 3.8 ng/kg bw/day and all PAH (PAH-19) of 166 ng/kg bw/day. High level intake for this age group was at 6.2 ng/kg bw/day and all PAH of 276 ng/kg bw/day.

Table 5-7: Estimate of dietary exposure to different PAHs by age group (ng/kg bw/day)
(EC 2002, chapter 2.3.3, Page 17-18, table 2.3.1)

Table 2.3.2 Dietary intakes of PAH for consumers of different age in UK (ng/kg bw/day). [a,b]

	Average intake									High level (97.5th percentile) intake							
		Schoolchildren			Toddlers					Schoolchildren			Toddlers				
		Age range (years)								Age range (years)							
PAH	Adults	15-18	11-14	7-10	4-6	3.5-4.5	2.5-3.5	1.5-2.5	1.5-2.5/ adults [d]	Adults	15-18	11-14	7-10	4-6	3.5-4.5	2.5-3.5	1.5-2.5	1.5-2.5/ adults [d]
Acenaphthylene	2.0	1.7	2.1	2.9	3.8	3.8	4.0	4.4	2.2	3.5	3.0	3.9	5.1	6.3	6.4	6.9	8.2	2.3
Acenaphthene	14	12	15	22	27	27	28	31	2.2	23	21	25	33	40	42	46	52	2.3
Fluorene	8	7.5	9.3	13	17	17	18	20	2.5	14	12	16	20	25	26	29	33	2.4
Anthracene	1.2	1.1	1.4	1.9	2.4	2.4	2.5	2.6	2.2	2.0	1.8	2.4	2.9	3.6	3.6	3.9	4.5	2.3
Phenanthrene	22	21	27	39	49	50	53	56	2.5	39	36	46	59	74	76	83	94	2.4
Fluoranthene	5.0	4.5	5.9	8.4	11	11	12	12	2.4	8.5	7.8	10	13	16	17	18	21	2.5
Pyrene	5.0	4.7	6.1	8.8	11	11	12	13	2.6	8.6	8.0	10	14	16	17	19	21	2.4
Cyclopenta[cd]pyrene	0.4	0.4	0.5	0.8	1.0	0.9	1.0	1.1	2.8	0.8	0.8	0.9	1.2	1.4	1.4	1.6	1.8	2.3
Benz[a]anthracene	0.8	0.8	1.0	1.4	1.7	1.7	1.8	1.8	2.3	1.4	1.4	1.6	2.2	2.6	2.5	2.8	3.1	2.2
Chrysene	1.6	1.4	1.8	2.6	3.3	3.2	3.3	3.5	2.2	2.7	2.6	3.0	3.9	4.8	4.8	5.2	5.9	2.2
Benzo[b]fluoranthene	1.5	1.4	1.7	2.5	3.2	3.0	3.3	3.6	2.4	2.6	2.4	2.9	3.8	4.8	4.6	5.2	6.0	2.3
Benzo[k]fluoranthene	1.3	1.2	1.4	2.1	2.7	2.6	2.8	3.2	2.5	2.2	2.0	2.5	3.3	4.3	3.9	4.7	5.4	2.5
Benzo[a]pyrene	1.6	1.4	1.8	2.6	3.3	3.1	3.4	3.8	2.4	2.7	2.5	3.0	4.0	5.0	4.8	5.4	6.2	2.3
Benzo[e]pyrene	0.8	0.7	0.9	1.3	1.7	1.6	1.7	1.8	2.3	1.4	1.3	1.6	2.1	2.5	2.5	2.7	3.0	2.1
Anthanthrene	0.3	0.3	0.3	0.5	0.6	0.6	0.7	0.8	2.7	0.5	0.5	0.6	0.8	1.0	0.9	1.1	1.3	2.6
Benzo[ghi]perylene	0.9	0.8	1.1	1.5	1.9	1.8	1.9	2.0	2.2	1.5	1.5	1.7	2.4	2.8	2.8	3.2	3.6	2.4
Indeno[1,2,3-cd]pyrene	1.4	1.3	1.6	2.2	2.9	2.8	3.0	3.4	2.4	2.4	2.2	2.6	3.6	4.5	4.3	4.9	5.8	2.4
Dibenz[a,h]anthracene	0.5	0.5	0.6	0.9	1.1	1.0	1.1	1.2	2.4	0.9	0.9	1.0	1.4	1.8	1.6	1.8	2.1	2.3
Sum of 19 PAHs [c]	69	63	80	115	145	146	155	166	2.4	116	106	131	172	208	217	236	276	2.4
mean									2.4									2.3

From: COT, 2002.

[a] Upper-bound estimates (i.e., by assuming 'not detected' values to be equal to the limit of detection).

[b] Years of consumption surveys: adults, 1986-87; schoolchildren, 1998; toddlers, 1992-93.

[c] PAHs are those listed in this table + benzo[b]naphto[2,1-d]thiophene.

[d] Ratio of the intake of age range 1.5-2.5 to that of adults.

5.5.2 Innere Exposition

For PAHs, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

The absolute oral bioavailability of PAH from soil is not directly available for humans. The absorption rate after oral exposure to food/water is poorly characterized, in particular in human studies (section 5.5.2.1), but some data suggest that it may be >90% for some PAH, incl. BaP. Therefore, SCAHT uses a conservative oral bioavailability from food of 100% for its assessment.

The Relative Oral Adjustment Factor (RAF) approach can be used to estimate the absolute oral bioavailability from soil. SCAHT proposes three approaches/scenarios to the use of the RAF, with consideration of the reliability and relevance of the underlying human (section 5.5.2.2) and animal (section 5.5.2.3) soil ingestion studies. No data were found for humans. The animal data show a broad range of relative bioavailability values for soils (<1-100%).

Therefore as a conservative approach, SCAHT applies a default RAF-value of 100% (*scenario 1*). Another approach is to use a RAF value of 50% (*scenario 2*) or of 29% (*scenario 3*), as already applied for health risk assessment purposes by several US State EPA Agencies. Using a lower RAF value is fairly well supported by the in vivo soil ingestion experimental studies (section 5.5.2.4).

All three approaches present uncertainties. While a RAF of 100% appears to be too conservative, the relevance of the RAF of 29% is uncertain, because the rat model used in the key study by Magee et al. (1996) is considered non physiologically relevant to humans, whereas no justification for using the RAF of 50% could be found. However, considering the range of relative bioavailabilities reported in vivo in soil ingestion experimental studies, using a RAF value of 50% might appear a more realistic compromise, yet entailed to a higer uncertainty.

In vitro studies which estimate the bioaccessbility of PAH from soil are available, but their reliability is considered to be insufficient to support the use of a RAF factor below 100% (section 5.5.2.5).

5.5.2.1 Oral bioavailability from food and/or water from dietary studies

PAHs are generally well absorbed orally and tend to be widely distributed to fatty tissues. Toxikokinetic data in rats suggest that the oral bioavailability of PAH from food will be in the range of 20-50% and that it increases with increasing content of lipophilic components in the food (SCF 2002, chapter 2.1.1, page A-53). A review by Ramesh et al. (2004) of the bioavailability of various orally ingested PAHs showed a range between 6-100%, depending on the dose, vehicle, and animal species. Additionally, bioavailability varies among individual PAH compounds. For example, phenanthrene bioavailability (86%), measured using an in vivo swine model, is greater than BaP bioavailability (31%) (Cavret et al., 2003). Ramesh et al. (2004) also reported bioavailability values up to >90% for several PAHs incl. BaP in rodents following administration of various dietary vehicles; based on human dietary studies, Ramesh et al. reported 90-99% absorption values for BaP and pyrene. This is also in line with a review by Magee et al. (1996) who suggested that bioavailability in humans may be complete following dietary exposure (e.g. as high as 98% for BaP), depending on the individual PAH compound and the type of food.

⇒ **Data are limited, in particular for humans, and contradictory results for rats have been reported (range: 20-90%); they suggest however that a fairly high absorption rate following oral exposure is possible for humans. Therefore SCAHT assumes a conservative oral bioavailability from food of 100%.**

5.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies and other sources in humans

No soil ingestion studies have been located in humans in the literature. Some data are available for dermal and inhalation absorption. Dermal absorption of PAHs by humans decreased from 24% to less

than 2% when applied in a soil matrix (NEPI 2000, page v). Inhalation is usually considered a minor exposure route due to the low volatility of PAHs, however inhaled particles can be removed from the lungs by mucocilliary clearance and swallowed, therefore soil-bound PAHs which are initially inhaled may contribute to the oral ingestion route of exposure (NEPI 2000, page 39-40).

5.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

The gastrointestinal absorption of PAH from contaminated soils has been reported in a limited number of in vivo studies in experimental animals, mainly rodents (e.g. Goon et al., 1991; Koganti et al., 1998; Magee et al., 1999; Stroo et al., 1999 reviewed *in* NEPI 2000, pp. 34-36). In general, available data show that there is a clear reduction in the *in vivo* bioavailability of PAHs when bound to soil. For example, Goon et al. (1991) reported that it can be as low as 34% when the PAHs have been in contact with the soil for a period of six months. In a recent review of the literature, Ruby et al (2016) reported that existing studies provide a strong basis for establishing that oral bioavailability of PAHs from soil is less than from diet, and an assumption of 100% relative bioavailability likely overestimates exposure to PAHs upon ingestion of PAH-contaminated soil. They conclude from the available literature that the oral bioavailability studies do not provide a broad understanding of how different PAH source materials, PAH concentrations, or soil chemistries influence the absorption of carcinogenic PAHs from soil.

- Goon et al. (1991) evaluated the effects of “aged” soil on BaP bioavailability in rats after administration by gavage of [14C]radiolabelled-BaP alone or absorbed to soil. At ageing times of 1-30 days BaP oral bioavailability was 44-53% and 61-64% for clay- and sandy soils, respectively, but for soils aged for 6 months it was lowered to 34% and 51%, respectively.
- Koganti et al. (1998) fed mice diets containing soil or organic extracts of four soil for two weeks and reported bioavailability estimates ranging from 9-75% based on 1-hydroxypyrene excretion and non-detectable to 76% when based on DNA adduct formation.
- Magee et al. (1999) fed mice diets containing soil or organic extracts of four soil for two weeks; based on the quantification of DNA adducts in the lungs and 3-hydroxyBaP urinary excretion in urine, they reported PAH bioavailability of 7-29% and 7-36%, respectively.
- Stroo et al. (2000) measured the uptake of phenanthrene, pyrene, chrysene, and BaP in rats following a one-time gavage and a 5-day feeding. In general, pure hydrocarbons and hydrocarbons freshly spiked onto soil were well-absorbed (90%) from the gastrointestinal tract. Absorption was reduced with treated soil (60%) and was considerably lower for PAH present on lamp black (25-50%).
- Recent studies of benzo(a)pyrene in soils gave relative bioavailabilities in minipigs of 14-39% (4 soils), respectively (DEPA 2003, citing Hack et al 2002).
- Roberts et al (2016) measured BaP bioavailability in rat following exposure to contaminated soil from three source materials: solvent (ca. 50%) soot (ca. 50%), and fuel oil (ca. 86%) to which BaP was added in a mixture of PAHs.
- Peters et al. (2016) used juvenile swine to model human exposure BaP and anthracene in certified reference material, spiked soil, spiked food, or spiked corn oil after one and seven days of dosing. Average BaP bioavailability for certified reference material, spiked soil, spiked food and corn oil was 71%, 0.72%, 0.03% and 0.97% respectively. Average anthracene bioavailability was 1.7% and 43% for corn oil and certified reference material, respectively. Anthracene was not detected above background in swine exposed to spiked food and spiked soil. Their results indicate that exposure media impacts bioavailability, but there is no statistical evidence that sub-chronic exposure affects systemic exposure.

5.5.2.4 Three scenarios for using the Relative Oral Absorption Factor (RAF) approach

One possible way to estimate the relative bioavailability of PAHs in soil compared to food or water, is to use the RAF approach proposed by the USEPA, as outlined in the Methodology section. RAF default medium-specific values have been proposed for PAHs (NRC 2003, Table 2.1 pp.69-70) (see **Table 5-8**).

In a literature review, Magee et al. (1996) identified adjustment factors for relative bioavailability for PAHs from soil and sediments of 29% and some US regulatory bodies (Massachussets Department of Environmental Protection, EPA Ohio and EPA Region 5) have applied this value for use in Human Health Risk Assessment (NRC 2003, pp. 86-87, Table 2-4). However, the RAF proposed by Magee et al. (1996) has been established based on *in vivo* rat studies, which are less physiologically relevant to humans than the juvenile swine model (which is considered the "gold standard").

1) In its initial assessment approach, SCAHT is using a RAF of 100%. Since SCAHT assumes a conservative default absolute oral bioavailability from foodstuffs, the absolute oral bioavailability from soil is 100%. This is line with NRC (2003). Given that in vivo studies demonstrate that the type of PAH source material can have a strong influence on PAH oral bioavailability, and that bioavailability following soil ingestion is likely to be reduced. Most of these studies however were established in rodents, which are less physiologically relevant than the juvenile swine model. This approach of a RAF value of 100% however may be over-conservative (scenario 1).
2) According to NRC (2003), another RAF value of 50% (scenario 2) has been used for semivolatile organic compounds (SVOCs) PAH for risk assessment by the US Michigan Department of Environmental Quality. However, the reasoning behind this approach is not given (personnal communication, as cited by NRC 2003).
3) An alternative approach would be to use a lower RAF. According to NRC, a RAF value of 29% has been used for human helath risk assessment purposes at Superfund Sites by various EPA State Agencies (Massachussetts, Ohio, EPA Region 5) based on Magee et al. (1996). In such a case, this would result to an absolute oral bioavailability from soil of 29% (scenario 3). However, the human relevance of the Magee study can be questioned.

⇒ **All three approaches present uncertainties. While a RAF of 100% appears to be too conservative, the relevance of the RAF of 29% is uncertain, whereas the justification for using a RAF of 50% is not made explicit. However, considering the range of relative bioavailabilities reported in vivo in soil ingestion experimental studies, using a RAF value of 50% might appear a more realistic compromise, yet entailed to a higer uncertainty.**

5.5.2.5 Summary of the in vitro bioaccessibility information

PAHs in soil exist predominantly as soil-bound species with very little transfer to the soil pore water or air phases, suggesting reduced mobility and availability. It has been shown that the bioaccessibility from soil will be reduced depending on the soil type, the interaction of soil organic matter, ageing and the extent of microbial degradation in soil (NEPI 2000, page v).

A broad range of values are found in the literature for *in vitro* "bioaccessibility" studies using surrogate test systems (e.g. Simplified Bioaccessibility Extraction Test, SBET or Physiologically Based Extraction Test, PBET) to estimate the bioaccessible PAH fraction from soil that is readily available for systemic absorption:

- Using a PBET system, Hack et al. (1996) found a bioaccessibility of soil-bound PAHs from 22 soils ranging from 7 to 95% (as reported in NEPI 2000, p. 58).

- James et al (2011) reported bioaccessibility of soil PAHs between 6-100%. Lower PAH values were associated with fasted conditions were employed in two models (Relative Bioaccessibility Leaching Procedure, RBALP, and in vitro digestion model, IVD
- The Danish EPA has identified bioaccessibility values between 10 and 90% for stomach and intestines (DEPA 2003, page 60, Table 7.4).
- The US NRC (2003) discussed the relevance and applicability of *in vitro* extraction systems and concluded that in general the more thorough extraction tests gave bioaccessibility results of 20-60% for PAHs from soils and solid wastes (NRC 2003, page 267).

Table 5-8 : Absolute and relative bioavailabilities for PAHs

PAH[a]	Oral bioavailability[b]	Absolute dermal Bioavailability from soil[c]	Relative Oral Bioavailability from soil[d]	Absolute oral bioavailability from soil[e]
Pyrene	suggested default 100%	10-18%	91% [f]	suggested default 100%
Acenaphthene		10-20%	100% [f]	
Anthracene		10-29%	91% [f]	
Benzo(ghi)perylene		10-18%	91% [f]	
Flouranthene		10-20%	100% [f]	
Fluorene		10-20%	100% [f]	
1-Methylnaphthalene		10%	100% [f]	
2-Methylnaphthalene		10%	100% [f]	
Naphthalene		10%	100% [f]	
Phenanthrene		10-18%	91% [f]	
Benzo(a)anthracene		10-18%	91% [f]	
Benzo(a)pyrene		10-18%	91% [f]	
Benzo(b)fluoranthene		10-18%	91% [f]	
Dibenz(a,h)anthracene		10-18%	91% [f]	
Indeno(123,cd)pyrene		10-20%	91% [f]	
Polycyclic Aromatic Hydrocarbons (semi-volatile organic compounds) [g]		1-15%	50% [h]	suggested default 50%

[a] List of PAHS according to NRC 2003, pp.69-70, table 2-1).

[b] SCAHT suggests a conservative default 100% oral bioavaiability, based on evidence from human and experimental animal studies.

[c] Absolute bioavailability of the compound in soil via the dermal route (NRC 2003, pp. 69-70, table 2-1).

[d] Relative absorption factor, equals the relative bioavailability of the compound (i.e. in soil vs in the medium used in the toxicity study) (NRC 2003, pp.69-70, table 2-1).

[e] The absolute oral bioavailability from soil is calculated based on the oral bioavailability adjusted by the relative oral absorption factor to account for reduced oral bioavailabilty from soil. SCAHT uses a conservatice default absolute oral bioavailability o PAHs in soil of 100%.

[f] Proposed State value by the Massachusetts Department of Environmental Protection (as cited in NRC 2003).

[g] Semivolatile organic compounds (SVOCs) have vapor pressures between 10^{-2} and 10^{-5} kPa; semi-volatile PAHs as defined by USEPA methods 8270, 525 and 625 are: fluorene, phenantrene, anthracene, fluoranthene, benzo(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(a)pyrene, indeno(123,cd)pyrene, dibenz(a,h)anthracene, benzo(ghi)perylene (*www.restek.com/pdfs/59411B.pdf)*

[h] Proposed State value by the Michigan Department of Environmental Quality (as cited in NRC 2003, pp.69-70, table 2-1). NRC further specifies that *"Michigan has set default relative bioavailability values by compound class for both oral and dermal exposures that are lower than EPA default values or any other state and are based primarily on the best professional judgment of Michigan Department of Environmental Quality scientists"* (NRC 2003, p.102).

5.6 Risikoabschätzung

The most critical health effect of PAH in humans is carcinogenicity. In its human health risk assessment arising from ingestion of PAH-contaminated soils the SCAHT has, therefore, focused on neoplastic leasions. Non-neoplastic effects have not been considered because it is assumed that thresholds for non-neoplastic effects will be clearly higher than the range of DMELs for neoplastic lesions. This is a generally accepted approach also used by official authorities (see also Deutschland 2010, page 52 for a similar approach).

- The threshold value for PAH-16 in the Swiss Contaminated Sites Ordinance (CSO) is set at 100 mg/kg soil. Therefore a child that ingests 250 mg of contaminated soil per day would be exposed 2 µg/kg bw/day assuming a body weight of 12.5 kg and a bioavailability of 100%.
- It should be noted that the use of the less conservative alternative scearios S2 and S3 would still require a reduction in the same order of magnitude.
- The threshold value for BaP in the Swiss CSO is set at 10 mg/kg soil. Therefore under the given risk assessment scenario exposure would be ten times lower than for the sum of PAH-16 (0.2 µg/kg bw/day assuming a bioaccessibility of 100%).

BUWAL describes the derivation of clean up values for PAHs based on indirect exposure pathways from soil and plants (BUWAL 1998, chapter 11.2, page 95). The former EU Scientific Committee on Food (SCF) gives another possible explanation for the ten-fold lower threshold value for BaP alone compared to PAH-16 in its dietary risk assessment for PAHs (EC 2002); it was concluded that a conservative estimate implied that the carcinogenic potency of total PAHs in food would be 10 times higher than expected from BaP alone.

In the absence of oral toxicity threshold values for PAH-16 the exposure from contaminated soil can be compared to the EFSA derived $BMDL_{10}$ values for oral toxicity of PAH-8 listed in **Table 5-3**. The comparison illustrates that exposure from ingestion of soil PAH-16 is low compared to the $BMDL_{10}$ value for PAH-8 which is associated with a 10% increase in cancer risk. The margin of exposure (MOE) is 245. For BaP alone a comparison of the $BMDL_{10}$ value would result in a MOE of 350 (see **Table 5-9**).

Table 5-9: Comparative overview of Margins of Exposure for BaP, PAH-8 and PAH-19

Comparison of the most recent EFSA-derived $BMDL_{10}$ values[6] for oral toxicity of BaP and PAH-8 with exposure from daily direct soil ingestion of soils contaminated with 100 mg/kg soil PAH-16, and 10 mg/kg soil PAH-16 respectively, and dietary exposure estimates for toddlers based on data in **Table 5-7**.

Group	Oral $BMDL_{10}$ (µg/kg bw/d)	Soil exposure (µg/kg bw/d)	Dietary exposure (µg/kg bw/d)	MOE BMDL/combined exposure
BaP	70	0.2 (BaP)	0.0038 – 0.0062	≈ 350
PAH-8 [a]	490	2 (PAH-16)	-	= 245 (soil exposure only)
PAH-19 [b]	490	2 (PAH-16)	0.166 - 0.276	≈ 220

[a] BaP, benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[ghi]perylene, chrysene, dibenz[a,h]anthra- cene, indeno[1,2,3-cd]pyrene.

[6] The scientific committee on food of the European commission (SCF) has performed a dietary risk assessment for PAHs in 2002, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) re-evaluated PAHs in 2005. A summary of the results can be accessed at https://www.reading.ac.uk/web/FILES/shes/CRETON.pdf.

[b] SCAHT assumes PAH-19 (see **Table 5-7)** is the best proxy for PAH-16, for which no dietary exposure assessment has been located. In the absence of BMDL values for PAH-16 or PAH-19, SCAHT further assumes that the oral BMDL for PAH-8 is the best proxy for PAH-19.

A comparison of the dietary exposure estimates for the youngest age group of the UK study (**Table 5-7**) and the SCAHT exposure estimate from soil ingestion reveals that soil exposure is the major route of exposure for small children with soil ingestion being several orders of magnitude higher than dietary exposure. The combined exposure from food and soil ingestion is not exceeding the EFSA-derived $BMDL_{10}$ values for oral toxicity. In the UK study (**Table 5-7**) dietary exposure estimates are consistently lower compared to the median EU levels (**Table 5-6**). Still the combined exposure from the higher EU median food intake and soil ingestion would not exceed the EFSA-derived $BMDL_{10}$ – values for oral toxicity. Calculating MOEs by dividing the lowest $BMDL_{10}$ values by the combined oral exposure from food and soil results in MOE well below 10'000 which, as proposed by the EFSA indicates a potential concern for consumer health and a possible need for risk management action (EFSA 2008, chapter 9, page 90 last sentence).

⇒ **Therefore the SCAHT recommends reconsidering the existing threshold values for BaP and PAH-16.**

The fact that the overall oral background exposure does not exceed the EFSA-derived oral $BMDL_{10}$ indicates a low additional health risk but under the discussed soil ingestion scenario, soil ingestion creates a massive additional exposure compared to the dietary background exposure.

Furthermore the EFSA-derived $BMDL_{10}$ is not risk free but already associated with a 10% increase in cancer risk. With respect to carcinogenicity children have to be considered a particularly sensitive sub-population both, in terms of an inherent greater sensitivity and their longer remaining life-span which is increasing the statistical risk for the development of cancer following exposure towards PAHs (Deutschland 2010, page 18, last paragraph).

To achieve the EFSA recommended minimal-MOE for carcinogens of >10000 soil clean up values have to be reduced by roughly 45-times for PAH-16 and by 29-times for BaP. This would result in new clean-up values of 2.1 mg/kg soil for PAH-16 and 0.3 mg/kg soil for BaP. These recommendations were derived based on MOEs initially calculated for exposures listed in **Table 5-8**.

- For example to increase MOE for BaP from 350 to 10000, exposure has to be reduced by a factor of 29 (29 = 10000/350). If for simplicity we assume that dietary exposure is negligible, because it is far lower than soil exposure, soil exposure must be reduced by a factor of 29 and the BaP soil clean up value must be reduced by a factor of 29 to 0.3 mg/kg soil.
- Similarly to increase MOE for PAH-16 from 220 to 10000, exposure has to be reduced by a factor of 45 (45 = 10000/220) and the PAH-16 soil clean up value must be reduced by a factor of 45 to 2.2 mg/kg soil. Here we assume that the BMDL established for PAH-8 is also valid for PAH-19 for which we have dietary exposure values. We also assume that exposure values for PAH-19 is a good proxy for PAH-16.

Further support for a reduction in clean-up values comes from e.g. Augusto et al. (2012) who argues that inhalation of resuspended soil particles present a major exposure pathway for PAHs. The SCAHT could not verify the robustness of the study and could not yet identify data to support an impact assessment for this exposure pathway but in principle this could be an exposure pathway. Furthermore as outlined in **Table 5-4** the DMELs for dermal toxicity are several orders of magnitude lower compared to $BMDLs_{10}$ for oral toxicity (**Table 5-3**), but dermal toxicity of PAH has not been the focus of this first tier risk assessment.

5.6.1 Which PAHs to prioritize for human health risk assessment?

Concern exists that the USEPA-16 list may not cover the most representative and useful compounds for risk assessment (Andersson and Achten, 2015; Keith LH, 2015). Three groups of polycyclic aromatic compounds are missing: larger and highly relevant PAHs, alkylated polycyclic aromatic compounds, and compounds containing heteroatoms. As a result, future research should focus on a better understanding of the toxicity, occurrence in the environment and chemical analysis, particularly of alkylated PAHs, higher molecular weight PAHs and substituted polycyclic aromatic compounds (amino-PAHs, cyano-PAHs). Alternative and updated lists have been proposed for practical use in the future such as (Andersson and Achten, 2015):

- a list of PAHs (including the 16 EPA PAHs) for the evaluation of ecological toxicity (40 EnvPAHs);
- a list of 23 NSO-heterocyclic compounds and 6 heterocyclic metabolites;
- lists including 10 oxy-PAHs and 10 nitro-PAHs.

5.6.1.1 The position of BfR and EFSA

The BfR argues that for consumer protection the focus should be on those PAH-8 which are explicitly known and legally classified as genotoxic carcinogens in Annex VI to Reg. No. 1272/2008 (CLP regulation (Deutschland 2010, chapter B. 1.4, page 34, paragraph 1), considering that that these eight PAH compounds (BfR PAH-8) exert their carcinogenic action by the same or (a) similar mechanism(s), albeit at different potencies and their action has therefore to be considered as being additive (Deutschland 2010, chapter B. 1.4, page 34, paragraph 1). Although consumers will often be exposed to many or even all of the PAH congeners it is assumed that by setting limits for both, BaP and the sum of all of the eight known carcinogenic congeners in a 'surrogate approach', a good part of the variability in the mixture composition is covered (Deutschland 2010, chapter B. 1.4, page 34, paragraph 4). The ‘surrogate’ approach takes BaP as a representative surrogate of the toxicity of the whole PAH mixture. A toxic equivalency factor (TEF) approach to the risk characterisation (like for dioxins) was not considered to be scientifically valid (EC 2002, FAO/WHO 2006, Deutschland 2010) because of the lack of data from oral carcinogenicity studies for different PAHs, their different modes of action and the evidence of poor predictivity of the carcinogenic potency of PAH mixtures based on the currently proposed TEF values (Deutschland 2010, page 48).

The EFSA opinion published in 2008 as a result of a dietary exposure assessment also argues that the focus should be on a limited number of PAH (compared to USEPA PAH-16 list). EFSA concluded that BaP alone is not a suitable indicator for the occurrence and toxicity of PAHs in food. Instead EFSA proposed that eight PAHs (EFSA PAH-8)[7], either individually or in a combination, are currently the only possible indicators of the carcinogenic potency of PAHs in food with EFSA PAH-8 not providing much added value compared to PAH-4 (EFSA 2008, chapter: conclusions, page 97, last paragraph).

5.6.1.2 The position of WHO/IARC and JECFA

WHO/IARC argues that a few polycyclic aromatic hydrocarbons seem to be more potent carcinogens

[7] However the list of PAH-8 defined by EFSA and BfR are not identical. EFSA PAH-8 includes benzo[a]pyrene, benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[ghi]perylene, chrysene, dibenz[a,h]anthracene, indeno[1,2,3-cd]pyrene. In the BfR PAH-8 list benzo[ghi]perylene and indeno[1,2,3-cd]pyrene are replaced by benzo[e]pyrene and benzo[j]fluoranthene (see also tables 5-1 and 5-2).

than benzo(a)pyrene. Of particular concern is dibenzo(a,l)pyrene which seems to be more than ten times more potent than benzo(a)pyrene in rats. IARC recommended that this potent polycyclic aromatic hydrocarbon compound should be measured routinely in the workplace and the environment. Another highly potent polycyclic aromatic hydrocarbon compound is dibenz(a,h)anthracene but it is already included in PAH-8 (Straif 2005, page 932, left column, second paragraph).

JECFA also identified an additional substance, benzo[c]fluorene, as a priority substance because it may contribute significantly to the formation of lung tumours after oral exposure to coal tar based on a much higher number of adducts than BaP (FAO/WHO 2006).

⇒ **In conclusion, the SCAHT also recommends reviewing whether or not the existing list of PAH-16 in the Swiss CSO is most appropriate to meet the risk management goals.**

⇒ **The SCAHT would recommend to keep monitoring the existing PAH-16 to allow comparison with historical data but to expand the list to cover dibenzo(a,l)pyren (CAS-191-30-0), benzo(c)fluoren (CAS 205-12-9), benzo[e]pyren (CAS 192-97-2), benzo[j]fluoranthen (CAS-205-82-3).**

5.7 Grenzwerte im internationalen Vergleich

In the context of remediation of polluted soils the Swiss Altlasten-Verordnung (AltlV 1998) defines clean up values for the sum of the USEPA-16 PAHs list. It is sometimes difficult to directly compare the clean up values (also referred to as remediation values, soil quality guidelines, soil quality standards or criteria, regulatory guidance values in the various existing regulations worldwide) for the sum of the PAH because the selection of the PAH may vary according to different priorities (e. g. Σ16, 10 or 12; Σ carcinogenic PAH only, individual PAH values only), in particular if the primary protection goal is human health and/or the environment (e.g. Carlon 2007; MfE 2011, p.144).

Based on a review of the scientific and regulatory literature in particular national soil remediation regulations in Europe, USA and Canada, it appears that the Swisss clean-up values are quite high for the sum of PAHs and the highest for BaP (refer to **Annex 1**):

Sum of the PAHs

US: not identified for sum of congeners but for individual PAHs (see below); CZ: 280 (Σ12); **CH: 100** (ΣEPA16); A: 50 (not specified); NL: 40 (Σ10); D: 10 (ΣEPA16); I: 10 (Σ10); S: 0.3 (Σ7 carcinogenic PAKs) and 20 (Σ9 non cacinogenic PAKs) (mg/kg dm).

BaP only

CH: 10; CZ: 2; A: 5; D: 4 &; CAN: 0.7; E: 0.2; I: 0.1; USA: 0.015 - 300 (mg/kg dm)

N.B: Jennings (2012b) reported RGV between 0.00018-860 (mg/kg dm) across US.

Other individual PAH: situation in the US

A regulatory guidance value (RGV) for the sum of PAH could not be identified in the US, but for individual PAH. Jennings reviewed RGVs across US juridisctions for 15 out of the 16 PAH on the USEPA-list (i.e. excluding napthalene). Jennnings (2012a) reported that the regulatory guidance values (RGV) used by the USEPA and many U.S. states are *"substantially higher than those applied elsewhere in the world",* and that they *"appear disproportionally in the upper half of the distributions".* Jennings (2012a, 2012b) reported that values for non carcinogenic PAHs and carcinogenic or mutagenic PAHs can differ by a factor of a million or more. For example, guidance values for benzo(g,h,i)perylene range between 0.026 and 380 000 mg/kg soil. Jennings noted: "*Analysis of PAH regulatory guidance values variability leads to several observations. The most obvious is that there is a great deal of variability. Some of this is unavoidable and easily justified, but values that differ by a factor of a million or more imply serious credibility issues. (...) Values that are random over wide ranges lead to questions about the credibility of the methods by which they are derived. (...) Different models, different toxicology data and/or alternative derivation methods also influence regulatory guidance values*" (Jennings 2012a).

Guidance values across U.S. regulatory jurisdictions:

- **non-carcinogenic PAH: acenaphthene (Table 5-10)**: 0.04-37'000; **acenaphthylene**: 0.03-18'000; **anthracene**: 0.14-230'000; **benzo(g,h,i) perylene**: 0.84-380'000; **fluroanthene**: 1.8-46000; **fluorene**: 0.04-27'000; **phenanthrene**: 0.99-99'000; **pyrene**: 0.034-29'000
- **carcinogenic and mutagenic PAH**: **benz(a)anthracene (Table 5-11)**: 0.0027-3'000; **benzo(a)pyrene**: 0.00018-860 **benzo(b)fluoranthene**: 0.016-3'000; **benzo(k)fluoranthene**: 0.00053-10'000; **dibenzo(a,h)anthracene**: 0.00015-300; **chrysene**: 0.4-10'000; **indeno(1,2,3-c,d)pyrene**: 0.0875-190'000 (mg/kg dm).

Table 5-10: US guidance values for 8 non carcinogenic PAHs (Jennings 2012a)

Table 2
Guidance values for noncarcinogenic polycyclic aromatic hydrocarbons from U.S. regulatory jurisdictions (all values in mg/kg).

Regulatory jurisdiction (reference) indicator[a]	Ace	Acy	Ant	BghiP	Fla	Flr	Phe	Pyr
U.S. Environmental Protection Agency (USEPA, 2011d)	3400	–	17,000	–	2300	2300	–	1700
National Oceanic and Atmospheric Admin. (NOAA, 2008)	–	–	–	–	–	–	5	10
Boeing Co., National Aeronautics and Space Admin., Dept. of Energy (Boeing/NASA/DOE, 2009) Table 4, child	–	–	–	–	–	–	23,000	–
(Boeing/NASA/DOE, 2009) Table 6, suburban[a]	–	–	–	–	–	–	17,000	–
(Boeing/NASA/DOE, 2009) Table 6, rural	–	–	–	–	–	–	520	–
Alabama Dept. of Environmental Mgmt. (ADEM, 2001a)	–	–	10.2	–	101	153	–	91.8
Alabama (ADEM, 2001b)	–	–	10.2	11.1	101	153	141	91.8
Alabama (ADEM, 2008)	370	–	220	228	230	270	202	230
Alaska Dept. of Environmental Conservation (ADEC, 2011)	2798	2798	20,566	1399	1865	2347	20,566	1399
Alaska (ADEC, 2009) – arctic	3800	3800	27,800	1900	2500	3200	27,800	1900
Alaska (ADEC, 2009) <40 in. ppt.	2800	2800	20,600	1400	1900	2300	20,600	1400
Alaska (ADEC, 2009) >40 in. ppt.	2300	2300	16,800	1100	1500	1900	16,800	1100
Arizona Administrative Code (ACC, 2009) Appx. A	3700	–	22,000	–	2300	2700	–	2300
Arizona (ACC, 2009) Appx. B	3900	–	20,000	–	2600	2600	–	2000
Arkansas Dept. of Environmental Quality (ADEQ, 2010)	3400	–	17,000	–	2300	2300	–	1700
Colorado Dept. of Public Health and Environment (CDPHE, 2007)	1000	–	1000	–	1000	1000	–	1000
Colorado Dept. of Labor and Employment (CDLE, 2004)	3700	–	18,000	–	2500	2500	–	1800
Connecticut Dept. of Energy and Environmental Protection (CDEEP, 2007)	–	1000	1000	–	1000	1000	1000	1000
Delaware Dept. of Natural Resources and Environmental Control (DDNREC, 1999)	270	–	1000	–	310	300	1000	230
Delaware (DDNREC, 2000)	10,300	–	51,400	–	6900	6900	5100	5100
Florida Dept. of Environmental Protection (FDEP, 2005a,b)	2400	1800	21,000	2500	3200	2600	2200	2400
Georgia Dept. of Natural Resources (GDNR, 2010)	300	130	500	500	500	360	110	500
Hawaii Dept. of Health (HDH, 2009)	140	130	2.5	27	40	130	18	56
Hawaii (HDH, 2000)	18	–	–	–	11	–	–	–
Idaho Administrative Code (IAC, 2011)	52.3	–	1040	–	364	54.8	–	359
Idaho Dept. of Environmental Quality (IDEQ, 2004)	52.3	78	1040	1188	364	54.8	79	359
Illinois Environmental Protection Agency (IEPA, 2011)	–	2300	–	2300	–	–	2300	–
Illinois Administrative Code (IAC, 2010) – Chicago	0.09	0.03	0.25	0.68	2.7	0.1	1.3	1.9
Illinois (IAC, 2010) – metro. areas	0.13	0.07	0.4	1.7	4.1	0.18	2.5	3
Illinois (IAC, 2010) – non-metro. areas	0.04	0.04	0.14	0.84	1.8	0.04	0.99	1.2
Illinois (IAC, 2010) – TACO	4700	–	23,000	–	3100	3100	–	2300
Indiana Dept. of Environmental Mgmt. (IDEM, 2009)	9500	1100	47,000	–	6300	6300	470	470
Iowa Dept. of Natural Resources (IDNR undated)	3400	1700	17,000	170	2300	2300	1700	1700
Kansas Dept. of Health and Environment (KDHE, 2010)	3420	–	18,000	–	2440	2360	–	1830
Kentucky Energy and Environment Cabinet (KEEC, 2011a)	10	10	10	10	10	10	10	10
Kentucky (KEEC, 2011b; USEPAIX, 2002)	3700	–	22,000	–	2300	2700	–	2300
Louisiana Dept. of Environmental Quality (LDEQ, 2003)	370	350	2200	–	220	280	2100	230
Maine Dept. of Environmental Protection (MDEP, 2009a)	3400	–	17,000	–	2300	2300	–	1700
Maine (MDEP, 2010) – Appx. I	4800	5100	22,000	3700	5000	4100	3500	3700
Maine (MDEP, 2010) – Appx. II	970	1000	4300	750	1000	830	700	750
Maine (MDEP, 2009b)	110	130	430	750	1000	200	470	750
Maryland Dept. of the Environment (MDE, 2008)	470	470	2300	230	310	310	2300	230
Maryland (MDE, 2003)	469	469	2346	235	313	313	2346	235
Massachusetts Dept. of Environmental Protection (MaDEP, 2009) M1-S1-GW3	1000	10	1000	1000	1000	1000	500	1000
Massachusetts (MaDEP, 2009) M1-S2-GW3	3000	10	3000	3000	3000	3000	1000	3000
Massachusetts (MaDEP, 2009) M1-S3-GW3	5000	10	5000	5000	5000	5000	3000	5000
Massachusetts (MaDEP, 2009) M2-S1-direct	1000	1000	1000	1000	1000	1000	500	1000
Massachusetts (MaDEP, 2009) M2-S2-direct	3000	3000	3000	3000	3000	3000	1000	3000
Massachusetts (MaDEP, 2009) M2-S -direct	5000	5000	5000	5000	5000	5000	3000	5000
Massachusetts (MaDEP, 2009) M3	10,000	10,000	10,000	10,000	10,000	10,000	10,000	10,000
Michigan Dept. of Environmental Quality (MDEQ, 2011)	41,000	1600	230,000	2500	46,000	27,000	1600	29,000
Minnesota Pollution Control Agency (MPCA, 2009)	1200	–	7880	–	1080	850	–	890
Mississippi Dept. of Environmental Quality (MDEQ, 2002)	4690	4690	23,500	2350	3130	3130	2350	2350
Missouri Dept. of Natural Resources (MDNR, 2011) Table 3-1	209	–	3140	–	1190	217	–	715
Missouri (MDNR, 2011) Table 7-1(a), sand	627	–	3140	–	1190	422	–	751
Missouri (MDNR, 2011) Table 7-2(a), silt	630	–	3150	–	1190	423	–	751
Missouri (MDNR, 2011) Table 7-3(a), clay	632	–	3160	–	1190	424	–	751
Missouri (MDNR, 2010) Table B-2, sand	3130	4180	15,700	1720	2280	2200	2170	1710
Missouri (MDNR, 2010) Table B-3, silt	3210	4310	16,100	1720	2280	2220	2220	1710
Missouri (MDNR, 2010) Table B-4, clay	3260	4390	16,400	1720	2280	2240	2250	1710
Montana Dept. of Environmental Quality (MDEQ, 2009)	400	–	2000	–	300	300	–	200
Nebraska Dept. of Environmental Quality (NDEQ, 2006)	1200	–	5900	–	570	780	–	590
Nevada Division of Environmental Protection (NDEP, 2009)	570	–	12,000	–	2300	560	–	1700
New Hampshire Code of Admin. Rules (NHCAR, 2008)	340	490	1000	960	960	77	960	720
New Hampshire Dept. of Environmental Services (NHDES, 2007)	1400	1400	7200	960	960	960	960	720
New Jersey Dept. of Environmental Protection (NJDEP, 2009)	3400	–	17,000	380,000	2300	2300	–	1700
New Jersey (NJDEP, 2008)	3400	–	10,000	–	2300	2300	–	1700
New Mexico Environmental Dept. (NMED, 2009)	3440	–	17,200	–	2290	2290	1830	1700
New York (NYDEC, 2010) Table 3	20	100	100	100	100	30	100	100
New York (NYDEC, 2010) Table 375-6.8(a)	20	100	100	100	100	30	100	100
New York (NYDEC, 2010) Table 375-6.8 (b) res.	100	100	100	100	100	100	100	100
New York (NYDEC, 2010) Table 375-6.8(b) restricted res.	100	100	100	100	100	100	100	100
North Carolina Dept. of Environment and Natural Resources (NCDENR, 2005)	8.16	11.4	995	6720	276	44.3	59.6	1.71

Table 2 (*continued*)

Regulatory jurisdiction (reference) indicator[a]	Ace	Acy	Ant	BghiP	Fla	Flr	Phe	Pyr
North Carolina (NCDENR, 2011)	680	–	3400	–	460	460	–	0.034
North Carolina (NCDENR, 2010)	940	469	4600	469	620	620	469	469
Ohio Administrative Code (OAC, 2009)	3500	–	18,000	–	2400	2400	–	1800
Ohio Environmental Protection Agency (OEPA, undated) adult – NC	20,000	–	10,000	9900	13,000	13,000	99,000	10,000
Ohio (OEPA, undated) child – NC	3500	–	18,000	1800	2400	2400	18,000	1800
Ohio (OEPA, 2005; USEPA, 2011d)	3400	–	17,000	–	2300	2300	–	1700
Ohio (OEPA, 2009; USEPA, 2011d)	340	–	1700	–	230	230	–	170
Oklahoma Dept. of Environmental Quality (OkDEQ, 2007; USEPA, 2011d)	3400	–	17,000	–	2300	2300	–	1700
Oregon Dept. of Environmental Quality (OrDEQ, 2009) res.	4700	–	23,000	–	2300	3100	–	1700
Oregon (OrDEQ, 2009) urban res.	9400	–	47,000	–	4600	6300	–	3400
Oregon (OrDEQ, 2005) acceptable	3700	–	22,000	–	2300	2700	–	2300
Oregon (OrDEQ, 2005) hot spot	37,000	–	100,000	–	23,000	27,000	–	23,000
Pennsylvania Dept. of Environmental Protection (PDEP, 2011a) 100 × GW	380	1600	6.6	0.026	26	190	110	13
Pennsylvania (PDEP, 2011a) generic	4700	18,000	350	180	3200	3800	10,000	2200
Pennsylvania (PDEP, 2011b) standard	–	–	350	180	–	3000	10,000	2200
Pennsylvania (PDEP, 2011b) action level	–	–	–	–	–	3800	–	–
Rhode Island Dept. of Environmental Management (RIDEM, 2004)	43	23	35	0.8	20	28	40	13
Tennessee Department of Environment and Conservation (TDEC, 2001; USEPA, 2011d)	3400	–	17,000	–	2300	2300	–	1700
Texas (TCEQ, 2011a) 0.5 A, N-C	3000	3800	18,000	1800	2300	2300	1700	1700
Texas (TCEQ, 2011a) 30 A, N-C	3000	3800	18,000	1800	2300	2300	1700	1700
Texas (TCEQ, 2011b) NC	4900	4900	25,000	2500	3300	3300	2500	2500
Texas (TCEQ, 2006a)	–	8200	41,000	4100	5500	5500	4100	4100
Texas TCEQ 2006b)	820	820	4100	410	550	550	410	410
Vermont Dept. of Environmental Conservation (VDEC undated a, USEPA, 2011d)	3400	–	17,000	–	2300	2300	–	1700
Vermont (VDEC undated b)	3400	–	17,000	–	2300	2300	–	1700
Virginia Dept. of Environmental Quality (VDEQ, 2009)	189	133	1700	170	230	230	170	170
Washington Dept. of Ecology (WDOC, 2011) C	–	–	–	–	–	–	–	2400
Washington (WDOC, 2011) NC	4800	–	24,000	–	3200	3200	–	–
West Virginia Dept. of Environmental Protection (WVDEP, 2009a)	3700	3800	22,000	1700	2300	2600	22,000	2300
West Virginia (WVDEP, 2009b)	4700	–	23,000	–	3100	3100	–	2300
Wisconsin Dept. of Natural Resources (WNDR, 2002) NC	939	–	4690	–	626	626	–	469
Wisconsin (WNDR, 1997)	900	18	5000	1.8	600	600	18	500
Wyoming Dept. of Environmental Quality (WDEQ, 2009)	3400	–	17,000	–	2300	2300	–	1700
(California) City of Oakland Public Works Agency (COPWA, 2000)	3100	3100	16,000	210	2100	2100	16,000	1600
(California) San Francisco Bay Regional Water Quality Control Board (SFBRWQCB, 2008)	500	340	3100	340	460	390	340	690
(California) Santa Barbara County Fire Dept. (SBCFD, 2007)	29	29	590	–	210	28	5	10
(Florida) Code of Miami-Dade County (CMDC, 2008)	2400	1800	21,000	2500	3200	2600	2200	2400
(New Mexico) City of Santa Fe Springs (CSFS, 2004; USEPA, 2011d)	3400	–	17,000	–	2300	2300	–	1700
(New York) Suffolk County Dept. of Health Services (SCDHS, 2010)	98	–	100	100	100	100	100	100
(New York) New York City (NYC, 2010; NYDEC, 2010) Table 3	20	100	100	100	100	30	100	100
(New York) (NYC, 2010; NYDEC, 2010) Table 375-6.8(a)	20	100	100	100	100	30	100	100
(NYC, 2010; NYDEC, 2010) Table 375-6.8(b) res.	100	100	100	100	100	100	100	100
(NYC, 2010; NYDEC, 2010) Table 375-6.8(b) rest. res.	100	100	100	100	100	100	100	100

[a] Value indicator (if necessary) for sources from which more than one value could have been selected.

Table 5-11: US guidance values for 7 carcinogenic or mutagenic PAHs (Jennings 2012b)

Table 2
Guidance values for carcinogenic or mutagenic polycyclic aromatic hydrocarbons from U.S. regulatory jurisdictions.

U.S. Regulatory Jurisdiction (reference) indicator[a]	BaA	BaP	BbF	BkF	Chr	DBahA	IPyr
U.S. Environmental Protection Agency (USEPA, 2011c)	0.15	0.015	0.15	1.5	15	0.015	0.15
National Oceanic and Atmospheric Admin. (NOAA, 2008)	1	1	1	1	–	1	1
Boeing Co., National Aeronautics and Space Admin., Dept. of Energy (Boeing/NASA/DOE, 2009) Table 4, res.	0.53	0.053	0.53	0.53	–	0.16	–
(Boeing/NASA/DOE, 2009) Table 6, suburban	0.36	0.036	0.36	0.36	–	0.11	–
(Boeing/NASA/DOE, 2009) Table 6, rural	0.0027	0.00018	0.0016	0.00053	–	0.00015	–
Alabama Dept. of Environmental Mgmt. (ADEM, 2001a)	33.7	15.7	18.5	9.84	6.37	–	–
Alabama (ADEM, 2001b)	33.7	15.7	18.5	9.84	6.37	–	–
Alabama (ADEM, 2008)	0.62	0.062	0.62	6.2	62	0.062	0.62
Alaska Dept. of Environmental Conservation (ADEC, 2011)	4.8866	0.4887	4.8866	48.8656	489	0.4887	4.8866
Alaska (ADEC, 2009) – arctic	6.6	0.66	6.6	66	660	0.66	6.6
Alaska (ADEC, 2009) <40 in. ppt.	4.9	0.49	4.9	49	490	0.49	4.9
Alaska (ADEC, 2009) > 40 in. ppt.	4	0.4	4	40	400	0.4	4
Arizona Administrative Code (AAC, 2009) Appx. A	0.69	0.069	0.69	6.9	68	0.069	0.69
Arizona (AAC, 2009) Appx. B	6.1	0.61	6.1	61	610	0.61	6.1
Arkansas Dept. of Environmental Quality (ADEQ, 2010)	0.15	0.015	0.15	1.5	15	0.015	0.15
California Office of Environmental Health Hazard Assessment (COEHHA, 2010)	–	0.038	–	–	–	–	–
Colorado Dept. of Public Health and Environment (CDPHE, 2007)	0.22	0.022	0.22	2.2	22	0.022	0.22
Colorado Dept. of Labor and Employment (CDLE, 2004)	0.61	0.061	0.61	6.1	6.1	0.061	0.61
Connecticut Dept. of Energy and Environmental Protection (CDEEP, 2007)	1	1	1	8.4	–	–	–
Delaware Dept. of Natural Resources and Environmental Control (DDNREC, 1999)	0.9	0.09	0.9	9	87	0.09	0.9
Delaware (DDNREC, 2000)	5.5	0.55	5.5	55	3.5	–	5.5
Florida Dept. of Environmental Protection (FDEP, 2005a,b)	1	0.1	1	10	100	0.1	1
Georgia Dept. of Natural Resources (GDNR, 2011)	0.66	0.66	0.66	0.66	0.66	0.66	0.66
Georgia (GDNR, 2010)	5	1.64	5	5	5	5	5
Hawaii Dept. of Health (HDH, 2009)	1.5	0.15	1.5	15	14	0.15	1.5
Hawaii (HDH, 2000)	–	1	–	–	–	–	–
Idaho Administrative Code (IAC, 2011)	0.422	0.0422	0.422	4.22	33.4	–	–
Idaho Dept. of Environmental Quality (IDEQ, 2004)	0.422	0.0422	0.422	4.22	33.4	0.0422	0.422
Illinois Administrative Code (IAC, 2010) – Chicago	1.1	1.3	1.5	0.99	1.2	0.2	0.86
Illinois (IAC, 2010) – metro. areas	1.8	2.1	2.1	1.7	2.7	0.42	1.6
Illinois (IAC, 2010) – non-metro areas	0.72	0.98	0.7	0.63	1.1	0.15	0.51
Illinois (IAC, 2010) – TACO	0.9	0.09	0.9	9	88	0.09	0.09
Indiana dept. of Environmental Management (IDEM, 2009)	5	0.5	5	50	500	0.5	5
Iowa Dept. of natural Resources (IDNR, undated)	3.1	0.31	3.1	31	310	0.31	3.1
Kansas Dept. of Health and Environment (KDHE, 2010)	10.9	1.09	10.9	109	1090	1.09	10.9
Kentucky Energy and Environment Cabinet (KEEC, 2011a)	0.15	0.3	0.3	0.3	15	0.3	0.3
Kentucky (KEEC, 2011b; USEPAIX, 2002)	0.62	0.062	0.62	6.2	62	0.062	0.62
Kentucky (KEEC, 2011b; USEPAIX, 2002) Cal-modified	–	–	–	0.38	3.8	–	–
Louisiana Dept. of Environmental Quality (LDEQ, 2003)	0.62	0.33	0.62	6.2	62	0.33	0.62
Maine Dept. of Environmental Protection (MDEP, 2009a)	0.15	0.015	0.15	1.5	15	0.015	0.15
Maine (MDEP, 2010) – Appx. I	2.6	0.26	2.6	26	260	0.26	2.6
Maine (MDEP, 2010) – Appx. II	0.26	0.026	0.26	2.6	26	0.026	0.26
Maine (MDEP, 2009b)	0.26	0.026	0.26	2.6	26	0.026	0.26
Maryland Dept. of the Environment (MDE, 2008)	0.22	0.022	0.22	2.2	22	0.022	0.22
Maryland (MDE, 2003)	875	87.5	875	8.7	87.5	87.5	875
Massachusetts Dept. of Environmental Protection (MaDEP, 2009) M1-S1-GW3	7	2	7	70	70	0.7	7
Massachusetts (MaDEP, 2009) M1-S2-GW3	40	4	40	400	400	4	40
Massachusetts (MaDEP, 2009) M1-S3-GW3	300	30	300	3000	3000	30	300
Massachusetts (MaDEP, 2009) M2-S1-direct	7	2	7	70	70	0.7	7
Massachusetts (MaDEP, 2009) M2-S2-direct	40	4	40	400	400	4	40
Massachusetts (MaDEP, 2009) M2-S-direct	300	30	300	3000	3000	30	300
Massachusetts (MaDEP, 2009) M3	3000	300	3000	10,000	10,000	300	3000
Michigan Dept. of Environmental Quality (MDEQ, 2011)	20	2	20	200	2000	2	20
Minnesota Pollution Control Agency (MPCA, 2009)	20	2	20	20	200	3.6	20
Mississippi Dept. of Environmental Quality (MDEQ, 2002)	0.875	0.0875	0.875	8.75	87.5	0.0875	0.875
Missouri Dept. of Natural Resources (MDNR, 2011) Table 3-1	1.84	0.19	1.84	18.4	183	0.184	–
Missouri (MDNR, 2011) Table 7-1(a) – sand	1.84	0.19	1.84	18.4	183	0.184	–
Missouri (MDNR, 2011) Table 7-2(a) – silt	1.84	0.19	1.84	18.4	183	0.184	–
Missouri (MDNR, 2011) Table 7-3(a) – clay	1.84	0.19	1.84	18.4	184	0.184	–
Missouri (MDNR, 2010) Table B-2 – sand	6.2	0.62	6.19	62	599	0.62	3.77
Missouri (MDNR, 2010) Table B-3 – silt	6.2	0.62	6.19	62	605	0.62	3.77
Missouri (MDNR, 2010) Table B-4 – clay	6.2	0.62	6.2	62	608	0.62	3.77
Montana Dept. of Environmental Quality (MDEQ, 2009)	0.2	0.02	0.2	2	20	0.02	0.2
Nebraska Dept. of Environmental Quality (NDEQ, 2006)	0.62	0.062	0.62	0.2	62	0.062	0.62
Nevada Division of Environmental Protection (NDEP, 2009)	0.15	0.015	0.15	1.5	15	0.015	0.15
New Hampshire Code of Admin. Rules (NHCAR, 2008)	1	0.7	1	12	120	0.7	1
New Hampshire Dept. of Environmental Services (NHDES, 2007)	1	0.1	1	12	120	0.1	1
New Jersey Dept. of Environmental Protection (NJDEP, 2009)	0.6	0.2	0.6	6	62	0.2	0.6
New Jersey (NJDEP, 2008)	0.9	0.66	0.9	0.9	9	0.66	0.9
New Mexico Environmental Dept. (NMED, 2009) NSMSSLs	6.21	0.621	6.21	62.1	621	0.621	6.21
New Mexico (NMED, 2006)	6.21	0.621	6.21	62.1	615	0.621	6.21
New York (NYDEC, 2010) Table 3	1	1	1	0.8	1	0.33	0.5
New York (NYDEC, 2010) Table 375-6.8(a)	1	1	1	0.8	1	0.33	0.5

Table 2 (*continued*)

U.S. Regulatory Jurisdiction (reference) indicator[a]	BaA	BaP	BbF	BkF	Chr	DBahA	IPyr
New York (NYDEC, 2010) Table 375-6.8(b) res.	1	1	1	1	1	0.33	0.5
New York (NYDEC, 2010) Table 375-6.8(b) restricted res.	1	1	1	3.9	3.9	0.33	0.5
North Carolina Dept. of Environment and Natural Resources (NCDENR, 2005)	0.343	0.0928	1.18	11.8	38.2	0.172	3.32
North Carolina (NCDENR, 2011)	0.15	0.015	0.15	1.5	15	0.015	0.15
North Carolina (NCDENR, 2010)	0.88	0.088	0.88	9	88	0.088	0.88
Ohio Administrative Code (OAC, 2009)	11	1.1	11	110	1100	1.1	11
Ohio (OEPA, undated) adult – C	18	1.8	18	180	1800	1.8	18
Ohio (OEPA, undated) child – C	11	1.1	11	110	1100	1.1	11
Ohio (OEPA, 2005; USEPA, 2011c) standard	0.15	0.015	0.15	1.5	15	0.015	0.15
Ohio (OEPA, 2005; USEPA, 2011c) adjusted	0.15	0.015	0.15	1.5	15	0.015	0.15
Oklahoma Dept. of Environmental Quality (OkDEQ, 2007; USEPA, 2011c)	0.15	0.015	0.15	1.5	15	0.015	0.15
Oregon Dept. of Environmental Quality (OrDEQ, 2009) res.	0.15	0.015	0.15	1.5	15	0.015	0.15
Oregon (OrDEQ, 2009) urban res.	0.34	0.034	0.34	3.4	34	0.034	0.34
Oregon (OrDEQ, 2005) acceptable	0.62	0.062	0.62	6.2	62	0.062	0.62
Oregon (OrDEQ, 2005) hot spot	62	6.2	62	620	6200	6.2	62
Pennsylvania Dept. of Environmental Protection (PDEP, 2011a) 100xGW	1.1	0.38	0.12	0.055	0.19	0.06	6.2
Pennsylvania (PDEP, 2011a) generic	960	860	170	610	230	270	190,000
Pennsylvania (PDEP, 2011b) standard	5.7	0.57	5.7	–	230	–	5.7
Pennsylvania (PDEP, 2011b) action level	320	46	170	–	–	–	28,000
Rhode Island Dept. of Environmental Mgmt. (RIDEM, 2004)	0.9	0.4	0.9	0.9	0.4	0.4	0.9
South Carolina Dept. of Health and Environmental Control (SCDHEC, 2001)	0.88	–	0.88	8.8	88	0.088	–
Tennessee Department of Environment and Conservation (TDEC, 2001; USEPA, 2011c)	0.15	0.015	0.15	1.5	15	0.015	0.15
Texas Commission on Environmental Quality (TCEQ, 2011a) 0.5 A, C	–	0.56	5.7	57	560	0.55	5.7
Texas (TCEQ, 2011a) 30 A, C	–	0.56	5.7	57	560	0.55	5.7
Texas (TCEQ, 2011b) C	8.3	0.83	8.3	83	830	0.83	8.3
Texas (TCEQ, 2006a)	0.63	0.063	0.63	6.3	63	0.067	0.63
Texas (TCEQ, 2006b)	0.63	0.063	0.63	6.3	63	0.0067	0.63
Vermont Dept. of Environmental Conservation (VDEC undated-a; USEPA, 2011)	0.15	0.015	0.15	1.5	15	0.015	0.15
Vermont (VDEC, undated-b) EPA RSL	0.15	0.015	0.15	1.5	15	0.015	0.15
Vermont (undated b) VDH	–	0.01	–	–	–	–	–
Virginia Dept. of Environmental Quality (VDEQ, 2009)	0.15	0.015	0.15	1.5	15	0.015	0.15
Washington Administrative Code (WAC, 2007)	10	0.1	10	10	100	10	10
Washington Dept. of Ecology (WDOC, 2011) C	1.4	0.14	1.4	14	140	0.14	1.4
West Virginia Dept. of Environmental Protection (WVDEP, 2009a)	0.62	0.062	0.62	6.2	62	0.062	0.62
West Virginia (WVDEP, 2009b)	0.88	0.088	0.88	8.8	88	0.088	0.88
Wisconsin (WNDR, 2002) C	0.0875	0.00875	0.0875	0.875	8.75	0.00875	0.0875
Wisconsin (WNDR, 1997)	0.088	0.0088	0.088	0.88	8.8	0.0088	0.088
Wyoming Dept. of Environmental Quality (WDEQ, 2009)	0.15	0.015	0.15	1.5	15	0.015	0.15
District of Columbia Dept. of the Environment (DDOE, 2011) res. child	0.916	0.0916	0.916	9.16	91.5	–	–
(California) City of Oakland Public Works Agency (COPWA, 2000)	0.25	0.025	0.25	0.25	2.5	0.074	0.25
(California) San Francisco Bay Regional Water Quality Control Board (SFBRWQCB, 2008)	0.38	0.038	0.38	0.38	62	0.062	0.62
(California) Santa Barbara County Fire Dept. (SBCFD, 2007)	0.08	0.062	0.2	0.38	3.8	0.062	0.62
(Florida) Code of Miami-Dade County (CMDC, 2008)	–	0.1	–	–	–	–	–
(New Mexico) City of Santa Fe Springs (CSFS, 2004; USEPA, 2011c)	0.15	0.015	0.15	1.5	15	0.015	0.15
(New York) Suffolk County Dept. of Health Services (SCDHS, 2010)	1	22	1.7	1.7	1	100	8
New York City (NYC, 2010; NYDEC, 2010) Table 3	1	1	1	0.8	1	0.33	0.5
(NYC, 2010; NYDEC, 2010) Table 375-6.8(a)	1	1	1	0.8	1	0.33	0.5
(NYC, 2010; NYDEC, 2010) Table 375-6.8(b) res.	1	1	1	1	1	0.33	0.5
(NYC, 2010; NYDEC, 2010) Table 375-6.8(b) restricted res.	1	1	1	3.9	3.9	0.33	0.5

[a] Value indicator (if necessary) for sources from which more than one value could have been selected.

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6 Blei

6.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 1'000 mg Pb/kg Boden sollte gemäss dem ALARA-Prinzip reduziert werden. SCAHT empfiehlt eine Reduktion auf 83 mg/kg Boden. Unter der Annahme einer oralen Bioverfügbarkeit von Blei aus dem Boden, einem Körpergewicht von 12.5 kg und einer Bodenaufnahmerate von 250 mg/Tag liegt die Exposition bei <0.5 µg Pb/kg KG/Tag, also niedriger als der $BMDL_{01}$ für Entwicklungsneurotoxizität.
Gefährdungspotential	Hoch	Blei akkumuliert im Körper, insbesondere in den Knochen: Biologische Halbwertszeit 5 - 30 Jahre. Entwicklungsneurotoxizität am kritischsten.
Kanzerogen	Ja	MAK stuft Blei als krebserzeugend beim Menschen ein, z. B. Bleichromat und Bleiarsenat. EU: Verdacht auf kanzerogenen Wirkung beim Menschen
Mutagen	Ja	Induktion von Chromosomenschäden
Reprotoxisch	Ja	EU: bekanntermassen reproduktionstoxischer Stoff
Neurotoxisch	Ja	Beeinträchtigung der kognitiven Entwicklung (IQ-Kinder ↓) am kritischsten
Andere	Ja	Herz-Kreislauferkrankungen und Nierenfunktionsstörungen bei Erwachsenen am kritischsten
Gesundheitsbasierter Referenzwert		Kein Schwellenwert für (neuro)toxische Effekte $BMDL_{01}$ (Verminderung des IQ um 1 Punkt bei Kindern): 0.5 µg Pb/kg KG/Tag $BMDL_{01}$ (Erhöhung des systolischen Blutdrucks bei Erwachsenen um 3 Punkte): 0.63 µg Pb/kg KG/Tag $BMDL_{10}$ (Reduktion der glomulären Filtrationsrate bei Erwachsenen): 1.5 µg Pb/kg KG/Tag
Exposition		
Äussere Exposition Boden (250 mg)		1'000 mg Pb/kg Boden = 250 µg Pb/250 mg Boden = 20 µg Pb/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability"		Bei 100% Bioavailability: 20 µg Pb/kg KG/Tag (KG: 12.5kg) Bei 30% absolute orale Bioavailability: 6.0 µg Pb/kg KG/Tag (KG: 12.5kg)

Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte tatsächliche mittlere Bleiaufnahme über die Nahrung (Kinder 1-3 Jahre): 1.3 – 3.3 µg Pb/kg KG/Tag (max. 5.5)
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Wahrscheinlich	Die geschätzte Aufnahmemenge alleine über die Nahrung überschreitet bereits den gesundheitsbasierten Referenzwert. Die geschätzte Bleiaufnahme durch direkte Bodenaufnahme ist vergleichbar mit der Bleiaufnahme über die Nahrung und etwa 5-fach höher als der gesundheitsbasierte Referenzwert. Ein zusätzliches Gesundheitsrisiko durch das Verschlucken von kontaminiertem Boden ist bereits unter der Annahme einer limitierten Bioverfügbarkeit des Bleis aus dem Boden von 30% wahrscheinlich. Gesundheitsbasierter Referenzwert $BMDL_{01}$ (Entwicklungsneurotoxizität): 0.5 µg Pb/kg KG/Tag Bleiaufnahme über die Nahrung: 1.3 – 3.3 µg Pb/kg KG/Tag (max. 5.5) Bleiaufnahme durch direkte Bodenaufnahme bei Kontamination mit 1000 mg Pb/kg Boden und oraler Bioverfügbarkeit von 30%: 6 µg Pb/kg KG/Tag
Grenzwert im Vergleich		**CH**: 1000; B: 700; NL: 530; A: 500; UK: 450; D & F & USA: 400; CZ: 300; CAN: 140; I: 100; S: 80; E: 60; (mg/kg dm)
Datenlage	Ausreichend	

6.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (AltlV)[1] festgelegte Sanierungswert für Blei für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 1000 mg Pb/kg Boden sollte gemäss dem ALARA-Prinzip reduziert werden.

Blei existiert in verschiedenen anorganischen und organischen Formen, wobei anorganische Pb^{2+}-Salze am häufigsten vorkommen. Blei hat keine bekannte biologische Funktion. Blei akkumuliert im Körper, insbesondere in den Knochen, mit einer Halbwertszeit zwischen 5 und 30 Jahren. Blei wirkt sich auf praktisch alle Organe unseres Körpers aus und ist mit einer Vielzahl von Effekten verbunden, darunter sind verschiedene neurologische Entwicklungsstörungen, Herz-Kreislauf-Erkrankungen, Bluthochdruck, Nierenfunktionsstörungen, Beeinträchtigung der Fruchtbarkeit und Schwangerschaftskomplikationen. Das kritischste Zielorgan für Blei ist das zentrale Nervensystem, insbesondere das sich entwickelnde Gehirn von Föten, Säuglingen und Kleinkindern. Dort kommt es selbst bei niedrigen Expositionen zur Beeinträchtigung der kognitiven Entwicklung und der geistigen Leistungsfähigkeit.

Für Blei gibt es keine sichere untere Wirkungsschwelle für den kritischsten toxikologischen Endpunkt der Neurotoxizität, gegenüber welchem Ungeborene und Kinder besonders empfindlich sind. Somit kann keine gesundheitlich unbedenkliche tolerable Aufnahmedosis festgelegt werden. Die EFSA hat stattdessen eine diätische Bleiexposition berechnet, die mit 95% Wahrscheinlichkeit das zusätzliche Risiko für Entwicklungsneurotoxizität auf 1% begrenzt ($BMDL_{01}$-Wert). Danach sollte die tägliche Exposition 0.5 µg/kg KG/Tag nicht überschreiten. Für Kinder zwischen 1 und 3 Jahren wurde eine mittlere tägliche Bleiaufnahme über Lebensmittel und Trinkwasser zwischen 1.1 und 3.1 µg/kg KG ermittelt, während das 95-Perzentil Werte bis zu 5.5 µg/kg KG und Tag erreicht. In der Altersgruppe 4 - 7 Jahre sind sowohl die mittlere nahrungsbedingte tägliche Bleiaufnahme mit Werten zwischen 0.8 und 2.6 µg/kg KG als auch das 95-Perzentil mit Werten bis zu 4.8 µg/kg KG etwas geringer. Somit überschreitet bei Kindern bereits die tägliche Bleiaufnahme über die Nahrung den $BMDL_{01}$-Wert für Entwicklungsneurotoxizität, ohne die Bleiaufnahme über andere Expositionsquellen und Expositionspfade zu berücksichtigen.

Das Verschlucken von bleibelastetem Boden stellt ein erhebliches zusätzliches Gesundheitsrisiko dar. Zur Bioverfügbarkeit von Blei aus dem Boden gibt es viele z. T. verschiedene Angaben und Vorgehensweisen einzelner Organisationen (in vivo Studien 12 - 40%, in vitro Studien 0.5 - 79%). Die Risikobeurteilung des SCAHT basiert auf der Annahme von 30% und entspricht dem Wert, den die US EPA in ihrem Modell zur Expositionsabschätzung von Kindern gegenüber Blei verwendet.

Der in der Schweizer Altlasten-Verordnung festgelegte Sanierungswert für Blei in Familiengärten ist auf 1000 mg Pb/kg Boden festgelegt. Unter der Annahme, dass ein Kind täglich 250 mg Boden verschluckt, der mit 1000 mg Pb/kg Boden kontaminiert ist, entsteht eine zusätzliche Belastung in Höhe von 250 µg Pb. Für ein Kind mit einem Körpergewicht von 12.5 kg bedeutet dies eine zusätzliche Belastung in Höhe von 20 µg/kg KG/Tag, d. h. alleine durch das Verschlucken kontaminierter Böden würde der von der EFSA abgeleitete $BMDL_{01}$-Wert von 0,5 µg/kg KG um das 40-fache überschritten.

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

Daher sollte nach Ansicht des SCAHT für die Festlegung des Sanierungswerts von Blei im Boden von Familiengärten das ALARA-Prinzip zur Anwendung kommen.

Unter der Annahme einer absoluten oralen Bioverfügbarkeit von Blei aus dem Boden von 30% und einer täglichen Aufnahme von 250 mg Boden pro Tag könnte ein Sanierungswert bei 83 mg Blei pro kg Boden festgelegt werden. Bei diesem Sanierungswert würde ein 12.5 kg schweres Kind zusätzlich < 0.5 µg Pb/kg KG/Tag aufnehmen. Diese Menge entspricht dem $BMDL_{01}$-Wert für Entwicklungsneurotoxizität und würde das zusätzliche Gesundheitsrisiko alleine durch die direkte Bleiaufnahme aus dem Boden auf 1% begrenzen. Alternativ könnte man über eine Absenkung des Sanierungswerts auf Höhe des aktuellen Prüfwerts für Blei in Höhe von 300 mg/kg TR nachdenken.

6.3 Gefährdungspotential

Blei existiert in verschiedenen anorganischen und organischen Formen. Elementares/metallisches Blei kommt selten in der Natur vor. Mehrheitlich findet man anorganische Bleisalze in den Oxidationsstufen Pb^{2+} und Pb^{4+}, wobei anorganische Pb^{2+}-Salze am häufigsten vorkommen. Die meisten anorganischen Salze sind schwer löslich (z. B. Bleichlorid) oder praktisch unlöslich (Bleisulfat) in Wasser; Ausnahmen sind Bleinitrat aber auch das organische Bleiacetat. Anorganische Salze haben in der Regel einen niedrigen Dampfdruck und sind bei Raumtemperatur nicht flüchtig. Anorganische Bleiverbindungen werden vom Körper nicht metabolisiert. Organische Bleiverbindungen wie Tetraethylblei und Tetramethylblei werden grosstechnisch hergestellt und sind hochflüchtige, lipidlösliche Flüssigkeiten, die in grossem Umfang hauptsächlich als Kraftstoffadditive verwendet wurden. Organische Bleiverbindungen können durch Dealkylierung in anorganische Bleisalze (Pb^{2+}) überführt werden. Organische Bleiverbindungen sind giftiger als anorganische Formen von Blei. Ihre Anwesenheit in der Umwelt resultiert im Wesentlichen aus der Verdampfung der Benzinadditive und ist für die Schweiz somit nicht mehr relevant.

- Blei hat keine bekannte biologische Funktion, sondern ahmt andere zweiwertige Metalle nach, die wesentlich für verschiedene biologische Funktionen sind. Insbesondere zerstört Blei die Eisen-Homöostase (ATSDR 2007, Kapitel 3.7, Seite 235-236).

- Blei akkumuliert im Körper. Die Halbwertszeit für anorganisches Blei im Blut beträgt etwa 30 Tage, in den Knochen dagegen zwischen 5 und 30 Jahren. Während der Schwangerschaft oder bei kleinen Kindern kann das Blei aus Knochen mobilisiert werden (BfR 2012, Seite 18). Aufgrund der langen Halbwertszeit im Körper sind chronische Expositionen auch gegenüber niedrigen Bleimengen relevant für die menschliche Gesundheit.

- Blei wirkt sich auf praktisch alle Organe unseres Körpers aus und ist mit einer Vielzahl von Effekten verbunden, darunter sind verschiedene neurologische Entwicklungsstörungen, Herz-Kreislauf-Erkrankungen, Bluthochdruck, Nierenfunktionsstörungen, Beeinträchtigung der Fruchtbarkeit und Schwangerschaftskomplikationen.

- Für Erwachsene wurden die kardiovaskulären Effekte (sensitivster Endpunkt ist die Erhöhung des systolischen Blutdrucks) und die Nephrotoxizität (Reduktion der glomulären Filtrationsrate als sensitivster Endpunkt der chronischen Nierentoxizität) von Blei als die kritischsten Endpunkte identifiziert, für Kinder die neurotoxischen Wirkungen (EFSA 2010, Abstract, Seite 1).

- Obwohl sich die Neurotoxizität des Bleis auch bei Erwachsenen äussert, sind Föten, Säuglinge und Kleinkinder besonders empfindlich, da sie sich in einer besonders vulnerablen Phase der Hirnentwicklung befinden. Blei passiert die Blut-Plazenta-Schranke und gelangt so in den Kreislauf des ungeborenen Kindes. Ausserdem geht Blei in die Muttermilch über (EFSA 2010, Kapitel 1, Seite 11, Paragraph 3) und die gastrointestinale Absorption von Blei ist bei Kindern um den Faktor 5 höher als bei Erwachsenen (BfR 2012, Kapitel 3.4.1, Seite 18 Paragraph 2).

- Zudem metabolisiert der Körper das aufgenommene anorganische Blei nicht, sondern scheidet es innerhalb weniger Wochen wieder aus. Allerdings werden bei Kindern nur 32% des aufgenommenen Bleis, bei Erwachsenen dagegen 99% ausgeschieden, so dass bei kontinuierlicher Exposition eine wesentlich stärkere Anreicherung des Bleis im Körper der Kinder und besonders in den Knochen stattfindet.

- Entwicklungsneurotoxizität hat man selbst bei niedrigen Expositionskonzentrationen beobachtet. Sie äussert sich in Form der Beeinträchtigung der kognitiven Entwicklung wie Aufmerksamkeits- und Reaktionsleistungen sowie Verhaltensstörungen, Hörschwellenverschiebungen und der

geistigen Leistungsfähigkeit (verminderter IQ) der Kinder. Bereits Bleikonzentrationen <100 µg/l im Blut von Kindern sind mit einem reduzierten Intelligenzquotienten assoziiert. Es werden auch Zusammenhänge zwischen dem hyperkinetischen Syndrom und leicht erhöhten Blutbleispiegeln berichtet. Das Risiko für diese Erkrankung bei Kindern (4 bis 15 Jahre) ist bei Blutkonzentrationen >20 µg Blei/l 4-fach höher als bei Konzentrationen <10 µg Blei/l (BfR 2012, Kapitel 3.4.1, Seite 18, Paragraph 6).

- Blei induziert Chromosomenschäden und ist im Tierversuch kanzerogen. Die MAK- Kommission stuft Blei als krebserzeugend (Kategorie 2, als krebserzeugend für den Menschen) ein. Auch die IARC hat Blei und seine anorganischen Verbindungen als wahrscheinlich krebserzeugend für den Menschen (Kategorie 2A) eingestuft. Die EU-Kommission hat eine Reihe von anorganischen Bleisalzen als Kanzerogene (Kategorie 2, Verdacht auf karzinogene Wirkung beim Menschen) und als reproduktionstoxische Substanzen (Kategorie 1A, bekanntermassen reproduktionstoxischer Stoff) eingestuft (BfR 2012, Kapitel 3.4.1, Seite 18, Paragraph 5).

6.4 Gesundheitsbasierter Referenzwert

2010 kommt die EFSA zu dem Schluss, dass für die negativen Effekte von Blei auf die Hirnentwicklung und den Intelligenzquotienten von Kindern keine wissenschaftlich fundierte Schwellendosis existiert (EFSA 2010, Zusammenfassung, Seite 5, Paragraph 3). Aus dem gleichen Grund hat auch die WHO/JECFA ihren ursprünglichen, unter der Annahme einer sicheren unteren Wirkungsschwelle abgeleiteten PTWI (provisorisch tolerierbare wöchentliche Aufnahme) von 25 µg/kg KG/Woche zurückgezogen (Benford 2010).

Da für die Bleitoxizität kein Schwellenwert festgelegt werden konnte, hat die EFSA anstelle des traditionellen NOAEL-Verfahrens das BMD-Verfahren (Benchmark-Dose-Verfahren) zur Risikocharakterisierung angewendet. Damit wurden auf der Basis epidemiologischer Studien diätische Bleiexpositionen berechnet, die mit 95% Wahrscheinlichkeit das zusätzliche Risiko für Entwicklungsneurotoxizität und kardiovaskuläre Erkrankungen auf 1% und das zusätzliche Risiko für Nierenerkrankungen auf 10% begrenzen. Der Bleigehalt im Blut wurde als Indikator für die Bleibelastung des Körpers verwendet.

Für Erwachsene wurde die Erhöhung des systolischen Blutdrucks als sensitivster Endpunkt für die kardiovaskulären Effekte des Bleis gewählt. Die Reduktion der glomulären Filtrationsrate diente als sensitivster Endpunkt für die Nierentoxizität. Für die neurotoxischen Wirkungen wurde eine Verminderung des IQ um einen vollen Punkt als sensitivster Parameter verwendet (EFSA 2010, Abstract, Seite 1).

Tabelle 6.1 fasst die Ergebnisse der BMDL-Berechnungen für die wichtigsten toxikologischen Endpunkte zusammen. Für den sensitivsten toxikologischen Endpunkt, die Entwicklungsneurotoxizität, sollte nach diesen Berechnungen die Exposition 0.5 µg/kg KG/Tag nicht überschreiten.

Tabelle 6-1: EFSA-Ansatz zur Risikocharakterisierung - BMDLs für die diätische Bleiexposition

(Quelle: EFSA 2010, Kapitel 8.6.2, Tabelle 37, Seite 101)

Endpoint	Population	BMDL B-Pb (µg/L)	Corresponding dietary Pb exposure µg/kg b.w. per day	µg/person per day
Developmental neurotoxicity	Children	12	0.50	10[(a)]
Nephrotoxicity	Adults	15	0.63	37.5[(b)]
Cardiovascular effects	Adults	36	1.50	90[(b)]

(a) Based on a 20 kg child; (b) Based on a 60 kg adult; B-Pb: blood lead; BMDL: benchmark dose lower confidence limit; b.w.: body weight.

6.5 Exposition

6.5.1 Äussere Exposition

Der Mensch kann Blei durch Einatmen, Verschlucken oder über die Haut aufnehmen. Die Beiträge der verschiedenen Expositionspfade sind in **Tabelle 6-2** dargestellt (EFSA 2010, Kapitel 7.5, Seite 62, Tabelle 29).

Tabelle 6-2: Geschätzte Bleibelastung durch Lebensmittel und andere Expositionen

(Quelle: EFSA 2010, Kapitel 7.5, Tabelle 29, Seite 62)

Source	Pathway	Range of calculated or reported exposures µg/kg b.w. per day	
		Average consumers	High consumers
Dietary exposure			
Adults[a]	Oral	0.36-1.24	0.73-2.43
Infants 3 months breast milk	Oral	0.21	0.32
Infants 3 months infant formula	Oral	0.27-0.63	0.40-0.94
Children 1-3 years	Oral	1.10-3.10	1.71-5.51
Children 4-7 years	Oral	0.80-2.61	1.30-4.83
Specific diets (game meat)	Oral	1.98-2.44	
Vegetarians	Oral	0.46-1.25	0.80-2.24
Women 20-40 years	Oral	0.38-1.28	0.68-2.60
Potential non-Dietary Exposure			
Soil and dust (children 2 years)[b]	Oral	0.18-0.80	
Outdoor air[c]	Inhalation	0.001-0.003	
Smoking (20 cigarettes)[d]	Inhalation	0.003-0.018	
Environmental Tobacco Smoke[e]	Inhalation	0.009-0.037 (adults) 0.012-0.052 (children)	

b.w.: body weight

(a) Age at which adulthood is assumed varies with country between 15 and 25 years in the different surveys. Details can be found at http://www.efsa.europa.eu/en/datex/datexfooddb.htm; (b) Exposure based on a mean and high lead content of 23 mg/kg and 100 mg/kg soil and dust, respectively, and ingestion of 100 mg soil and dust per day by a 12.5 kg child; (c) Exposure based on a mean and high lead content of 0.003 µg/m^3 and 0.010 µg/m^3, respectively, and 17 m^3 respired air and 60 kg b.w.; (d) Exposure based on 0.2 to 1.1 µg lead per person per day; (e) Exposure based on 0.03 to 0.13 µg/m^3 and 17 m^3 air respired by a 60 kg adult or 5 m^3 air respired by a 12.5 kg child.

- Nahrungsmittel stellen die grösste Einzelquelle für Bleibelastungen des Menschen dar. Die 2010 von der EFSA abgeschätzten Aufnahmemengen von Blei über Lebensmittel und Trinkwasser zeigen, dass Erwachsene im Durchschnitt 0.36 – 1.24 µg/kg KG und Tag aufnehmen, während das 95-Perzentil Werte von 0.73 – 2.43 µg/kg KG und Tag erreicht.

- Bei Kindern ist die alimentäre Bleiaufnahme bezogen auf das Körpergewicht höher als bei Erwachsenen. Bei jüngeren Kindern ist eine höhere alimentäre Bleiaufnahme zu beobachten als bei älteren. Für Kinder zwischen 1 und 3 Jahren wurde eine mittlere tägliche Bleiaufnahme über Lebensmittel und Trinkwasser zwischen 1.1 und 3.1 µg/kg KG ermittelt, während das 95-Perzentil Werte bis zu 5.5 µg/kg KG und Tag erreicht. In der Altersgruppe 4 - 7 Jahre sind sowohl die mittlere nahrungsbedingte tägliche Bleiaufnahme mit Werten zwischen 0.8 und 2.6 µg/kg KG als auch das 95-Perzentil mit Werten bis zu 4.8 µg/kg KG etwas geringer.

- Zusätzlich sind bei Kindern Verhaltensweisen zu berücksichtigen, die relevant zur Bleiaufnahme beitragen können. Hierzu gehört der häufige Hand-Mund-Kontakt, Krabbeln und Spielen auf dem Fussboden verbunden mit Staubingestion oder das Verschlucken von Bodenpartikeln. So führen

Hausstaub, Bodenpartikel und Hand-Mund-Aktivitäten bei kleineren Kindern zu höherer Bleikonzentration im Blut als bei älteren. Für zweijährige Kinder schätzt die EFSA eine Bleiaufnahme über Boden- und Staubpartikel zwischen 0.18 und 0.8 µg/kg KG und Tag. Allerdings ist das Verschlucken von bleihaltigem Hausstaub i.d.R. relevanter als die direkte Bodenaufnahme (Turner 2011). Eine Meta-Analyse zum Beitrag des Hausstaubs zur Gesamtbleibelastung des Blutes hat gezeigt, dass Hausstaub und Innenfarbe ein weit grösseres Risiko darstellen als Blei aus dem Boden (Lanphear et al 1998). Allerdings tragen Innenraumfarbe, Strassenstaub und Gartenerde wesentlich zur Bleibelastung des Hausstaubs bei und die Zusammensetzung der Hausstäube korreliert mit der Zusammensetzung der Gartenböden (Alloway 2004). Die zusätzliche Exposition über Spielzeug wurde bei den Schätzungen der EFSA nicht berücksichtigt, kann aber je nach Szenario den $BMDL_{01}$ bereits überschreiten (BfR 2012, Kapitel 3.4, Seite 19 letzter Paragraph – Seite 20 erster Paragraph).

- Weitere Expositionswege für Blei sind die inhalative Aufnahme über die Aussenluft und das Passivrauchen. Der primäre Beitrag der Umgebungsluft an der Gesamtbleibelastung geht in der Regel auf das Verschlucken von Blei nach dessen Ablagerung in Böden und Stäuben zurück, nicht aber durch das Einatmen von Luft (US EPA 2013). Staub und Bodenpartikel, die mit Blei belastet sind, liegen typischerweise als grössere Partikel vor, die nicht mehr lungengängig sind und daher abgehustet oder verschluckt werden (US EPA 2013).

- Der Beitrag des Einatmens von Luft, dem Rauchen oder dem Passivrauchen an der Gesamtbleibelastung ist extrem gering. Metallisches Blei und anorganische Bleiverbindungen haben einen niedrigen Dampfdruck und sind bei Zimmertemperatur nicht flüchtig. Organische Bleiverbindungen sind hochflüchtige Flüssigkeiten. Seit dem Verbot dieser Verbindungen als Kraftstoffadditive ist der Konsument diesen Verbindungen nicht mehr ausgesetzt. Eine inhalative Exposition gegenüber organischen Bleiverbindungen besteht somit vor allem im beruflichen Umfeld.

- Die dermale Absorption von Blei ist im Allgemeinen niedrig. Staub und Schmutz, die Blei enthalten, gelangen auf die Haut, ebenso wie billige Schmuckstücke, die hohe Bleigehalte aufweisen können. Allerdings kann nur ein kleiner Teil des Bleis die Barriere der gesunden Haut durchdringen und in den Blutkreislauf gelangen. Die einzigen Arten von Bleiverbindungen, die leicht in die Haut eindringen, sind die Zusatzstoffe in verbleitem Benzin, das nicht mehr vermarktet wird. Es ist daher unwahrscheinlich, dass die breite Öffentlichkeit durch dermale Exposition gegenüber Blei exponiert ist (ATSDR 2007).

6.5.2 Innere Exposition

For lead, SCAHT applies the TIER 1-strategy as outlined in the methodology section.

The absolute oral bioavailability of lead from soil is directly available for humans, based on the US EPA IEUBK-Model[2] (NRC, 2003, p.71; USEPA, 2007), which has been widely used by regulatory Authorities worldwide since its introduction in 1994 (ANSES, 2013; USEPA 2007, 2013; DEPA, 2003; NEPI, 2000; NRC, 2003). For children, the USEPA IEUBK-Model presupposes a 50% absolute bioavailability from water or food, a relative bioavailability of soil lead of 60% and an aboslute oral bioavailability of 30% of lead in soil. These assumptions are well supported by the available database:

[2] IEUBK: Integrated Exposure Uptake Biokinetic Model

- Human kinetics are well characterized, though more in adults that shildren. Studies for children indicate that oral absorption is ca. 40-50% vs 3-10% for adults (section 6.5.2.1).
- One human soil ingestion study has shown a 26% absolute oral bioavailability in fasted adults vs only 2.5% in the non fasted state (section 6.5.2.2).
- There are many *in vivo* soil ingestion studies in experimental animals with a large range of relative bioavailabilites from soil (section 6.5.2.3). Collectively, juvenile swine studies indicate a mean of 49% (median 51%) (USEPA 2013).
- Some in vivo studies in rats and swine have been used by US Federal and State Agencies for health risk assessment based on absolute oral bioavailabilites from soil between 12-40% (section 6.5.2.4).

6.5.2.1 Oral bioavailability from food and/or water from dietary studies

The extent and rate of gastrointestinal absorption of ingested inorganic lead are influenced by physiological states of the exposed individual (e.g., age, fasting, nutritional calcium and iron status) and physicochemical characteristics of the lead-bearing material ingested (e.g., particle size, mineralogy, solubility). In adults, estimates of absorption of ingested water-soluble lead compounds (e.g., chloride, nitrate, acetate) range from 3 to 10% in fed subjects. The absence of food in the GI tract increases absorption of water-soluble lead in adults. Reported estimates of soluble lead absorption range from 26 to 70% in fasted adults (USEPA 2013, chapter 3.2.1.2, page 3-37).

Limited evidence demonstrates that gastrointestinal absorption of water-soluble lead is higher in children than in adults. Estimates derived from dietary balance studies conducted in infants and children (ages 2 weeks to 8 years) indicate that ca. 40-50% of ingested lead is absorbed (USEPA 2013, chapter 3.2.1.2, page 3-37). According to Hettiarachchi and Pierzynski (2004), estimates of lead absorption from dietary sources in infants and children range from 40 to 53%, while adults typically absorb 7-15% of lead ingested from a dietary source.

- In its IEUBK-Model, the USEPA assumes that the absolute bioavailability of lead in the food and water is 50% for children.

⇒ **SCAHT assumes a conservative oral bioavailability from the diet of 50% for its risk assesssment.**

6.5.2.2 Oral bioavailability from in vivo soil ingestion studies in humans

One study of lead uptake for human adults following ingestion of mine waste-contaminated soil have shown a 26% oral absolute bioavailability for ingested lead in fasted individuals vs 2.5% in fed individuals (Maddaloni et al., 1998, reviewed in NRC 2003, pp.285-286).

- Maddaloni et al. (1998) utilized the stable isotopes of lead[3] that exist naturally to measure the absolute bioavailability of lead in six human adult volunteers from a residential yard soil at a mining-impacted federal Superfund site. A <250 μm fraction was used for the experiments to better reflect realistc ingestion scenario through hand-to-mouth activities. One group received a soil dose (250 μg Pb per 70 kg body weight, i.e., 85.5 mg soil) in a gelatin capsule) after an overnight fast, while the second group received the same dose immediately after a standardized, high-fat breakfast. From the change in blood

[3] The unique existence of naturally occurring stable isotopes in different ratios in soils and individuals from different areas) make this approach difficult to reproduce for other chemicals.

concentration and isotope ratio, the percent of the lead dose in the blood compartment of the subjects could be calculated. It was found that the average absolute bioavailability of lead for fasted subjects from the soil samples was 26% percent. For non-fasted subjects, the absolute bioavailability was much lower, averaging only 2.5%.

⇒ **SCAHT considers that the value of 26% absolute bioavailability from soil in the Maddaloni study is well aligned on the 30% absolute bioavailability value used in the USEPA IEUBK-Model.**

6.5.2.3 Oral bioavailability from in vivo soil ingestion studies in experimental animals

There are numerous in vivo studies (primarily rodents and juvenile swine) available in the literature. Experimental studies provide further evidence for greater absorption of Pb from the gut in young animals compared to adult animals (reviwed by USEPA 2013, chapter 3.2.1.2, page 3-37).

According to USEPA (2013), collectively, published studies conducted in swine have provided mean relative bioavailability estimates from 25 soils of 49% (±29% [SD]), median 51%, and 5th to 95th percentile range of 12% to 89%.

- Ruby et al. (1999) reported that studies of relative lead bioavailability from soil at mining and smelting sites in a weanling rat model showed RAFs between 8.7 and 41%, whereas similar studies in swine (EPA Region VIII) showed values between 6-90% (mean 50%).
- Similarly, Casteel et al. (2006) found that the relative bioavailability of lead acetate in a variety of soil and soil-like test materials ranged from 6 to 105%. Studies in minipigs reported bioavailabilities of 22-72% following ingestion of lead from six differnet type of soils (DEPA 2003, citing Hack et al., 2002). Based on data for 18 soil materials assayed in swine, relative bioavailability of lead mineral phases were categorized into “low” (<25%), “medium” (25 to 75%), and “high” (>75%) categories.

6.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

Some of these studies have been used for health risk assessment by various US Federal and State Agencies, to estimate the absolute oral bioavailability of lead of 12-40% , based on the IEUBK model (NRC 2003, Seite 86-87, Tabelle 2.4):

- in vivo rat 24% relative bioavailability from soil, with an absolute oral bioavailability of 12% (EPA region 8)
- in vivo rat 40% relative bioavailability from soil, with an absolute oral bioavailability of 20% (US Oklahoma DEQ)
- in vivo swine relative bioavailability from different soils 60% and 80%, with an absolute oral bioavailability of 30% and 40% (EPA region 7)
- in vivo swine relative bioavailability from soil 60%, with an absolute oral bioavailability of 30% (EPA region 3)

⇒ **In conclusion, SCAHT considers that the available database supports well the assumptions of the USEPA IEUBK-Model for children, which presupposes a 50% absolute bioavailability from water or food, a relative bioavailability of soil lead of 60% and an absolute oral bioavailability of lead from soil of 30%.**

6.5.2.5 Summary of the in vitro bioaccessibility information

The bioaccessibility of lead from soil is like other metals dependent of its chemical form, the particle size of the mineral fraction and the physico-chemical properties from the soil. The major factors governing lead mobility and bioaccessibility in soils are: soil pH; soluble organic matter content; hydrous metal oxide content; clay content and type; presence of inorganic and organic ligands (e.g. iron, fulvic and humic acids), and competition from other metal ions (e.g. Hettiarachchi and Pierzynski 2004; Hernandez-Soriano and Jimenez-Lopez, 2012). Walraven et al. (2015) showed that lead bioaccessibility was correlated with pH, organic matter and reactive iron.

There are numerous in vitro studies that tried to estimate the bioaccessibility of lead from various type of soils. The range of reoprted values is usally large, e.g. between 0.5% - 79.0% in the Walraven et al (2015) study. Lead is the only case where in vitro bioaccessibility has been shown to be a good predictor of bioavailability (DEPA 2003). Indeed it has been shown that the in vitro physiologically-based extraction test (PBET) of Ruby et al. (1996) which does not use food in the extraction to mimic fasting conditions, has been shown to predict accurately relative bioavailable lead in contaminated soil and media (Ruby et al., 1999). Denys et al (2012) also demonstrated that there was good correlations for lead between bioaccessibility data as produced with the Unified BARGE Method test compared with bioavailability measurements in the juvenile swine model.

6.6 Risikoabschätzung

EFSA und WHO/JECFA bestätigen, dass es für Blei keine sichere untere Wirkungsschwelle für den kritischsten toxikologischen Endpunkt der Neurotoxizität gibt und dass Föten, Säuglinge und Kinder besonders empfindlich gegenüber den neurotoxischen Effekten des Bleis sind.

Für diesen sensitivsten toxikologischen Endpunkt, die Entwicklungstoxizität, hat die EFSA eine diätische Aufnahmemenge für Blei in Höhe von 0.5 µg/kg KG und Tag berechnet, die mit 95% Wahrscheinlichkeit das zusätzliche Risiko für Entwicklungsneurotoxizität auf 1% begrenzt.

Bei Kindern überschreitet bereits die tägliche alimentäre Bleiaufnahme den von der EFSA abgeleiteten $BMDL_{01}$-Wert für Entwicklungsneurotoxizität von 0.5 µg/kg KG um ein Mehrfaches. Aus dem Vergleich der modellierten BMDL-Daten (Kapitel 6.3, **Tabelle 6-1**) mit der geschätzten diätischen Exposition (Kapitel 6.4.1, **Tabelle 6-2**) kann man eine sog. Margin of Exposure (MOE)[4] berechnen (MOE = BMDL / Exposition), um die Grösse des Gesundheitsrisikos abzuschätzen. Dabei zeigt sich, dass die MOE vor allem für die Neurotoxizität bei Kindern <1 ist, d. h. dass die Exposition über dem BMDL liegt (**Tabelle 6-3**).

Als sicheren Abstand zwischen dem BMDL-Wert und der täglichen Bleiaufnahme ohne ein nennenswertes Risiko für einen klinisch signifikanten Effekt auf den Intelligenzquotienten definiert die EFSA einen MOE (Margin of Exposure) von 10 oder grösser. Allerdings liegt der ermittelte MOE für Kinder zwischen 1 und 3 Jahren zwischen 0.16 und 0.45 und ist damit deutlich unter 1. In der Altersgruppe von 4 - 7 Jahren war der MOE nur geringfügig höher. Daher folgert die EFSA: „In children (...) there is potential concern at current levels of exposure to lead for effects on neurodevelopment" (EFSA 2010, Kapitel 9.4, Seite 106). Bereits die alimentäre Bleiaufnahme führt bei Kindern also zu erheblicher Besorgnis. Weitere kinderspezifische Quellen für die Bleiaufnahme wie Hausstaub, Bodenpartikel oder auch Spielzeug wurden dabei noch nicht berücksichtigt.

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten, Standorten) festgelegte Sanierungswert für Blei für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, ist auf 1'000 mg Pb/kg Boden festgelegt. Unter der Annahme, dass ein Kind täglich 250 mg Boden verschluckt, der mit Blei kontaminiert ist, entsteht so eine zusätzliche externe Exposition in Höhe von 250 µg/kg Boden.

Unter der Annahme einer absolute orale Bioverfügbarkeit aus dem Boden von 30%, wie sie standardmässig vom NRC angenommen wird, bedeutet dies für ein Kind mit einem Körpergewicht von 12.5 kg eine zusätzliche Belastung in Höhe von 6 µg/kg KG/Tag. Das bedeutet, dass alleine durch das Verschlucken kontaminierter Böden der von der EFSA abgeleitet $BMDL_{01}$-Wert von 0.5 µg/kg KG um das 12-fache überschritten wird, bzw. die orale Aufnahme von Blei über den Boden im Vergleich zur Aufnahme über die Nahrung bei einem durchschnittlich belasteten 1 - 3-jährigen Kind (1,1 -3,1 µg/kg KG laut Tabelle 6.2) um mehr als das Zwei- bis Fünffache gesteigert werden kann.

Nach Ansicht des SCAHT sollte daher für die Festlegung des Sanierungswerts von Blei im Boden von Familiengärten das ALARA-Prinzip zur Anwendung kommen.

- Das ALARA-Prinzip kommt zur Anwendung, wenn für einen Stoff aus toxikologischer Sicht

[4] Der MOE (Margin of Exposure) ist ein von Risikobewertern verwendetes Instrument zur Abwägung möglicher Sicherheitsbedenken in Bezug auf Substanzen ohne Schwellenwert. Beim MOE handelt es sich um das Verhältnis zwischen der Dosis, bei der man eine kleine, jedoch messbare negative Auswirkung erstmalig feststellt, und dem Expositionsniveau der betrachteten Substanz für eine gegebene Population

kein sicherer Schwellenwert abgeleitet werden kann, bis zu dem ein gesundheitliches Risiko praktisch ausgeschlossen ist, oder wenn bereits die Aufnahme aus anderen Quellen, beispielsweise aus der Nahrung und dem Trinkwasser, einen solchen Schwellenwert überschreitet.

- Im vorliegenden Fall kommt erschwerend hinzu, dass die direkte Aufnahme von Blei über den Boden einen wesentlichen Expositionspfad darstellt.

Für das Risikomanagement ist entscheidend abzuklären, welcher Sanierungswert gemäss dem ALARA-Prinzip als „so gering wie vernünftigerweise erreichbar" anzusehen ist. Eine limitierte Anzahl von Messungen deutet darauf hin, dass Familiengärten in der Schweiz häufig mit weniger als 100 mg Pb/kg Boden belastet sind, allerdings gibt es auch hier Ausnahmen.

Unter der Annahme einer Bioverfügbarkeit von Blei aus dem Boden von 30% und einer täglichen Aufnahme von 250 mg Boden pro Tag könnte ein Sanierungswert bei 83 mg Blei pro kg Boden festgelegt werden (siehe nachfolgende Rechnung):

Der $BMDL_{01}$-Wert für Entwicklungstoxizität liegt bei 0.5 µg/kg KG. Ein 12.5 kg schweres Kind könnte demnach täglich 6.25 µg/Tag zu sich nehmen, ohne den $BMDL_{01}$-Wert zu überschreiten. Unter der Annahme, dass ein Kind 250 mg belasteten Boden pro Tag verschluckt, berechnet sich der Grenzwert wie folgt: 6.25 µg Blei pro 250 mg Boden x 4 = 25 µg Blei pro 1000 mg Boden = 25 mg Blei pro 1 kg Boden bei einer 100% Bioverfügbarkeit. Unter der Annahme einer Bioverfügbarkeit von 30% erhöht sich der Wert von 25 mg auf 83 mg.

Bei diesem Sanierungswert würde ein 12.5 kg schweres Kind zusätzlich <0.5 µg/kg KG/Tag aufnehmen. Diese Menge entspricht dem $BMDL_{01}$-Wert für Entwicklungsneurotoxizität und würde das zusätzliche Gesundheitsrisiko alleine durch die direkte Bleiaufnahme aus dem Boden auf 1% begrenzen.

Tabelle 6-3: EFSA-Ansatz zur Risikocharakterisierung - MOEs für die diätische Bleiexposition

(Quelle: EFSA 2010, Kapitel 9.4, Seite 106)

Population/Diet	Endpoint	MOE	
		Average consumer	High consumer
Adult	Cardiovascular effects[a]	1.2 - 4.2	0.62 - 2.1
	Nephrotoxicity[b]	0.51 - 1.8	0.26 - 0.86
Vegetarians	Cardiovascular effects	1.2 - 3.3	0.67- 1.9
	Nephrotoxicity[b]	0.50 - 1.4	0.28 - 0.79
Specific diet (game meat)	Cardiovascular effects	0.76	0.61
	Nephrotoxicity	0.32	0.26
Infants 3 months breast milk	Developmental neurotoxicity[c]	2.4	1.6
Infants 3 months infant formulae	Developmental neurotoxicity	0.79 - 1.9	0.53 - 1.3
Children 1-3 years	Developmental neurotoxicity	0.16 - 0.45	0.09 - 0.29
Children 4-7 years	Developmental neurotoxicity	0.19 - 0.63	0.10 - 0.38
In utero exposure(a)	Developmental neurotoxicity	0.39 - 1.3	0.19 - 0.74

(a) For cardiovascular effects the MOE was calculated by dividing the $BMDL_{01}$ intake value of 1.50 µg/kg b.w. per day by the respective dietary exposure estimates taken from Table 29; (b) For nephrotoxicity the MOE was calculated by dividing the $BMDL_{10}$ intake value of 0.63 µg/kg b.w. per day by the respective dietary exposure estimates taken from Table 29; (c) For neurodevelopmental toxicity, the MOE was calculated by dividing the $BMDL_{01}$ intake value of 0.50 µg/kg b.w. per day by the respective dietary exposure estimates taken from Table 29. The MOE range for *in utero* exposure was derived from the 20 to 40 year old female consumer data; MOE: margin of exposure

6.7 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften in Europa, USA und Kanada (z.B. Carlon 2007; Provoost et al, 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden (siehe **Anhang 1**).

CH: 1000; B: 700; NL: 530; A: 500; UK: 450; D & F & USA: 400; CZ: 300; CAN: 140; I: 100; S: 80; E: 60; (mg / kg dm).

6.8 Literatur

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7 Antimon

7.1 Datenblatt

Handlungsbedarf	Nein	Aktueller Sanierungswert von 50 mg Sb/kg Boden kann beibehalten werden. Rein rechnerisch kann aus humantoxikologischer Sicht der Sanierungswerte auf 2010 mg/kg Boden erhöht werden.
Gefährdungspotential	Gering (oral) Hoch (inhalativ)	Verdacht auf Kanzerogenität nach inhalativer Exposition im Menschen. Gering nach oraler Exposition: Anorganisches Antimontrioxid kommt am häufigsten vor, es ist aber schlecht bioverfügbar und von geringer Toxizität. Die gut wasserlöslichen organischen Kalium-und Natriumtartrate des Antimon werden als Human- und Veterinärarzneimittel eingesetzt. Auch hier ist die orale Bioverfügbarkeit gering (<5%).
Kanzerogen	Ja	MAK stuft Antimon als krebserzeugend beim Menschen ein. Vor allem nach inhalativer Exposition gegenüber hohen Dosen am Arbeitsplatz. Nach chronischer oraler Gabe im Tierversuch ohne Krebsbefund (Studien alt und nur begrenzt relevant).
Mutagen	Nein	Nicht-mutagenes Kanzerogen: Hemmung der DNA-Reparaturmechanismen Kanzerogene Wirkung durch Generierung von oxidativem Stress infolge der Senkung des Glutathionspiegels
Reprotoxisch	?	Östrogene Wirkung - in vitro; Plazentagängig - in vivo; Keine teratogenen Effekte - in vivo
Neurotoxisch	Nein	
Andere	Ja	Irritationen des Magen-Darm-Trakts
Gesundheitsbasierter Referenzwert		TDI: 6 µg Sb/kg KG/Tag
Exposition		
Äussere Exposition Boden		50 mg Sb/kg Boden = 12.5 µg Sb/250 mg Boden = 1 µg Sb/kg KG/Tag (KG: 12.5kg)

(250 mg)		
Innere Exposition Boden „Bioavailability“		Bei 100% Bioavailability: 1 µg Sb/kg KG/Tag (KG: 12.5kg) Bei 10% Bioavailability: 0.1 µg/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte tatsächliche mittlere Antimonaufnahme aller verschiedenen Quellen (Kinder): 1.98 µg Sb/kg KG/Tag (Beitrag Nahrung bis zu 50%)
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Unwahrscheinlich	Die geschätzte Gesamtaufnahmemenge über alle Expositionsquellen inklusive des Verschluckens von kontaminiertem Boden beträgt nur etwa ein Drittel des gesundheitsbasierten Referenzwerts. Ein zusätzliches Gesundheitsrisiko durch das Verschlucken von kontaminiertem Boden ist selbst unter der Annahme einer maximalen Bioverfügbarkeit des Antimons aus dem Boden von 100% unwahrscheinlich. Gesundheitsbasierter Referenzwert TDI: 6 µg Sb/kg KG/Tag Geschätzte Antimonaufnahme über Nahrung, Luft, Staub, Kleidung: 1.98 µg Sb/kg KG/Tag Geschätzte Antimonaufnahme durch direkte Bodenaufnahme: 0.1-1 µg Sb/kg KG/Tag bei 10% bzw 100% Bioaccessibility.
Grenzwert im Vergleich		F: 100; **CH: 50**; CAN: 20; NL: 15; I: 10; E: 6; A: 5 (mg/kg dm)
Datenlage	Unzureichend	Es gibt keine Studien zur Bioverfügbarkeit von Antimon aus dem Boden im Mensch, und kaum Tierstudien. ADME und Toxizität Studien im Mewnsch oder Tier sind gering. Aber da die Exposition im Vergleich Hintergrundbelastung und TDI klein ist, bestehen keine Unsicherheitbezügl. der Risikobeurteilung.

7.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten) (AltlV)[1] festgelegte Sanierungswert für Antimon (Sb) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 50 mg Sb/kg Boden bietet hinreichend Schutz vor gesundheitlichen Schäden, selbst unter der Annahme einer 100% oralen Bioverfügbarkeit nach direkter Bodenaufnahme .

Antimon ist ein Element, das nur in geringen Mengen in der Erdkruste enthalten ist und das trotz seiner möglichen Giftigkeit grundsätzlich kein besonderes Problem für die Allgemeinbevölkerung darstellt, trotz des Einsatzes von Antimon und seiner Verbindungen in verschiedenen industriellen und therapeutischen Anwendungen und der damit verbundenen Umweltexposition.

Antimon hat keine bekannte biologische Funktion. Es gibt viele Wissenslücken hinsichtlich seiner geochemischen oder biologischen Eigenschaften. Allgemein wird angenommen, dass sich Antimon aufgrund seiner Stellung im Periodensystem der Elemente in vielen Fällen ähnlich wie Arsen verhält (Gebel, 1999a, 1999b *in* FOEN 2007; ATSDR 1992).

Alle akut-toxischen Wirkungen von Antimon werden durch Ionen verursacht. Das anorganische Antimontrioxid (Sb_2O_3, ATO) kommt am häufigsten in der Umwelt vor. Für Antimon konnte *in-vitro* eine östrogene Wirkung gezeigt werden. Hinweise aus *in-vivo*-Experimenten liegen bislang keine vor. Die Datenlage bezüglich der Genotoxizität von Antimontrioxid *in-vitro* ist widersprüchlich. Die MAK-Kommission hat Antimon und seine anorganischen Verbindungen aufgrund der Datenlage zur Genotoxizität, Bioverfügbarkeit und chemischen Ähnlichkeit zum Arsen in die Kanzerogenitätskategorie 2 (krebserregend im Menschen) eingestuft. Die grössten Bedenken hinsichtlich der Kanzerogenität von Antimonverbindungen besteht im Hinblick auf die inhalative Exposition. In älteren oralen chronischen Tierstudien hat man keine Hinweise auf ein mögliches Krebsrisiko gefunden. Diese Studien entsprechen allerdings nicht den heutigen Qualitätsstandards und sind deshalb nur bedingt relevant für die Risikobeurteilung.

Die Aufnahme über die Nahrung stellt den wichtigsten Expositionspfad für Antimon in der Allgemeinbevölkerung dar, aber die Exposition durch natürlich vorkommendes Antimon über die Lebensmittelkette ist gering. Es gibt wenige Daten zur diätischen Exposition, aber Studien aus Frankreich und UK geben eine mittlere diätische Exposition von 0.03 µg/kg KG/Tag für Erwachsene und 0.05 µg/kg KG/Tag für Kinder an. Die Exposition kann durch Stillen verdoppelt werden. Das Trinkwasser hat einen wesentlich kleineren Anteil an der Antimonbelastung des Körpers.

Zur Bioverfügbarkeit von Antimon aus dem Boden konnten keine expliziten Angaben in der Literatur identifiziert werden. Das SCAHT geht daher standardmässig von einer 100% Bioverfügbarkeit von Antimon aus dem Boden aus. Dieser Ansatz ist konservativ. Weil sich Antimon im Boden wenig löst und eine eingeschränkte Mobilität zeigt, ist eher zu erwarten, dass die Bioverfügbarkeit aus dem Boden gering ist.

Die von der WHO im Jahre 2003 festgelegte tolerierbare tägliche Aufnahmemenge (TDI-Wert) beträgt 6 µg Sb/kg KG/Tag (WHO 2003). Die tägliche Hintergrundaufnahme von Antimon bei Kindern aus unterschiedlichen Quellen (orale Aufnahme von Antimon über Nahrung, Trinkwasser, Muttermilch, Hausstaub und Spielzeug, eine dermale Exposition über Textilien und eine inhalative Aufnahme über die Atemluft) beträgt 1.98 µg Sb/kg KG/Tag. Damit wird der TDI zu ca. einem Drittel

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

ausgelastet. Selbst bei einer weiteren Belastung in Höhe von 4.02 µg/kg KG/Tag würde der TDI nicht überschritten.

Unter der Annahme, dass ein Kind täglich 250 mg Boden verschluckt, der mit 50 mg Antimon pro kg Boden kontaminiert ist, würde eine zusätzliche Gesamtbelastung von 12.5 µg oder 1 µg/kg KG/Tag für ein 12.5 kg schweres Kind entstehen. Unter Berücksichtigung einer limitierten Bioverfügbarkeit von Antimon aus dem Boden von 30% reduziert sich die Belastung auf 0.3 µg/kg KG/Tag. Ein zusätzliches Gesundheitsrisiko durch das Verschlucken kontaminierter Böden ist unwahrscheinlich.
Die Gesamtexposition gegenüber Antimon aus der unvermeidbaren Hintergrundbelastung (1.98 µg Sb/kg KG/Tag) und dem Verschlucken von kontaminiertem Boden (0.3 µg Sb/kg KG/Tag) beträgt weniger als etwa 2.3 µg/kg KG/Tag, das entspricht etwa 40% der zulässigen täglichen Aufnahmemenge.

7.3 Gefährdungspotential

Antimon existiert in 4 Oxidatiosstufen: Sb(-III), Sb(0), Sb(+III), and Sb(+V). In der Umwelt kommt Antimon in den trivalenten und pentavalenten Oxidationsstufen vor, unter sauerstoffreichen Bedingungen dominiert Sb(+V) (Garbos et al 2000 *in* USEPA 2014).

Antimon ist ein Element, das nur in geringen Mengen in der Erdkruste enthalten ist und das trotz seiner möglichen Giftigkeit grundsätzlich kein besonderes Problem für die Allgemeinbevölkerung darstellt, trotz des Einsatzes von Antimon und seiner Verbindungen in verschiedenen industriellen und therapeutischen Anwendungen und der damit verbundenen Umweltexposition. Im Jahr 2001 wurden auf dem Schweizer Mark mehr als 70 antimonhaltige Produkte für metallurgische und nicht metallurgische Anwendungen (Flammschutzmittel Kunststoff, Katalysator, Glas, Pyrotechnik, Munition, Gummi, Schmiermittel, Pigmente) (FOEN 2007) identifiziert.

Alle akut-toxischen Wirkungen von Antimon werden durch Ionen verursacht, die aufgrund ihrer Affinität zu Thiol- und Imidazolgruppen zur Inhibition von Enzymen nach Bindung an entsprechende funktionelle Gruppen führen. Ein weiterer diskutierter Wirkmechanismus beruht auf der Senkung des zellulären Gehalts an Glutathion (GSH), der zu oxidativem Stress führt (BfR 2012, Kapitel 3.1.1, Seite 4, Paragraph 4).

Die akute Toxizität der Antimonverbindungen wird im Wesentlichen von der Wasserlöslichkeit und damit von der Bioverfügbarkeit bestimmt.

- Das anorganische Antimontrioxid (Sb_2O_3, ATO) kommt am häufigsten in der Umwelt vor und geht ausschliesslich auf die technische Anwendung der Substanz, z. B. als Flammschutzmittel oder Katalysator bei der Polyethylenterephthalat (PET)-Produktion zurück. Trotz dieser Umweltbelastung ist es aus humantoxikologischer Sicht wenig relevant, weil die Verbindung aufgrund der schlechten Wasserlöslichkeit kaum bioverfügbar ist. Die akute orale Toxizität von ATO ist gering (LD_{50} Ratte > 20.000 mg/kg KG) (BfR 2012, Kapitel 3.1.1, Seite 4, Paragraph 4).

Die gut wasserlöslichen organischen Kalium- und Natriumtartrate des Antimon (APT und AST) werden als Veterinär- und Humanarzneimittel eingesetzt, um Erbrechen zu induzieren oder Infektionskrankheiten und menschliche Parasiten zu behandeln. Auch hier ist die systemische Bioverfügbarkeit im Menschen nach oraler Aufnahme bedingt durch die niedrige Absorptionsrate aus dem Magendarmtrakt gering. Vergiftungsfälle mit APT deuten auf eine Absorptionrate von etwa 5% im Menschen hin. Die LD_{50}-Werte für das wasserlösliche Kaliumantimontartrat liegen je nach Versuchstierart zwischen 15 mg/kg KG (Kaninchen), 115 mg/kg KG (Ratte) bis 600 mg/kg KG. Beim Menschen bewirkt die einmalige orale Aufnahme entsprechender Mengen löslicher Antimonsalze starke irritative Effekte vor allem auf den Gastrointestinaltrakt mit Krämpfen und Durchfall sowie toxische Effekte auf das Herz. Die minimale Letaldosis für eine orale Intoxikation durch APT liegt bei 300 mg APT bei einem Kind und 1200 mg APT für einen Erwachsenen. Die akuten Symptome ähneln denen einer akuten oralen Intoxikation durch Arsen. Bezüglich möglicher irritativer Effekte auf die Haut liegen für den Menschen eine Reihe von Fallstudien vor, die darauf hindeuten, dass Antimontrioxid zu einer Dermatitis („Antimon-Dermatitis“) im Bereich schweissfeuchter Hautstellen führt (BfR 2012, Kapitel 3.1.1, Seite 4, Paragraph 5).

Für Antimon konnte *in-vitro* eine östrogene Wirkung gezeigt werden. Hinweise aus *in-vivo*-Experimenten liegen bislang keine vor (BfR 2012, Kapitel 3.1.1, Seite 5, Paragraph 1, letzter Satz).

- Antimon ist plazentagängig und wurde in der Milch von Versuchstieren nachgewiesen. Eindeutige teratogene Effekte wurden für keine der bisher getesteten Antimonverbindungen beobachtet (BfR 2012, Kapitel 3.1.1, Seite 5, Paragraph 2, erster Satz).

Die Datenlage bezüglich der Genotoxizität von Antimontrioxid *in- vitro* ist widersprüchlich (BfR 2012, Kapitel 3.1.1, Seite 5, Paragraph 2).

- Die MAK-Kommission hat Antimon und seine anorganischen Verbindungen aufgrund der Datenlage zur Genotoxizität, Bioverfügbarkeit und chemischen Ähnlichkeit zum Arsen in die Kanzerogenitätskategorie 2 (krebserregend im Menschen) eingestuft. Antimontrioxid ist gemäss Verordnung (EG) 1272/2008 als Kanzerogen der Kategorie 2 eingestuft. Als Wirkmechanismus wird eine Hemmung u. a. der an der DNA-Reparatur beteiligten Enzyme und die Generierung von oxidativem Stress postuliert (BfR 2012, Kapitel 3.1.1, Seite 5, Paragraph 2).

Die grössten Bedenken hinsichtlich der Kanzerogenität von Antimonverbindungen besteht im Hinblick auf die inhalative Exposition.

- Das Einatmen von Antimontrioxid führte im Tierexperiment zu Lungentumoren bei weiblichen Ratten. Als Ursache für die Auslösung der Tumoren wird eine nicht substanzspezifische Lungenschädigung bei chronischer Inhalation angesehen, die durch chronische Entzündungsprozesse bei „overload“ mit unlöslichen Partikeln entsteht. Für den Menschen gibt es zwar einige Fallstudien mit Personen, die am Arbeitsplatz gegenüber Antimontrioxid exponiert waren. Ein eindeutiger Beleg für eine erhöhte Inzidenz für das Auftreten von Lungentumoren fehlt, weil die Fälle vielfach bezüglich der Expositionsbedingungen schlecht dokumentiert sind (BfR 2012, Kapitel 3.1.1, Seite 5, Paragraph 3).

- Für entsprechende Effekte bei inhalativer Exposition gegenüber anderen Antimonverbindungen liegen nur wenige Daten vor (BfR 2012, Kapitel 3.1.1, Seite 5, Paragraph 2).

- In älteren oralen chronischen Tierstudien hat man keine Hinweise auf ein mögliches Krebsrisiko gefunden. Diese Studien entsprechen allerdings nicht den heutigen Qualitätsstandards und sind deshalb nur bedingt relevant für die Risikobeurteilung.

7.4 Gesundheitsbasierter Referenzwert

Von der WHO wurde basierend auf einer Studie von Poon *et al.* im Jahre 2003 ein TDI-Wert von 6 µg Antimon/kg KG/d abgeleitet (Poon et al 1998; WHO 2003).

- Bei der Ableitung des TDI-Wertes ist die WHO von einem aus einer subchronischen Trinkwasser-Studie mit Kaliumantimontartrat ermittelten NOAEL (No Observed Adverse Effect Level) von 6 mg Antimon/kg KG/Tag ausgegangen (BfR 2012, Kapitel 3.1.1, Seite 4, Paragraph 3).

- Es wurde ein Sicherheitsfaktor von 1000 (10x10x10) für Unterschiede zwischen den Arten und innerhalb einer Art, sowie für die Extrapolation von subchronischer zu chronischer Exposition berücksichtigt.

7.5 Exposition

7.5.1 Äussere Exposition

Antimon ist ein in der Natur selten vorkommendes Halbmetall, mit dem Kinder neben einer Hintergrundexposition über Lebensmittel, Muttermilch, Trinkwasser, Hausstaub und Atemluft in nennenswertem Umfang auch über Bedarfsgegenstände (kosmetische Mittel, Polyesterfasern in Textilien, Spielwaren, Farbpigmente) und pharmazeutischen Produkten in Kontakt kommen können (Tabelle 7.1).

- Die Aufnahme über die Nahrung stellt den wichtigsten Expositionspfad für Antimon in der Allgemeinbevölkerung dar, aber die Exposition durch natürlich vorkommendes Antimon über die Lebensmittelkette ist gering. Es gibt nur sehr begrenzte Daten zur ernährungsbedingten Exposition gegenüber Antimon. Leblanc et al (2005) gibt für Europa die tägliche Exposition gegenüber Antimon aus der Nahrung mit 4 µg/Tag an. Das entspricht Werten im oberen Bereich von Studien in UK, wo das 97,5-Perzentil mit weniger als 2 µg/Tag angegeben wurde (Leblanc et al 2005, EC/HC 2010). In einer Studie der Französischen Agentur für Lebensmittelsicherheit (AFSSA) aus dem Jahr 2006 lagen die mittleren Expositionswerte bei 0.03 µg/kg Körpergewicht/ Tag für Erwachsene und bei 0.05 µg/kg Körpergewicht/Tag bei Kindern (Arnich et al 2012). Diese Werte stehen im Einklang mit australischen Studien, wo man eine durchschnittliche Aufnahmemenge von <0.01 bis 0.08 µg/kg Körpergewicht/Tag bei Erwachsenen und von <0.01 bis 0.09 µg/kg Körpergewicht/ Tag bei Kindern geschätzt hat (FSANZ 2003 *in* Arnich et al 2012). Die diätische Exposition kann durch Stillen verdoppelt werden. Das Trinkwasser hat einen wesentlich kleineren Anteil an der Antimonbelastung des Körpers.

- Die orale Aufnahme von Hausstaub ist eine spezifische Expositionsquelle für Kinder. Kinder nehmen zwischen 50 und 100 mg Hausstaub pro Tag auf. Unter der Annahme, dass ein 10 kg schweres Kind 100 mg Hausstaub mit einem Gehalt von 60 µg/g Antimontrioxid pro Tag aufnimmt, würde daraus eine Belastung in der Grössenordnung von 0.6 µg/kg KG/d (Tabelle 7.1) resultieren.

- Die hauptsächliche Aufnahme aus Spielzeug erfolgt dermal über Spielzeug aus Polyester-Material und Flammschutz -ausgerüstetem Material (Gummi- und Kunststoffprodukte, Textilien) sowie oral durch Verschlucken von Spielzeugmaterial und durch Kauen und Lutschen von Antimon-haltigem Spielzeug. Für den Übergang von Antimon durch Kauen und Lutschen von Antimon-haltigem Spielzeug gibt es keine quantitativen Daten.

- In der Schweiz wurden im Rahmen des nationalen Bodenbeobachtungsprogramms (NABO) die Belastungen von Böden gemessen (Keller und Desaules 2001, FOEN 2007). Über 500 Bodenproben (0 - 20 cm) wurden gemessen. Die durchschnittliche Antimonkonzentration lag bei 8.6 mg/kg. Einer der bedeutendsten Eintragspfade sind Schiessübungen auf Schiessständen. Ein weiterer wichtiger Eintragspfad ist der diffuse Eintrag von Antimon auf Böden aus der Erosion von Bremsbelägen in Autos (FOEN 2007).

Tabelle 7-1: Exposition von Kindern gegenüber Antimon
(basierend auf BfR 2012, Kapitel 3.1.2, Seite 5, Tabelle 3).

Expositionsquelle	µg Sb/kg KG /Tag
Lebensmittel	0.10
Muttermilch	0.09
Aufnahme Hausstaub	0.6
Spielzeug (8 mg abschabbares Material)	0.6
Textilien (max. chron. Belastung; 200 mg Sb/kg)	0.5
Atemluft (460 ng/Tag und Person)	0.06
Trinkwasser (2 L/Tag)	0.03
Gesamtexposition:	1.98
TDI	6

Wie aus **Tabelle 7-1** ersichtlich wird, lastet die Gesamtexposition eines 12.5 kg schweren Kindes den TDI zu 33% aus, wenn man standardmässig von einer 100% Bioverfügbarkeit des Antimon aus dem Boden ausgeht.

7.5.2 Innere Exposition

For antimony, SCAHT applies the TIER 3-strategy as outlined in the methodology section.

Many data gaps exist for antimony. The absolute oral bioavailability of antimony from soil is not directly available for humans. Data on antimony absorption rate are poorly characterized in humans (section 7.5.2.1). Furthermore, there are no data following ingestion of soil in humans (section 7.5.2.2) and simiilar in vivo data in experimental animals are largely lacking (section 7.5.2.3). Therefore, given all these limitations, the Relative Oral Adjustment Factor (RAF) approach cannot be used to estimate the absolute oral bioavailability from soil (section 7.5.2.4).

In TIER 3, an alternative approach is considered based on information from in vitro bioaccessibility studies (section 7.5.2.5). Bioaccessibility could be used in certain cases as a predictor of bioavailability, provided that information on kinetics is available. However, in vitro studies with antimony showed that bioaccessibility data cannot be used as a surrogate for bioavailability. Therefore, SCAHT takes a conservative approach to the RAF-value (100%), which is in line with USEPA recommendations (USEPA 2007) for such situations.

In conclusion, considering a conservative dietary oral bioavailability of 10% in humans and a RAF of 100% to account for the higher uncertainty of the database, SCAHT uses an absolute oral bioavailability from soil of 10% for its risk assessment.

7.5.2.1 Oral bioavailability from food and/or water from dietary studies

Precise quantitative information regarding antimony absorption, distribution, and retention in humans is lacking. Toxicokinetic studies showed that oral absorption is slow and an oral absorption rate of 1% has been proposed for Sb(III) compounds such as antimony trioxide (ATO) (EC/HC 2010). Absorption rates between 5% and 20% have been observed in animals when administered in drinking water; examination of four persons after involuntary acute intoxication with Sb(IIII) potassium antimony tartrate revealed an absorption rate of 5% (WHO, 2003). Therapeutic use of antimonial compounds for the treatment of parasitic diseases (e.g. Sb(V) meglumine antimoniate, Sb(IIII) piperazine di-antimonyl tartrate) has also demonstrated poor systemic bioavailability (SCAHT notes:

not quantified) following oral exposure in humans. Data on absorption of antimony compounds with food were not located.

⇒ **From these data, SCAHT concludes that oral bioavailability of antimony compounds is well below 10%, but takes a conservative estimate of 10%.**

7.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

No studies have been located in the literature.

7.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

Only one study was located (Denys et al., 2012). Relative bioavailability values were obtained in juvenile swine (as measured in urine) for 11 soils from three different minining/smelting sites and were: mean 1-11% (range 0.2-20.9%) (Denys et al., 2012, Supplementary information, table S3).

7.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of antimony in soil compared to food or water, is to use the RAF approach proposed by the USEPA, as outlined in the Methodology section. A default medium-specific RAF value of 0.5 (50%) has been proposed for inorganics by the US Michigan State Department of Environmental Quality (NRC 2003, Table 2.1 pp.69-70). However, the justification for this value is not made explicit in the NRC report (personnal communication).

⇒ **Given all these data limitations, it is not possible to use the default Relative Oral Adjustment Factor (RAF) of 0.5 (50%) proposed for inorganics (NRC 2003, Table 2.1 pp.69-70) as outlined in the methodology section (TIER 2).**

⇒ **A further step would be to consider information from in vitro bioaccessibility studies (TIER 3) to potentially inform on relative absorption from soil (see section 7.5.2.5). It has been shown indeed that bioaccessibility could be used in certain cases as a predictor of bioavailability (DEPA 2003; Denys et al., 2012; Wragg and Cave, 2003; Wragg et al., 2011).**

7.5.2.5 Summary of the in vitro bioaccessibility information

Die Bioverfügbarkeit von Antimon aus dem Boden („Bioaccessibility“) ist wie bei anderen Metallen abhängig von seiner chemischen Form, der Partikelgrösse und den physikalisch-chemischen Eigenschaften des Bodens. Boden-pH-Wert, löslicher Gehalt organischer Substanzen, Metall-Hydroxid-Gehalt, Tongehalt und -art, die Anwesenheit organischer und anorganischer Liganden und die Konkurrenz durch andere Metallionen haben einen wesentlichen Einfluss auf die Mobilität des Antimons. Antimon, und hier ganz besonders die pentavalente Spezies, adsorbiert stark an organische oder anorganische Bodenmatrixbestandteile durch Adsorption an wasserhaltige Oxide von Eisen, Mangan und Aluminium (Blay 2000 *in* BAFU 2007; Hooda 2010; Leuz et al 2006 *in* USEPA 2014) und organische Stoffe. Antimon löst sich wenig im Boden und zeigt eine eingeschränkte Mobilität.

- For example, Pascaud et al (2014) using the BARGE-unified protocol could not measure antimony bioaccessibility from soil neither in the gastric nor the intestinal phase (results < detection limit); this was due to the nature of the mineral fraction (antimony-bearing phase); in their study, antimony was shown to be associated with the stable beudantite structure [$PbFe_3(OH)_6$ (SO_4) (AsO_4)]. Other studies suggest also that low antimony bioaccessibility might be explained by the association of antimony and soil bearing phases like iron oxy-hydroxides, sulphides, and refractory soil constituents (Denys et al., 2009, 2012; Gal et al.,

2007; Johnson et al., 2005) that are not easily dissolved by the artificial digestive solutions used in disgestive extraction tests.

⇒ **In general, it is assumed that the bioaccessibility of antimony from soil matrices will be low (ATSDR 1992; USEPA 2014).**

This is confirmed by the few in vitro bioaccessibility studies available from the literature; collectively, and however limited, they suggest that the human bioaccessible fraction of antimony from soil tends to be in the 5-15% range:

- Denys et al. (2008) measured antimony bioaccessibility in the soils using the unified Bioaccessibility Group Research Europe (BARGE) Method (UBM) digestion test. They found bioaccessibility values from soil for total antimony between 1.5 and 12%. Based on sequential extractions and physical analysis on the most contaminated soil, they found (i) that antimony was mostly occurring in the iron oxide and sulphide phases and in the pentavalent form; and (ii) that no change of this speciation [SB(V)] was occurring during the digestion process. Denys et al (2009) also observed bioaccessibility values of antimony from mining soils between 1-11%.
- The predominance of Sb(V) in the gastric fluid was also demonstrated by Bhagerifam et al. (2014), who found bioacccessibility values from a calcareous soil between ca. 3-20% using SBET.
- Wilson et al. (2013) measured by SBET oral bioaccessibility of antimony for two types of soils and found that the oral bioaccessible fraction was <3 % for total antimony in both soils.
- Li et al (2014) reported average antimony bioaccessibility values of 5.89 ± 6.44% (range: < 1-12%) for the SBET extraction; 7.83 ± 9.82% (range: < 1-17%) for the PBET (gastric) extraction; and 3.03 ± 3.53% (range: < 1-6%) for the PBET (intestinal) extraction, respectively.

7.5.2.5.1 Can bioaccessibility be used as a predictor of bioavailability? (TIER 3)

Denys et al. (2012) aimed to validate the UBM bioaccessibility data against in vivo relative bioavailability in a juvenile swine model, i.e to demonstrate that bioaccessibility data can be used as a surrogate measurement for its relative bioavailability. However, the UBM for antimony did not achieve validation in-vivo, except in urine, because of its low concentration in soil samples.

- The relative bioavailability values of antimony were approximately 10% or less for all soils and it was difficult to measure the amount of Sb absorbed into the target organs, apart from urine, for all but two highly contaminated soils (ca. 50'000 mg Sb/kg). The small relative bioavailability range covered was therefore not suitable for calibrating antimony bioaccessibility measurements from in vitro testing methods/protocoles.

⇒ **Therefore, since bioaccessibility information cannot be used in the present case as a reliable predictor of relative bioavailability in soilSCAHT takes a conservative approach to the RAF-value (100%), which is in line with USEPA recommendations (USEPA 2007) for such situations. This is justified by the limited database and therefore estimating relative or absolute oral bioavailability from soil is associated with a high uncertainty.**

⇒ **In conclusion, considering a conservative dietary oral bioavailability of 10% in humans and a RAF of 100% to account for the higher uncertainty of the database, SCAHT uses an absolute oral bioavailability from soil of 10% for its risk assessment.**

7.6 Risikoabschätzung

Von der WHO wurde im Jahre 2003 ein TDI-Wert von 6 µg Antimon/kg KG/Tag abgeleitet (WHO 2003).

Die Summe der in **Tabelle 7-1** berücksichtigten Expositionen aus unterschiedlichen Quellen ergibt eine tägliche orale Aufnahme von Antimon bei Kindern über Nahrung, Trinkwasser, Muttermilch und Hausstaub sowie eine inhalative Aufnahme über die Atemluft von 0.88 µg/kg KG/Tag. Damit wird der TDI von 6 µg/kg KG/Tag über die Hintergrundaufnahme nur zu 15% ausgelastet. Die Gesamtexposition, einschliesslich Spielzeug und Textilien beträgt 1.98 µg/kg KG/Tag und lastet den TDI zu 33% aus. Rein rechnerisch könnte eine zusätzliche Belastung in Höhe von 4.02 µg/kg KG/Tag geduldet werden, ohne den TDI zu überschreiten.

In der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten) ist für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, ein Konzentrationswert von 50 mg Sb/kg Boden festgelegt.

Unter der Annahme, dass ein Kind täglich 250 mg Boden verschluckt, der mit 50 mg Antimon pro kg Boden kontaminiert ist, würde eine zusätzliche Gesamtbelastung von 12.5 µg oder 1 µg/kg KG/Tag für ein 12.5 kg schweres Kind entstehen. Unter Berücksichtigung einer limitierten Bioverfügbarkeit von Antimon aus dem Boden von 10% reduziert sich die Belastung auf 0.1 µg/kg KG/Tag.

Ein zusätzliches Gesundheitsrisiko durch das Verschlucken kontaminierter Böden ist unwahrscheinlich, weil die Gesamtexposition gegenüber Antimon aus der unvermeidbaren Hintergrundbelastung (1.98 µg Sb/kg KG/Tag) und dem Verschlucken von kontaminiertem Boden (0.1 µg Sb/kg KG/Tag) weniger als etwa 2.1 µg/kg KG/Tag beträgt. Das entspricht etwa 35% der zulässigen täglichen Aufnahmemenge. Rein rechnerisch besteht aus humantoxikologischer Sicht ein grosser Spielraum zur Erhöhung des bestehenden Sanierungswertes. Geht man von einer zulässigen täglichen Höchstzufuhr in Höhe des TDI von 6 µg/kg KG/Tag Tag aus und einer Hintergrundbelastung durch in Höhe von 1.98 µg/kg KG/Tag, könnten zusätzlich 4.02 µg Sb/kg KG/Tag aufgenommen werden. Unter der Annahme einer 10% oralen Bioverfügbarkeit von Antimon nach direkter Bodenaufnahme würde das Verschlucken von 250 mg Boden der mit etwa 2010 mg Sb/kg Boden[2] kontaminiert ist, wahrscheinlich kein Gesundheitsrisiko darstellen.

⇒ Der bestehende Grenzwert von 50 mg Sb/kg Boden könnte also um den Faktor 40 auf 2010 mg Sb/kg Boden angehoben werden, unter der Annahme einer 10% Bioverfügbarkeit von Antimon aus dem Boden. Selbst bei der Annnahme einer 100% oralen Bioverfügbarkeit von Antimon nach direkter Bodenaufnahme, könnte unter Berücksichtigung der Hintergrundexposition der bestehende Grenzwert noch um etwa den Faktor 2[3] angehoben werden.

⇒ Ob dies aus Gründen des Umwelt- und Gewässerschutzes vertretbar ist, muss evaluiert werden. Die Belastung durch das Verschlucken von kontaminiertem Boden beträgt beim

[2] Der derzeitige Sanierungswert von 50 mg Sb/Kg Boden führt zu einer zusätzlichen Exposition in Höhe von 0.1 µg /Kg KG/Tag. Eine zusätzliche Exposition in Höhe von 4.02 µg /Kg KG/Tag durch das Verschlucken von Boden würde bei einer Kontamination des Bodens mit 2010 mg Sb/Kg Boden stattfinden [2010=(4.02x50)/0.1].

[3] Der TDI liegt bei 6 µg/Kg KG/Tag, die Exposition nach Verschlucken von belastetem Boden liegt bei 1 µg/Kg KG/Tag und die Hintergrundbelastung bei 1.98 µg /Kg KG/Tag. Die Gesamtbelastung liegt als bei 2.98 µg/Kg KG/Tag und damit um den Faktor 2 niedriger als der TDI.

aktuellen Sanierungswert 15% der Hintergrundbelastung. Inwiefern eine Erhöhung der zusätzlichen Belastung ein breite Akzeptanz in der Bevölkerung findet, ist eine Frage der Risikokommunikation.

⇒ **Antimon ist als krebserregend im Menschen eingestuft. Aufgrund der unzureichenden Datenlage zur kanzerogenen Wirkung im Menschen ist aus Sicht des SCAHT eine Erhöhung des Sanierungswertes nicht wünschenswert.**

7.7 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften in Europa, USA und Kanada (z.B. Carlon 2007; Provoost et al, 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden (siehe **Anhang 1**).

F: 100; **CH: 50**; USA: 31; CAN: 20; NL: 15; I: 10; E: 6; A: 5 (mg/kg dm).

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8 Non dioxin-like (NDL)-PCBs

8.1 Datenblatt

Handlungsbedarf	Nein	Aktueller Sanierungswert von 1 mg NDL-PCBs/kg Boden kann beibehalten werden. Auch dioxinartige PCBs sollten aufgrund ihrer toxikologische Eigenschaften und der Persistenz in der Umwelt in den Anhang 3 AltV aufgenommen werden[1].
Gefährdungspotential	Hoch	Multiorgantoxizität (in vivo und im Menschen) einschliesslich Kanzerogenität. Akkumulation im Fettgewebe.
Kanzerogen	Ja	IRAC: Wahrscheinlich kanzerogen für den Menschen (basierend auf in vivo-Daten)
Mutagen	Nein	Keine Effekte auf Gene oder Chromosomen (in vitro und in vivo) aber kanzerogene Effekte infolge von DNA-Schäden als sekundärer Effekt von oxidativem Stress.
Reprotoxisch	Ja	Endokrine und reprotoxikologische Effekte (Hormonhaushalt) (in vivo, im Menschen vermutet).
Neurotoxisch	Ja	Entwicklungsneurotoxizität (verzögerte Entwicklung) und Verhaltensauffälligkeiten („neurobehavioural“) (in vivo, im Menschen vermutet).

[1] Dioxins and dioxin-like PCBs (due to their similar toxicological properties) are often considered together within the context of public health (see e.g. at EFSA level, http://www.efsa.europa.eu/en/topics/topic/dioxins.

Dioxins and polychlorinated biphenyls (PCBs) are toxic chemicals that persist in the environment and accumulate in the food chain. Their presence in the environment in Europe has declined since the 1970s, following concerted efforts by public authorities and industry. In the context of EFSA’s work, ‘dioxins’ refers to two groups of compounds: Polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs). Dioxins have no technological or other use, but are generated in a number of thermal and industrial processes as unwanted and often unavoidable by-products. In contrast to dioxins, PCBs had widespread use in numerous industrial applications, and were produced in large quantities for several decades, until they were banned in most countries by the 1980s.

Dioxins and PCBs are found at low levels in many foods. Longer-term exposure to these substances has been shown to cause a range of adverse effects on the nervous, immune and endocrine systems, and impair reproductive function. They may also cause cancer. Their persistence and the fact that they accumulate in the food chain, notably in animal fat, therefore continues to cause some safety concerns.

Dioxins and some PCBs referred to as dioxin-like PCBs (due to their similar toxicological properties) are often considered together within the context of public health. Other PCBs referred to as ‘non dioxin-like PCBs’ have a different mechanism of toxicity but can also cause adverse effects on health.

Andere	Ja	Bei den nicht neoplastischen Läsionen stehen neben den reprotoxischen und neurotoxischen Effekten die Immuntoxizität im Vordergrund: Morphologische Veränderungen der lymphatischen Organe (Thymus, Knochenmark) Funktionelle Störungen der humoral- und zellvermittelten Immunantwort
Gesundheitsbasierter Referenzwert		Obwohl es sich um nicht-mutagene Kanzerogene handelt, kann kein Schwellenwert abgeleitet werden, weil NDL-PCBs immer in Mischungen mit DL-PCBs und/oder Dioxinen auftreten. Anstatt einer Einzeldosis wird die Gesamtbelastung des Körpers (internal body burden: BB) durch Akkumulation der NDL-PCB im Körper nach wiederholter Exposition als Gesundheitsindikator verwendet. NOAEL BB: 500 µg NDL-PCBs/kg KG (basierend auf NDL-PCB-6)
Exposition		
Äussere Exposition Boden (250 mg)		1 mg NDL-PCB-6/kg Boden = 0.25 µg / 250 mg Boden = 0.02 µg NDL-PCB-6/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 100% Bioavailability: 0.02 µg NDL-PCB-6/kg KG/Tag (KG: 12.5kg) = 20 ng NDL-PCB-6/kg KG/Tag (KG: 12.5kg) Bei 50% Bioavailability: 0.01 µg NDL-PCB-6/kg KG/Tag (KG: 12.5kg) = 10 ng NDL-PCB-6/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte mittlere NDL-PCB-6-Aufnahme über die Nahrung (Kinder 1-3 Jahre): 8.3 – 52.7 ng NDL-PCP-6/kg KG/Tag
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Wahrscheinlich	Die geschätzte Aufnahmemenge von NDL-PCB-6 liegt in der gleichen Grössenordnung wie die Aufnahmemenge über die Nahrung. Entscheidend für die Risikobeurteilung ist aber die Akkumulation von NDL-PCB-6 im Körper (BB), sie sollte 500 µg NDL-PCBs/kg KG nicht überschreiten. Durch das Verschlucken von kontaminiertem Boden über einen Zeitraum von drei Jahren nimmt der Körper insgesamt 10.95 µg NDL-PCB-6/kg KG/3 Jahre auf, wenn man eine Bioaccessibility von 50%

		annimmt. Das entspricht nur ≈ 2.2% des zulässigen NOAEL BB und ein zusätzliches Gesundheitsrisiko ist unwahrscheinlich. Auch wenn man 100% Bioaccessibility annimmt, ist der Beitrag durch Verschlucken von NDL-PCP-6 aus dem Boden mit 4.3% des NOAEL BB gering. Geschätzte NDL-PCB-16-Aufnahme über die Nahrung: 8.3 – 52.7 ng NDL-PCP-6/kg KG/Tag Geschätzte NDL-PCB-16-Aufnahme durch direkte Bodenaufnahme: 12 ng NDL-PCB-6/kg KG/Tag Gesundheitsbasierter Referenzwert NOAEL BB: 500 µg NDL-PCBs/kg KG (basierend auf NDL-PCB-6) Geschätzte NDL-PCB-16-Aufnahme durch direkte Bodenaufnahme über drei Jahre: 10.95 µg NDL-PCB-6/kg KG ≈ 2.2% von NOAEL BB: 500 µg NDL-PCBs/kg KG.
Grenzwert im Vergleich		UK: 8 (nicht spezifiziert); CZ: 5 (ΣPCB7); CAN: 1.3; A (ΣPCB7) & NL 1; CH: 1 (ΣPCB6); B: 0.9 (nicht spezifiziert); D: 0.8 (ΣPCB6); USA, 0.5 (nicht spezifiziert); E: 0.08 (nicht spezifiziert); S: 0.02 (nicht spezifiziert); I: 0.001 (nicht spezifiziert) (mg / kg dm)
Datenlage	Zufriedenstellend	Es gibt keine Studien zur Bioverfügbarkeit von NDL-PCBs aus dem Boden im Menschen, aber es gibt einige Tierstudien. Epidemiologische Studien erlauben keine Zuordnung der Befunde zu den einzelnen Mischungskomponenten. PCBs findet man in der Regel als Mischung von NDL-PCBs und DL-PCBs zusammen mit Verunreinigungen mit anderen Dioxinen. Die Verwendung eines Toxizitätsäquivalenzfaktors, wie er bei Dioxinen eingesetzt wird, scheitert daran, dass die Wirkungsmechanismen der NDL-PCBs nicht einheitlich sind (keine Bindung an den AhR-Rezeptor).

8.2 Zusammenfassung

There are currently no sound scientific data which would support a change in the current clean up value for non dioxin-like polychlorinated biphenyls ((NDL)-PCBs) of 1 mg/kg soil for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly, as outlined in the Swiss Contaminated Sites Ordinance (CSO)[1].

The general population is primarily exposed to PCBs via the food. PCBs bio-accumulate mainly in animal fatty tissues and can bio-magnify along the food chain. PCBs are not mutagenic but they target multiple organs and exert a vast array of toxicological effects such as endocrine, reproductive, immune, neurodevelopmental and carcinogenic effects. The most sensitive effects in humans are liver and thyroid toxicity.

No health based guidance value for humans can be established for NDL-PCBs. EFSA concluded that despite the absence of mutagenicity, which would justify a threshold approach for the hazard characterisation, no health based guidance value for NDL-PCBs could be established because simultaneous exposure to dioxins (i.e. polychlorinated dibenzo-p-dioxins/polychlorinated dibenzofurans PCDD/PCDF) and dioxin-like PCBs (DL-PCBs) hampers the interpretation of the results of the toxicological and epidemiological studies, and the toxicological database on effects of individual NDL-PCB congeners is rather limited. EFSA concluded that a margin of exposure approach (MOE)[2] should be applied using NOAELs and BMDLs as a reference point for the risk characterisation.

Since PCBs accumulate in the human body as a consequence of continuous exposure and are slowly excreted due to long biological half-life, EFSA considered it was most appropriate to base its evaluation on internal body burden (BB)[3] calculations.

EFSA derived a human NOAEL body burden (NOAEL BB) of 500 µg/kg body weight (bw) that is supposed to be without adverse effects on human health. This was considered to be a conservative body burden at the NOAEL which applies to all individual NDL-PCBs and for the sum of NDL-PCBS occurring in human tissues.

A comparison of the estimated actual body burden from dietary exposure with the EFSA NOAEL BB for NDL-PCBs in human tissues of 500 µg/kg bw reveals a NOAEL Margin of body burden (MoBB) of about 10. This safety margin seems small and from that perspective additional exposure to PCBs such as from direct ingestion of contaminated soil should be avoided.

The Swiss Contaminated Sites Ordinance (CSO) set a clean up value for the sum of the six indicator NDL-PCB at 1mg/kg. At that level, a daily accidental ingestion of 250 mg NDL-PCB-contaminated soil by a 12.5 kg child would contribute to an additional external exposure of 0.02 µg/kg bw/day. Assuming an oral bioavailability of NDL-PCBs from soil of 50%, the internal exposure would be reduced to 0.010 µg/kg bw/day or 10 ng/kg bw/day. Based on this exposure scenario NDL-PCB

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

[2] The MOE is a tool used by risk assessors to consider possible safety concerns arising from the presence in food and feed of substances which are both genotoxic (that is, which may damage DNA, the genetic material of cells) and carcinogenic. The MOE is a ratio of two factors which assesses for a given population the dose at which a small but measurable adverse effect is first observed and the level of exposure to the substance considered. A higher MOE is associated with a lower health risk.

[3] BB describes the total amount of a harmful substance in a live body. If bioaccumulants are present in the environment, the body burden will likely increase with time.

uptake from soil would be in the same order of magnitude as the lower bound dietary exposure of toddlers and other children.

However, cumulative exposure to NDL-PCBs from daily soil ingestion over 3 years would result in an additional exposure of 10.95 µg/kg bw which accounts for only 2.2% of the EFSA-derived NOAEL BB of 500 µg/kg bw. Therefore the SCAHT argues that the additional health risk from soil ingestion appears to be low.

8.3 Gefährdungspotential

Polychlorinated biphenyls (PCBs) are a widespread class of persistent organic chemicals that accumulate in the environment and humans and are associated with a broad spectrum of adverse health effects. Depending on the number of chlorine atoms and their position 209 theoretically possible congeners exist. Based on these structural characteristics and their toxicological effects PCBs can be divided into two groups: a group of 12 congeners with dioxin-like planar structure which show toxicological properties similar to dioxins and are therefore termed "dioxin- like PCBs" (**DL-PCBs**); and a remaining group of 197 congeners with non-planar structure due to chlorine substitution at ortho position that have a different toxicological profile and are therefore referred to as "non dioxin-like PCBs" (**NDL-PCBs**). PCBs are usually found as mixtures of NDL-PCBs and DL-PCBs, along with impurities of other dioxins such as polychlorinated dibenzo-p-dioxins (PCDDs), or polychlorinated dibenzofurans (PCDFs). The different compositions as well as the presence of toxicologically relevant impurities of dioxins affect the toxicological profile of the individual mixtures.

Technical PCB mixtures such as Aroclors® (USA), Kanechlors® (Japan) and Clophens® (Germany), were manufactured and used worldwide as dielectric fluids in capacitors and transformers, heat transfer fluids, hydraulic fluids, lubricating oils, and as additives in pesticides, paints, copy paper, adhesives and plastics between the 1930's and the mid-1970s (WHO 1993 *in* US EPA 2003, as cited). PCBs were banned in the late 1970s in many countries of North America and Western Europe, 1986 in Switzerland and 2004 worldwide by the Stockholm Convention on POPs. Despite the ban on the manufacture, processing and distribution of PCBs their entry into the environment still occurs, especially due to improper disposal practices or leaks in electrical equipment and hydraulic systems still in use. PCBs can also enter soil and surface water through wet or dry deposition because they are long-range pollutants that are globally circulated by atmospheric transport. Their environmental fate is primarily governed by their lipophilic properties and high stability against chemical and microbiological degradation. PCBs bio-accumulate mainly in animal fatty tissues and can bio-magnify along the food chain. Altogether, this makes PCBs ubiquitous pollutants in all environmental media and biota.

8.3.1 Toxicological profile of PCB mixtures

PCBs target multiple organs and exert a vast array of toxicological effects such as endocrine, reproductive, immune, neurodevelopmental, neurobehavioural and carcinogenic effects. PCB structural properties as well as toxic effects have not been completely elucidated yet. From a mechanistic point of view the NDL-PCBs elicit different types of biological responses than the dioxins and DL-PCBs. These effects occur via multiple toxicity pathways with several underlying modes of action (see **Table 8-1**), but do not involve binding to the aryl hydrocarbon receptor (AhR) (EFSA 2005, pp. 85-86).

Table 8-1: Mechanistic aspects of PCBs toxicity

Endpoint	Mode of action
Endocrine effects	Interaction with the androgen oestrogen and progesterone receptors as well as thyroid hormone receptor and transporter
Immunotoxicity	Morphological changes in lymphoid organs, functional impairment of humoral- and cell-mediated immune responses Reduced lipopolysaccharide induced proliferative response in splenocytes, reduced antibody secretion and impaired neutrophil function
Neurotoxicity	Alteration in cellular signalling pathways (PKC), homeostasis (calcium) and neurotransmitters (dopamine, acetylcholine) levels Alteration in gross motor and cognitive functions development, behavioural changes

Many toxicity studies have been performed with commercially available PCB mixtures (marketed e. g. under the trade name Aroclor® 1242, 1248, 1254,1260, etc.[4]) of varying composition and chlorine content (ATSDR 2000, 2011) as well as individual PCB congeners (NDL- or DL-PCBs).

⇒ The exact composition of technical PCB mixtures (e. g. Aroclors) used in experimental toxicity studies is generally not known, and it is therefore difficult to allocate the observed effects to NDL-PCBs or DL-PCBs. Besides, for those effects related to NDL-PCBs exposure, they are often not specific for NDL-PCBs alone but are also to be seen following exposure to polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs), and DL-PCBs (EFSA 2005, pp.61-62). Similarly, existing epidemiological or occupational exposure data do not allow an estimation of the toxicity that can specifically be attributed to the NDL-PCBs.

Experimental studies (mainly monkeys and rats) that have investigated either oral exposure to **technical PCB mixtures** (e. g. Aroclor 1242, 1248, 1254, 1260) or **individual NDL-PCBs congeners** (including i. a. PCB 28, 52, 101, 153, 180) showed multi-target organ toxicity with effects primarily on the gastrointestinal tract, liver, thyroid, lymphoid organs and the developing brain as well as endocrine, reproductive and carcinogenic effects. The most sensitive effects (i. e. in term of LOAEL) were liver and thyroid toxicity. Dose-dependent effects are often observed, in particular for endocrine, reproductive and developmental endpoints.

Among non-cancer effects reported to be associated with environmental PCB exposure (mixtures), adverse reproductive outcomes, delayed neurodevelopment and impairment of the developing immune system are considered to be the most important. The epidemiological studies however do not allow differentiation between the effects caused by NDL-PCB and DL-PCB, and PCDD/PCDF (EFSA 2005, p.96). No studies on chronic toxicity and carcinogenicity have so far been published for any individual NDL-PCBs (EFSA 2005, p.68).

8.3.1.1 Endocrine effects

Experimental animal studies with Aroclors have shown a broad range of reproductive related endocrine effects, such as altered litter sex ratio, altered serum luteinizing hormone and other sex related hormones levels across the estrous cycle in a two generation rat study (Aroclor 1221) (ATSDR 2011, p.3); decreased serum levels of thyroid hormones (T3, T4) in rats and enlarged thyroid glands in Rhesus monkeys, together with histological changes in the thyroid (Aroclor 1254) (EFSA 2005, p.63); increase of corticosterone levels and decrease of adrenal cortex hormones and DHEA levels in rats (Aroclor 1242, 1221) (EFSA 2005, p.63). Available human studies are scarce but it was suggested that exposure to PCB-153 (and other PCBs) is associated with the prevalence of type 2 diabetes (ATSDR 2011, pp.2-3).

8.3.1.2 Reproductive and developmental toxicity

Experimental animal studies with Aroclors (1248, 1254, 1260) have shown oestrous cycle modifications, decreased conception rate and increased foetal mortality in monkeys, as well as reduced litter sizes in rats (EFSA 2005, pp.63-64). Acute exposure of pregnant rats to NDL-PCB 132 resulted in decreased epididymal weight, sperm count, and motility in their male offspring at adulthood (ATSDR 2011, p.7). Some epidemiological studies have suggested an association with prenatal and/or postnatal exposure to PCBs and adverse reproductive effects in humans, e. g. cryptorchidism in boys (PCB total, Brucker-Davis et al., 2008), reduced oestradiol or testosterone

[4] Produced by Monsanto between 1930 and 1977, the Aroclors are identified by a four-digit numbering code in which the first two digits indicate the type of mixture and the last two digits indicate the approximate chlorine content by weight percent (ATSDR 2000).

levels (sum of the six indicators PCB- 28, 52, 101, 138, 153, and 180, Cao et al., 2008), delayed and/or reduced genital development (PCB-138, -153 and -180, Den Hond et al 2002) (reviewed by ATSDR 2011, pp.7-9).

8.3.1.3 Immunotoxicity

Experimental studies with Aroclors (1248, 1254) on monkeys have shown reduced levels of circulating immunoglobulines (IgG, IgM), pathological changes in lymphoid tissues (e. g. thymus) and functional impairment of humoral- and cell-mediated immune responses (e. g. reduced B cell numbers, reduced cytotoxic T-lymphocyte response, and reductions in plaque forming cell response) (EFSA 2005, pp. 64-65). In humans, prenatal exposure to PCBs has been associated with reduced thymus size at birth and possible impaired immunologic development, whereas perinatal exposure to PCBs has been associated with impaired immune responses to vaccinations and deficient immune function in children. Another study in humans suggests a potential immunomodulatory effect of PCBs on the prevalence of anti-GAD antibodies (which are positively associated with type 1 diabetes or latent autoimmune diabetes in adults) (reviewed in ATSDR 2011, p.4).

8.3.1.4 Neurodevelopmental/neurobehavioural toxicity

In experimental studies, neuro-developmental effects were associated with modulation of motor activity, learning and memory, neural damage and abnormal brain development, particularly in the offspring of rodents following *in utero* exposure to PCBs (ATSDR 2011, p.5). Impaired performance on a spatial learning and memory task was also observed in the progeny of monkeys exposed to Aroclor 1248 (Levin et al., 1988 *in* EFSA 2005, p.65). Neurobehavioural effects were associated in rodents with reduced maternal licking and grooming, decreased social interaction and increased anxiety level following exposure to DL-PCB 77 and 126 (ATSDR 2011, p.5). In humans, many epidemiological studies have investigated the association between prenatal or postnatal exposure to PCBs and adverse neurodevelopmental and/or neurobehavioural outcome (e. g. Goodman et al., 2010). While studies suggest that prenatal exposure to PCBs is associated with neurodevelopmental effects there is limited evidence to support that postnatal exposure may be associated with neurodevelopmental deficit in young children or later in life. For example, a US occupational cohort study suggested that females would be susceptible to neurodegenerative disease from PCBs exposure but not men (Steenland et al., 2006 *in* ATSDR 2011, p.4) (data were recently reviewed by ATSDR 2011, pp.7-9).

8.3.1.5 Mutagenicity

Results of *in vitro* and *in vivo* genotoxicity studies indicate that PCBs are not mutagenic at the gene or chromosome level. Some NDL-PCBs, in particular the lower chlorinated congeners caused DNA damage, probably resulting from the formation of reactive oxygen species. Available information on in vivo genotoxic effects of PCBs in humans is limited by confounding exposures that involved mixtures of chemicals (EFSA 2005, p.3).

8.3.1.6 Carcinogenicity

No studies on chronic toxicity and carcinogenicity have so far been published for any individual NDL-PCB (EFSA 2005, p. 68).

The International Agency for Research on Cancer (IARC) classified PCBs in Group 2A (probably carcinogenic to humans), based on limited evidence in humans and sufficient evidence in animals. In two-stage initiation-promotion studies, technical PCB mixtures containing NDL-PCBs as well as DL-PCBs promote liver carcinogenesis in rats following initiation with genotoxic carcinogens. Data from animal experiments with several technical mixtures (Aroclor 1016, 1242, 1254 and 1260) indicate that PCBs can cause liver and thyroid neoplasms in rats. Evaluation of the cancer studies in rats with technical PCBs mixtures and comparison with data obtained with TCDDs indicate that the dioxin-like

components in technical PCB mixtures are likely to be responsible for the carcinogenic response of these mixtures. No peer-reviewed data are available on the carcinogenicity of individual NDL-PCB congeners (EFSA 2005, p.3).

Occupational exposures to PCBs have been reported to be associated with an increased risk of cancer of the digestive system and possibly other sites. Some studies suggest that environmental PCB exposure may be linked to the development of breast cancer, although perhaps only in certain vulnerable sub-groups (EFSA 2005, p.96).

Some epidemiological data suggest also a possible association between PCBs exposure and an increased risk of developing a non-Hodgkin's lymphoma (PCBs-156, -180, -194), testicular cancer or prostate cancer (PCB-153) (ATSDR 2011, pp.10-11).

8.4 Gesundheitsbasierter Referenzwert

In 2005, the EFSA CONTAM Panel concluded that no health based guidance value for NDL-PCBs could be established based on the facts that: i) simultaneous exposure to PCDDs/PCDFs and DL-PCBs hampered the interpretation of the results of the toxicological and epidemiological studies; ii) human data on environmental exposure to PCB mixtures could not differentiate between the effects of NDL-PCBs, DL-PCBs and PCDDs/PCDFs; iii) the toxicological database on health effects of technical PCB mixtures was not suitable for the separate assessment of individual NDL-PCBs; and iv) the toxicological database on effects of individual NDL-PCB congeners was rather limited (EFSA 2005).

As a result, and despite the absence of mutagenicity of NDL-PCBs which would have justified a threshold approach for their hazard characterisation, the Panel used a Margin of Exposure approach based on estimated human internal body burden (BB) for the health risk characterisation. Since PCBs accumulate in the human body as a consequence of continuous exposure and are slowly excreted due to long biological half-life, the Panel considered it was most appropriate to base its evaluation on internal BB calculations which are more appropriate than evaluations based on the external dose. Therefore, EFSA derived a concservative human NOAEL body burden (NOAEL BB) of 500 µg/kg bw that is supposed to be without adverse effects on human health, and which applies to all individual NDL-PCBs and for the sum of NDL-PCBs occurring in human tissues.

EFSA's MoE approach to derive the overall NOAEL BB was based on the following considerations:

- **First**, the NOAELs of the most sensitive toxicological effects (liver and thyroid toxicity) seen in 90-day rat studies with three individual NDL-PCB congeners (PCB 28, 128, and 153) were identified to be between 30 - 40 µg/kg bw/day.
- **Second**, the EFSA's CONTAM Panel estimated the total body burden from accumulation of the three individual PCBs over the study period. A NOAEL of 400, 800, and 1'200 µg/kg bw respectively was estimated for PCB 28, 128, and 153.
- **Third**, the Panel compared the estimated BBs at the NOAEL for different effects in animals with the estimated median human body burden derived from the analyses of human milk. The "margin of body burdens" at the NOAEL (NOAEL MoBB) was calculated by dividing the estimated animal body burden with the estimated median human body burden.

  ⇒ NOAEL MoBBs of 900, 6'300, and 85 were obtained for the effects on liver and/or thyroid of PCB 28, 128, and 153, respectively.

  ⇒ Although PCB 28, 128, and 153 showed similar potencies in the 90-day toxicity studies PCB 153 had the lowest NOAEL MoBB due to its abundance in human tissues. Application of the same approach to experimental animal studies on reproductive and developmental effects, oestrogenicity, thyroid effects and effects on the immune system, and the developing nervous system revealed NOAEL MoBBs that were higher than 1'600 (EFSA 2005, p.4).

- **Fourth**, the panel compared toxicological data of other congeners present in food and human tissues and identified that the LOAEL BB for the most sensitive effects (liver, thyroid) were 10 times higher than the NOAEL BB (400, 800, and 1'200 µg/kg bw for PCB 28, 128, and 153, respectively). Based on this observation the panel chose an **overall body burden of 500 µg/kg bw** as a representative conservative body burden at the NOAEL (NOAEL BB) for all individual NDL-PCB and for the sum of NDL-PCB occurring in human tissues.
- **Fifth**, based on the median total concentration of all NDL-PCB measured in human milk sampled in European countries of about 240 ng/g fat and assuming 20% fat content in the human body a median human body burden of about 50 µg/kg bw was estimated. Consequently, the overall NOAEL MoBB is about 10.

8.5 Exposition

Based on their human health and/or environmental toxicological relevance and potential for exposure six NDL-PCBs, i. e. PCB 28, 52, 101, 138, 153 and 180, are often considered as appropriate indicators for different PCB exposure patterns in various sample matrices (e. g. soil, food). However, there is still some inconsistency in the use of these indicator PCBs for regulatory purposes, whether it deals with soil protection or dietary exposure assessment. In the context of dietary exposure assessement EFSA's evaluation (2012) of human health risk from dietary exposure to PCB is also based on the sum of the six PCB congeners. It is assumed that the sum of these six indicator PCBs represents about 50% of the total NDL-PCBs in food (EFSA 2012). However, the reporting of human dietary NDL-PCB exposure data can be based on the sum of three PCB congeners (PCB 138, 153 and 180), six PCBs (28, 52, 101, 138, 153, 180) or seven PCBs congeners (28, 52, 101, 118, 138, 153, 180).

8.5.1 Äussere Exposition

The general population is exposed to PCBs, primarily via consumption of contaminated foods. PCBs bio-accumulate in animal fatty tissues and bio-magnify in the food chain. To a minor extent PCBs can also accumulate in terrestrial vegetation. Strong sorption of PCBs to soil organic matter and clay inhibits to a certain extent the uptake of PCBs in plants through the roots. Children are exposed to PCBs in the same manner as the general population. Exposure also may occur by transfer of PCBs that have accumulated in women's bodies to the fetus across the placenta. Because PCBs are lipophilic substances they can accumulate in breast milk and be transferred to nursing infants.

In 2012, EFSA updated the monitoring of levels of dioxins and PCBs in food and feed (EFSA 2012). Depending on the population group average exposure to the sum of the six NDL-PCB indicators was estimated to be between 4.3 - 25.7 ng/kg bw/day and at the 95th percentile between 7.8 - 53.7 ng/kg bw/day. When comparing 2002 - 2004 data with data from 2008 - 2010 a decrease in the dietary exposure was observed in almost all (61/68) population groups, estimated to be between 2.0 and 75.6 %.

Results showed that younger age groups (infants, toddlers and other children) were more exposed than other population groups. In particular, toddlers seem to be the most exposed group with average exposures between 8.3 and 52.7 ng/kg bw/day and 95th percentile exposures between 8.8 and 53.5 ng/kg bw/day (see **Table 8-2**). These levels are in the range of those reported from exposure studies between 1994 and 2004 with averages between 13.5 and 25 ng/kg bw/day for the sum of the 6 indicator NDL-PCBs, as referenced in the opinion of the CONTAM Panel on NDL-PCBs (EFSA 2005).

Table 8-2: Dietary exposure to the sum of the six NDL-PCBs indicators for the period 2008 - 2010 expressed in ng/kg bw per day estimated across the different population groups

(Source: EFSA Journal 2012;10(7)2832, Table 22, pp.53-54)

Country	Survey acronym	N[a]	Lower bound		Upper bound	
			Mean[b]	P95[c]	Mean[b]	P95[c]
Infants						
Bulgaria	NUTRICHILD	860	7.2	17.7	11.0	35.4
Italy	INRAN SCAI 2005 06	16	8.3	31.7	8.5	35.4
Toddlers						
Belgium	Regional Flanders	36	10.8	20.0	11.8	23.5
Bulgaria	NUTRICHILD	428	12.8	33.2	23.0	53.5
Finland	DIPP	497	13.6	41.0	15.9	46.1
Germany	DONALD 2006	92	12.5	27.9	13.5	29.3
Germany	DONALD 2007	85	11.4	26.1	12.3	27.2
Germany	DONALD 2008	84	11.2	23.4	11.8	23.4
Italy	INRAN SCAI 2005 06	36	16.9	36.6	19.2	39.8
Netherlands	VCP kids	322	8.3	18.2	8.8	20.5
Spain	enKid	17	18.9	52.7	25.7	52.7
Other children						
Belgium	Regional Flanders	625	9.3	24.4	10.2	26.9
Bulgaria	NUTRICHILD	433	11.3	36.7	19.6	50.6
Czech Republic	SISP04	389	12.4	41.7	15.5	44.7
Denmark	Danish Dietary Survey	490	10.8	24.3	12.8	26.7
Finland	DIPP	933	13.5	33.8	15.6	37.0
Finland	STRIP	250	7.4	19.9	8.2	21.7
France	INCA2	482	14.7	31.6	17.1	33.6
Germany	DONALD 2006	211	8.4	19.2	9.3	21.5
Germany	DONALD 2007	226	8.2	17.4	9.3	19.2
Germany	DONALD 2008	223	8.8	19.2	9.7	23.2
Greece	Regional Crete	839	8.4	22.7	9.6	24.1
Italy	INRAN SCAI 2005 06	193	16.1	45.4	18.8	47.2
Latvia	EFSA TEST	189	6.2	17.0	8.1	22.8
Netherlands	VCP kids	957	7.3	16.6	7.8	16.7
Spain	enKid	156	13.7	38.5	18.1	42.6
Spain	NUT INK05	399	15.0	38.8	18.5	42.1
Sweden	NFA	1,473	9.2	20.9	10.3	22.7
Adolescents						
Belgium	Diet National 2004	584	3.7	12.4	4.5	13.1
Cyprus	Childhealth	303	4.7	15.9	5.9	17.1
Czech Republic	SISP04	298	9.3	29.2	11.0	30.8
Denmark	Danish Dietary Survey	479	6.0	11.8	7.2	14.9
France	INCA2	973	7.4	16.7	8.8	18.2
Germany	National Nutrition Survey II	1,011	3.3	8.5	4.3	11.3

Table 8-2: cont'd

Country	Survey acronym	N[(a)]	Lower bound		Upper bound	
			Mean[(b)]	P95[(c)]	Mean[(b)]	P95[(c)]
Adults						
Belgium	Diet National 2004	1,304	4.6	14.7	5.4	15.3
Czech Republic	SISP04	1,666	6.2	19.7	7.4	21.3
Denmark	Danish Dietary Survey	2,822	5.4	10.8	6.3	11.8
Finland	FINDIET 2007	1,575	6.1	18.6	6.9	19.7
France	INCA2	2,276	6.7	14.3	8.0	15.9
Germany	National Nutrition Survey II	10,419	4.3	14.4	5.3	15.9
Hungary	National Repr Surv	1,074	4.1	9.5	5.6	11.8
Ireland	NSIFCS	958	4.8	10.9	6.7	13.5
Italy	INRAN SCAI 2005 06	2,313	7.8	31.9	8.7	33.0
Latvia	EFSA TEST	1,306	4.6	16.0	5.9	17.6
Netherlands	DNFCS 2003	750	3.8	8.1	4.5	9.5
Spain	AESAN	410	8.0	21.0	9.6	25.0
Spain	AESAN FIAB	981	9.5	24.2	11.5	26.7
Sweden	Riksmaten 1997 98	1,210	5.7	12.8	6.0	13.1
United Kingdom	NDNS	1,724	4.1	9.8	5.3	11.7
Elderly						
Belgium	Diet National 2004	518	6.0	17.4	6.6	17.4
Denmark	Danish Dietary Survey	309	6.9	14.2	7.7	15.9
Finland	FINDIET 2007	463	7.5	23.0	8.1	23.2
France	INCA2	264	7.3	16.5	8.4	18.1
Germany	National Nutrition Survey II	2,006	5.1	17.3	5.9	18.3
Hungary	National Repr Surv	206	3.3	6.4	4.5	9.5
Italy	INRAN SCAI 2005 06	290	6.7	26.3	7.7	28.0
Very elderly						
Belgium	Diet National 2004	712	5.9	17.3	6.5	17.3
Denmark	Danish Dietary Survey	20	9.5	36.0	10.3	36.5
France	INCA2	84	6.7	14.5	7.7	15.7
Germany	National Nutrition Survey II	490	5.4	17.7	6.2	18.6
Hungary	National Repr Surv	80	3.5	5.6	4.4	7.8
Italy	INRAN SCAI 2005 06	228	4.7	13.2	5.6	13.5

(a): number of subjects. (b): mean exposure. (d): P95: 95th percentiles of exposure. (e): percentage of individuals with an exposure above the TWI with its corresponding 95% confidence interval. **Reminder: in case of too few observations (less than 60 observations for the 95th percentile), the estimation of high percentiles may be biased and must consequently be interpreted cautiously.**

Air, dust and soil represent additional routes of exposure. EFSA estimated the contribution from non dietary sources such as ambient air, ingested soil or dust and through dermal contact (see Table 8.3 below). However, NDL-PCBs from air (ambient, indoor), dust and soil contribute only a few percent to the body burden of NDL-PCBs of the general population (EFSA 2005, pp.51-52).

Since children spend a lot of time playing on the ground, both indoors and out, they come into more contact with contaminants found on **dust and dirt particles**. Soils are the major sink for PCBs in the terrestrial environment. PCBs, particularly the highly chlorinated congeners adsorb strongly to sediment and soil where they tend to persist with half-lives in the order of months to years (EFSA 2005, p.93; ATSDR 2000, p.507). Children may be exposed to PCBs by dermal contact with **PCB-contaminated soil** and by ingesting contaminated soil from their unwashed hands and other hand-

to-mouth behaviour. Dermal uptake of PCBs is generally only a very minor pathway for their uptake, typically about three to four orders of magnitude lower than the average dietary intake (EFSA 2005, pp.52-53).

Table 8-3: Relative importance of PCB exposure from air and soil compared to exposure from food

(Source: reconstructed from EFSA 2005, p.52 and Table 22, pp.53-54)

Exposure type	**Source**	**Pathway**	**Range of calculated or reported exposures** (ng/kg bw/day)	
			children	**adults**
Dietary exposure	Food mean consumers[a]	Oral	12.9 - 15.8	5.7 - 6.9
	Food high consumers[b]	Oral	31.0 - 35.1	15.8 - 17.5
Non-dietary exposure	House dust[c]	Oral	0.06 - 0.6	-
	Ingested soil[c]	Oral	0.06 - 0.6	-
	Air[d, e]	Inhalation	0.05 - 0.5	0.03 - 0.3
	Skin contact[f]	Dermal	0.005	0.00076

[a] Mean for Lower Bound (LB) – Upper Bound (UB) for toddlers and adults across the different country surveys, according to table 8.2.

[b] 95th percentile for Lower Bound (LB) – Upper Bound (UB) for toddlers and adults across the different country surveys, according to table 8.2.

[c] Calculated by EFSA (2005) for children, based on soil concentrations of 10 - 100 ng PCB/g dry matter and assuming ingestion of 100 mg soil or dust per day.

[d] Calculated by EFSA (2005) for children, based on ambient air levels ranging from about 0.1 - 1 ng/m^3, a body weight of 15 kg and an inhalation rate of 7.5 m^3/day.

[e] Calculated by EFSA (2005) for adults, based on ambient air levels ranging from about 0.1 - 1 ng/m^3, a body weight of 70 kg and an inhalation rate of 20 m^3/day.

[f] Calculated by EFSA (2005) for children and adults, based on an USEPA (2000) average dermal absorption rate of 14% (USEPA 2000 *in* EFSA 2005) and a highly contaminated soil (1,000 ng PCB/g dry matter).

8.5.2 Innere Exposition

For PCBs SCAHT applies the TIER 2-strategy as outlined in the methodology section.

Many data gaps exist for antimony. Information on absolute oral bioavailability from soil for PCBs is not directly available for humans. Data on PCB absorption rate are poorly characterized in humans (section 8.5.2.1). Furthermore, there are no data following ingestion of soil in humans (section 8.5.2.2). There are several in vivo data in experimental animals (rat, goat, swine) (section 8.5.2.3), which allows the application of the proposed RAF methodology (section 8.5.2.4). In particular, juvenile swine data support the use of a proposed RAF value of 0.5 (50%) as a more realistic estimate of garden soil.

In conclusion, considering a conservative dietary oral bioavailability of 100% in humans and a RAF of 50%, SCAHT uses an absolute oral bioavailability of PCBs from soil of 50% for its risk assessment.

8.5.2.1 Oral bioavailability from food and/or water from dietary studies

The bioavailability of PCBs in experimental animals has been shown to be quite high, e.g. 75% for the higher chlorinated congeners and >90% for the lower chlorinated congeners. PCB absorption from the gastrointestinal tract occurs by passive diffusion and there is yet no evidence of specific transporters for PCB (EFSA 2005, p.53).

For humans, it has been suggested that PCBs entering the body from the airways and from the gastrointestinal tract are readily absorbed (EFSA 2005, p.52). Highly chlorinated PCB congeners with only isolated non-chlorinated carbons show the longest elimination half-lives and therefore the greatest bioaccumulation potential (e. g. PCB 138, 153, 170, and 180) (EFSA, p.57).

⇒ **From these data, SCAHT uses a 100% oral bioavailability, as a conservative estimate.**

8.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

Quantitative information regarding the bioavailability and amount of PCBs that children are exposed to through direct contact with contaminated soils is not available (ATSDR 2000, p. 573; Delannoy et al., 2014a; Kimbrough et al., 2010).

8.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

Some *in vivo* studies were conducted in rats, goats and swine to estimate the oral bioavailability following ingestion of soil.

- *Rats*. The oral uptake of PCBs in soil by rats was found to range from 66 to 99%, with less chlorinated PCBs exhibiting greater absorption (NEPI 2000, page v, last paragraph).
- *Goats*. Feidt et al. (2013) reported that the relative oral bioavailability of goats following ingestion of PCB contaminated soil varied from 36 to 50% for PCB 118, 138, and 153 and it was 73% for PCB 180; when considered globally, the response obtained with mainly PCB forms 153, 180, and 138 was estimated to 51% (Feidt et al., 2013, abstract).
- *Swine*. Delannoy et al. (2014a, 2014b, 2015) investigated the impact of soil characteristics (organic matter, clay content, pH) on relative bioavailability (RBA) of NDL-PCBs in a serie of experiments using the juvenile swine model following ingestion of soil spiked with Aroclor 1254 for 10 days.

  Delannoy et al. (2014a) RBA factors for the sum of PCBs: they found that condensed organic matter (activated carbon) strongly reduces bioavailability (RBA factors for the sum of PCBs were 6.4%, 9.9% and 3.0% in adipose tissue, muscle and liver, respectively), whereas the less condensed one (fulvic acid) does not seem to have a significant effect (RBA factors for the sum of PCBs were 80.0%, 76.9% and 67.8% in adipose tissue, muscle and liver, respectively) compared to the standard soil (RBA factors for the sum of PCBs were 75.0%, 101.8% and 74.8% in adipose tissue, muscle and liver, respectively).

  In a subsequent experiment, Delannoy et al. (2014b) showed that a fulvic acid reduced slightly the bioavailability of NDL-PCBs (mean RBA of 82.7% for the sum of PCB) compared to spiked corn oil (mean RBA of 100% for the sum of PCB). Humic acid (mean RBA of 46.6% for the sum of PCB) and Sphagnum peat (mean RBA of 61.1% for the sum of PCB) or Sphagnum peat and activated carbon (mean RBA of 42.4% for the sum of PCB) reduced it significantly higher, whereas activated carbon alone reduced it the most (mean RBA of 16.7% for the sum of PCB). RBA estimate for each congener increased for each soil type along with the chloration degree (PCB-52<PCB-101<PCB-138<PCB 153<PCB-180).

  Delannoy et al. (2015) determined the impact of organic carbon, black carbon, clay contents and pH of ten contaminated soils on the bioavailability of NDL-PCBs PCB 101, 138, 153 and 180 (Aroclor 1254) in five juvenile male piglets exposed to increasing oral amounts of each of the soils for 10 days. Despite high variations in the amount of black carbon (0.05-0.6% d.w.) and organic matter (1.2-18% d.w.), only 3 soils exhibited a significantly lower RBA for all NDL-PCBs, compared to the oil-group. High levels of organic carbon (>10%) and black carbon content (0.3%) were related to a significant reduction in RBA. Overall, RBA was higher than 45% independently of the soil and the PCB congener.

8.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of PCBs from soil compared to food or water, is to use the Relative Oral Adjustment Factor (RAF) approach proposed by the USEPA, as outlined in the methodology section (TIER 2 approach).

- A default medium-specific oral relative absorption factor of 0.5 (50%) for PCB Aroclors 1254 and 1242 has been proposed by the Michigan Department of Environmental Quality (NRC 2003, table 2.1, page 69). However, the justification for this value is not made explicit in the NRC report (personnal communication).
- The available *in vivo* soil ingestion studies in juvenile swine show a wide range of relative bioavailability values depending on the soil type, as shown by the Delannoy studies. Two scenarios can be proposed here. A conservative approach, using a relative bioavailability of 100%, based on relative bioavailability values in the range 75-90%. found for standard soils or fulvic acid enriched soils. The other approach considers a relative bioavailability of 50% as a realistic estimate for soils enriched with humic acid, activated carbon and/or moss which is assumed to be more representative of garden top soils which show in general a higher total organic matter content (Alloway, 2004) compared to other (e.g. urban, industrial, agricultural) soil types.

⇒ **Based on these data, and assuming a conservative 100% oral bioavailability (systemic absorption rate), SCAHT uses an absolute oral bioavailabilty of PCBs in soil of 50% for its risk assessment.**

8.5.2.5 Summary of the in vitro bioaccessibility information

The bioaccessibility of PCBs from the soil matrix is governed by the properties of the soil (particle size, organic content, etc.) and by the low solubility, high K_{ow} and low K_{oc} properties of PCBs (ATSDR 2000, p.499; USEPA 2003, p.8). PCBs are generally stable and strongly sorbed to soils, in particular to particles of organic matter and clay, and dust particles. Delannoy et al. (2014b, 2015) found that organic matter content is of major impact on relative bioavailability. Mobility/leaching is assumed to be generally low, particularly in soils with high organic carbon such as garden topsoil. PCBs, particularly the highly chlorinated congeners, tend to persist with half-lives on the order of months to years (ATSDR 2000, p.487, 499).

- NRC 2003 discussed the relevance and applicability to PCBs of in vitro extraction systems (i.e. "bioaccessibility" studies) (NRC 2003, p.267). Their report concludes that in general the more thorough extraction tests gave bioaccessibility results of 20 - 60% for PCBs (as well as for PAHs and PCDD/PCDF) from soils and solid wastes.

8.6 Risikoabschätzung

Based on the median total concentration of all NDL-PCBs measured in human milk sampled in European countries of about 240 ng/g fat and assuming 20% fat content in the human body, a median human body burden of about 50 µg/kg bw was estimated. A comparison of this accumulated internal exposure with the EFSA defined body burden at the NOAEL (NOAEL BB) for NDL-PCBs in human tissues of 500 µg/kg bw reveals a NOAEL MoBB of about 10^4.

Therefore the safety margin is small and from the perspective of human health protection SCAHT concludes that there would hardly be any room for an additional exposure to PCBs such as from direct ingestion of contaminated soil.

However, EFSA argues that although this margin appears rather small it should be stressed that the endpoints considered in the evaluation of the individual NDL-PCB congeners can also be observed after treatment with PCDD/PCDF or DL-PCBs. Since a number of these latter compounds have relatively high potencies for these effects in rats minor contamination (in the range of 0.1%) of the NDL-PCB congeners studied with potent dioxin-like compounds might be sufficient to explain the effects observed. Thus, any estimate of a NOAEL for NDL-PCBs is hampered by the uncertainty in the extent to which NDL-PCB congeners might have been contaminated with polychlorinated dibenzofurans and/or DL-PCBs. Therefore the "true" NOAEL MoBB for NDL-PCBs might be larger, i. e. resulting in more safety. On the other hand, the MoBB was calculated on the basis of the median concentrations of NDL-PCBs in human milk and some populations in Europe may have considerably higher body burdens.

The Swiss Contaminated Sites Ordinance (CSO) set a clean up value for the sum of the six indicator NDL-PCBs at 1mg/kg. At that level a daily accidental ingestion of 250 mg PCB-contaminated soil by a 12.5 kg child would contribute to an additional external exposure of 0.02 µg/kg bw/day, assuming a conservative absolute oral bioavailability for NDL-PCBs of 100%. Assuming half of this value, i.e 50%, the internal exposure would be reduced to 0.01 µg/kg bw/day or 10 ng/kg bw/day. Based on this exposure scenario NDL-PCB uptake from soil would be in the same order of magnitude as the lower bound dietary exposure of toddlers and other children.

However, *cumulative exposure* to NDL-PCBs from soil ingestion over 3 years would result in an additional exposure of 10.95 µg/kg bw[2] which accounts for only ≈ 2.2% of the EFSA-derived NOAEL body burden of 500 µg/kg bw.

⇒ **Therefore the SCAHT argues that the additional health risk from soil ingestion seems to be low.**

[4] The detailed calculation to derive that NOAEL MoBB is the following: under the given exposure scenario, daily exposure would account for 0.01 µg/kg bw x 365 day/year x 3 years = 10.95 µg/kg bw/3 years.

8.7 Grenzwerte im internationalen Vergleich

In the context of remediation of polluted soils the Swiss Contaminated Sites Ordinance (CSO) defines clean up values for the sum of these six indicator NDL-PCBs. The AltlV 1998 gives a clean up value for PCB in residential gardens and playgrounds of 1 mg/kg, defined as the sum of 6 indicator NDL-PCB congeners x 4.3 = no. 28, 52, 101, 138, 153, 180. It should be noted that the VBBo (Verordnung über Belastungen des Bodens (VBBo) vom 1. Juli 1998, Stand am 1. Juni 2012). defines a soil clean up value based on PCB-7 (NDL-PCB-6 plus DL-PCB 118).

It is sometimes difficult to directly compare the clean up values (also referred to as remediation values, soil quality guidelines, soil quality standards or criteria in the various national regulations on soil remediation at international level) for the sum of the PCBs because the selection of the indicator PCBs (NDL-PCB, DL-PCB) may vary according to different priorities, in particular if the primary protection goal is human health and/or the environment (e. g. Carlon 2007; MfE 2011, p.144). Some countries use the sum of the six PCBs congeners while others use the sum of seven PCB congeners (i. e. the sum of the six indicator NDL-PCBs plus PCB 118 which is a DL-PCB) or even the total sum of PCBs without further indication. Some national regulations have no provisions related to the soil remediation of PCBs-contaminated sites.

Based on a review of the scientific and regulatory literature, in particular national soil remediation regulations in Europe, USA and Canada, it appears that the clean up value as defined by the Swiss Ordinance on Polluted Soils is in the ***middle range*** (refer to **Annex 1**):

UK: 8 (not specified); CZ: 5 (ΣPCB7); CAN: 1.3; A (ΣPCB7) & NL 1; **CH: 1** (ΣPCB6); B: 0.9 (not specified); D: 0.8 (ΣPCB6); USA, 0.5 (not specified); E: 0.08 (not specified); S: 0.02 (not specified); I: 0.001 (not specified) (mg / kg dm).

8.8 Literatur

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9 Arsen

9.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 50 mg As/kg Boden sollte überprüft werden.
Gefährdungspotential	Hoch	Krebserzeugend beim Menschen nach hoher inhalativer Exposition am Arbeitsplatz. Krebserzeugend beim Menschen nach hoher oraler Exposition über Trinkwasser.
Kanzerogen	Ja	Krebserzeugend beim Menschen nach hoher inhalativer Exposition am Arbeitsplatz und nach hoher oraler Exposition über Trinkwasser: Blasen-, Haut-, Lungenkrebs aber auch Leber-, Nieren- und Prostatakrebs.
Mutagen	Nein	Es wird ein Schwellenwertmechanismus für die Krebsentstehung angenommen.
Reprotoxisch	Ja	
Neurotoxisch	Ja	
Andere	Ja	Hautläsionen (Hyperpigmentierung, Hyperkeratose) und Herzkreislauferkrankungen
Gesundheitsbasierter Referenzwert		Kein gesundheitlich unbedenklicher Referenzwert festgelegt, aufgrund von Unsicherheiten bei der Dosis-Wirkungsbeziehung. $BMDL_{01}$ (Hautläsionen und Krebs): 0.3 – 8 µg As/kg KG/Tag
Exposition		
Äussere Exposition Boden (250 mg)		50 mg As/kg Boden = 12.5 µg As/250 mg Boden = 1 µg As/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 100% Bioavailability: 1 µg As/kg KG/Tag (KG: 12.5kg) Bei 50% Bioavailability: 0.5 µg As/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte tatsächliche mittlere Arsenaufnahme über die Nahrung (Kinder): 0.32 – 2.09 µg As/kg KG/Tag

Risiko Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung	Wahrscheinlich	Die tägliche Arsenaufnahme über Nahrung und das Trinkwasser liegt im unteren Wertebereich des $BMDL_{01}$ und ist somit risikobehaftet. Die geschätzte tägliche Aufnahmemenge durch das Verschlucken von kontaminiertem Boden liegt in der gleichen Grössenordnung wie die risikobehaftete tägliche Hintergrundbelastung und stellt somit ein zusätzliches Gesundheitsrisiko dar. Aufgrund der grossen Unsicherheit bei der Dosis-Wirkungsbeziehung ist der Risikobeitrag der einzelnen Komponenten schwer abzuschätzen. Gesundheitsbasierter Referenzwert $BMDL_{01}$: 0.3 – 8 µg As/kg KG/Tag Geschätzte Arsenaufnahme über Nahrung: 0.32 – 2.09 µg As/kg KG/Tag Geschätzte Arsenaufnahme durch direkte Bodenaufnahme: 0.5 - 1 µg As/kg KG/Tag (KG: 12.5kg)
Grenzwert im Vergleich		BE: 110; CZ: 70; NL: 55; D: 50; A, **CH: 50**; F: 37; E: 30; I, UK: 20; S: 15; USA: 19; CAN: 12 (mg/kg dm).
Datenlage	Ausreichend	

9.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten)[1] festgelegte Sanierungswert für Arsen für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 50 mg As/kg Boden sollte gemäss dem ALARA-Prinzip reduziert werden.

Der Mensch ist sowohl gegenüber anorganischem Arsen mit verschiedenen Oxidationsstufen (meist +3, +5) als auch gegenüber organisch gebundenem Arsen exponiert. Die Unterschiede in der Toxizität der verschiedenen Oxidationsstufen sind vergleichsweise gering. Unter den organischen Arsenverbindungen befinden sich Arsenobetaine, Arsenozucker und Arsenolipide. Für keine dieser Verbindungen gibt es ausreichende toxikologische Daten für eine umfassende Risikobeurteilung, noch gibt es hinreichende Daten zur Exposition. Das anorganische Arsen steht deshalb im Fokus dieser Risikobeurteilung.

Eine erhöhte chronische Aufnahme von anorganischem Arsen wirkt nachweislich krebserzeugend beim Menschen und zwar vor allem nach inhalativer Exposition höherer Dosen, wie man sie im arbeitsbedingten Umfeld beobachtet hat. Durch zahlreiche epidemiologische Studien an exponierten Arbeitern aber auch in Populationen mit hoher Exposition über Trinkwasser wurde ein kausaler Zusammenhang zwischen der Exposition gegenüber anorganischem Arsen und der Entstehung von Blasen-, Haut- und Lungenkrebs beim Menschen belegt. Einige Studien weisen auch auf Leber-, Nieren- und Prostatatumore hin. Neben einem erhöhten Krebsrisiko werden bei chronischer Aufnahme von anorganischem Arsen auch andere toxische Effekte beobachtet. Berichtet werden Hautläsionen (Hyperpigmentierung, Hyperkeratose), Herz-Kreislauf-Erkrankungen, reprotoxische und neurotoxische Effekte.

Für die verschiedenen für anorganisches Arsen diskutierten Mechanismen der Krebsentstehung wird von einem Schwellenwertmechanismus ausgegangen. Aufgrund der Unsicherheiten bei den Dosis-Wirkungsbeziehungen kann nach Ansicht der EFSA keine tolerable Aufnahmedosis in Form von TDI- oder PTWI-Werten festgelegt werden. Stattdessen wurde ein $BMDL_{01}$-Wertebereich zwischen 0.3 bis 8 µg/kg KG/Tag festgelegt, der eine tägliche Aufnahmedosis charakterisiert, bei der ein zusätzliches 1%-iges Risiko für verschiedene toxikologische Endpunkte besteht. Die zugrunde gelegten gesundheitlichen Effekte waren Hautläsionen, Haut-, Lungen- und Blasenkrebs.

Die von der EFSA geschätzte ernährungsbedingte tägliche Exposition für Kinder im Alter von 1 - 3 Jahren gegenüber anorganischem Arsen liegt zwischen 0.32 und 2.09 µg/kg KG/Tag. Ein Vergleich des von der EFSA abgeleiteten $BMDL_{01}$-Wertebereichs zwischen 0.3 bis 8 µg/kg KG/Tag mit den aktuellen Schätzwerten für die tägliche Exposition gegenüber anorganischem Arsen zeigt, dass für Kinder die tägliche Arsenaufnahme über Lebensmittel und Trinkwasser im Bereich der unteren Grenze dieses BMDL-Wertebereiches liegt. Da dieser Wertebereich bereits risikobehaftet ist, besteht zwischen den Arsen-Aufnahmemengen und den Dosen, ab denen Arsen Gesundheitsbeeinträchtigungen verursachen kann, kein Sicherheitsabstand. Daher können alleine durch die Arsenaufnahme über Nahrung und Trinkwasser gesundheitliche Risiken nicht ausgeschlossen werden. Jede zusätzliche Arsenbelastung durch das Verschlucken kontaminierter Böden könnte das Risiko gesundheitlicher Beeinträchtigungen erhöhen.

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten) festgelegte Sanierungswert für Arsen für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, ist auf 50 mg As/kg Boden festgelegt. Ein 12.5 kg schweres Kind, das täglich 250 mg Boden verschluckt, nimmt unter der Annahme einer 50% orale Bioverfügbarkeit des Arsens aus dem Boden zusätzlich 0.5 µg/kg KG/Tag auf.

Aufgrund der Streuung des $BMDL_{01}$-Wertebereiches von 0.3 bis 8 µg/kg KG/Tag ist das zusätzliche Gesundheitsrisiko durch die Aufnahme von Arsen über den Boden in Höhe von 0.5 µg/kg KG/Tag schwer abzuschätzen. Im vorliegenden Szenario liegt die tägliche Exposition gegenüber anorganischem Arsen aus dem Boden im unteren Bereich der mittleren täglichen Arsenaufnahme über Lebensmittel und Trinkwasser von 0.32 - 2.09 µg/kg KG/Tag und im Bereich der unteren Grenze des $BMDL_{01}$-Wertebereiches von 0.3 bis 8 µg/kg KG/Tag, der mit einem kleinen zusätzlichen Gesundheitsrisiko verbunden ist. Obwohl nach Meinung des SCAHT das zusätzliche Gesundheitsrisiko durch die direkte Arsenaufnahme über den Boden eher gering ist, stellt die Exposition über den Boden einen Hauptaufnahmepfad in der gleichen Grössenordnung wie die diätische Exposition dar. Deshalb sollte standardmässig für die Festlegung des Sanierungswerts das ALARA-Prinzip zur Anwendung kommen. Die Wirksamkeit einer Reduzierung des Sanierungswertes für Arsen im Boden sollte aber im Zusammenhang mit anderen möglichen Risikominimierungsmassnahmen evaluiert werden.

9.3 Gefährdungspotential

Arsen wurde durch mehrere internationale Gremien bewertet. Das SCAHT bezieht sich in seiner Risikobeurteilung im Wesentlichen auf eine zusammenfassende Bewertung, die das BfR (2012) auf Grundlage dieser internationalen Bewertungen zusammengestellt hat. In 2014 hat EFSA ihre Schätzwerte für die ernährungsbedingte Exposition gegenüber anorganischem Arsen von 2009 nach unten korrigiert (EFSA 2014). Dies wurde in der vorliegenden Bewertung berücksichtigt.

Der Mensch ist sowohl gegenüber anorganischem Arsen in verschiedenen Oxidationsstufen (meist +3, +5) als auch gegenüber organisch gebundenem Arsen exponiert. Die Unterschiede in der Toxizität der verschiedenen Oxidationsstufen sind vergleichsweise gering (BfR 2012, Kapitel 3.2.1, Seite 9, Paragraph 2). Unter den organischen Arsenverbindungen befinden sich Arsenobetaine, Arsenozucker und Arsenolipide. Für keine dieser Verbindungen gibt es ausreichende toxikologische Daten für eine umfassende Risikobeurteilung, noch gibt es hinreichende Daten zur Exposition (EFSA 2009). Ohnehin findet man diese Stoffe in Seafoods. Deshalb sind sie für die vorliegende Risikobeurteilung nicht relevant.

Das anorganische Arsen steht deshalb im Fokus dieser Risikobeurteilung.

- Wasserlösliches anorganisches Arsen wird meist schnell und fast vollständig absorbiert. Allerdings haben die Löslichkeit und die Gegenwart anderer Lebensmittelbestandteile einen relevanten Einfluss. Die Absorption verschiedener organischer Arsenverbindungen liegt generell über 70%. Die Verteilung im Körper ist unabhängig vom Aufnahmeweg und erfolgt in alle Organe, die Plazentaschranke wird passiert (BfR 2012, Kapitel 3.2.1, Seite 9, Paragraph 3).

- Bei akuter und subakuter Vergiftung mit anorganischem Arsen sind fast alle physiologischen Systeme, wie der Magen-Darm-Trakt (Erbrechen, Durchfall), das Herz-Kreislauf-System und das Nervensystem betroffen. In geringerem Masse können auch Atmung, Leber, Haut und das Blutsystem beeinträchtig sein. Akutes Organversagen kann zum Tod führen. ATSDR (2007) berichtet eine akute letale Dosis nach Verschlucken von 100 bis 300 mg (1 bis 5 mg/kg KG), wobei Arsenit (Salz der Arsenigen Säure) und/oder Arsenat (Salze der Arsensäure) als aufgenommene Spezies angenommen werden (BfR 2012, Kapitel 3.2.1, Seite 9, Paragraph 4).

- Eine erhöhte subchronische Aufnahme von anorganischem Arsen beeinflusst den Magen-Darm-Trakt, das Blutsystem und die Haut. Für die subchronischen Effekte wurde ein LOAEL (Lowest Observed Adverse Effect Level) zwischen 0.05 und 0.1 mg/kg KG/Tag abgeleitet (BfR 2012, Kapitel 3.2.1, Seite 9, Paragraph 5).

- Eine erhöhte chronische Aufnahme von anorganischem Arsen wirkt nachweislich krebserzeugend beim Menschen. Durch zahlreiche epidemiologische Studien an exponierten Arbeitern oder in Populationen mit hoher Exposition über Trinkwasser wurde ein kausaler Zusammenhang zwischen der Exposition gegenüber anorganischem Arsen und der Entstehung von Blasen-, Haut- und Lungenkrebs beim Menschen belegt. Während bei inhalativer Aufnahme der Primärtumor im Wesentlichen in der Lunge, untergeordnet aber auch in der Leber, Haut und im Verdauungstrakt entsteht, führt die chronische orale Aufnahme bevorzugt zu Hauttumoren, jedoch sind auch hier Blasen- und Lungentumore berichtet worden. Einige Studien weisen auch auf Leber-, Nieren- und Prostatatumore hin. Für die verschiedenen für anorganisches Arsen diskutierten Mechanismen der Krebsentstehung wird von einem Schwellenwertmechanismus ausgegangen. Anorganische Arsenverbindungen werden von der IARC (Stufe 1), der US-EPA (Gruppe A) und der EU (Kategorie 1A) als humankanzerogen klassifiziert (BfR 2012, Kapitel 3.2.1, Seite 9, Paragraph 6 - Seite 10, Paragraph 1).

  Neben einem erhöhten Krebsrisiko werden bei chronischer Aufnahme von anorganischem Arsen

auch andere toxische Effekte beobachtet. Berichtet werden Hautläsionen (Hyperpigmentierung, Hyperkeratose) als empfindliche Indikatoren für eine chronische Aufnahme von anorganischem Arsen, die bereits bei Trinkwasserkonzentrationen <100 µg/l beobachtet wurden. Dermatitis wurde bei Arbeitern beobachtet, die gegenüber Arsen exponiert waren (BfR 2012, Kapitel 3.2.1, Seite 10, Paragraph 2).

Zahlreiche Studien belegen eine Assoziation zwischen einer chronischen Arsenexposition durch kontaminiertes Trinkwasser und Herz-Kreislauf-Erkrankungen, Gefässerkrankungen, koronare Herzkrankheiten und Myokardinfarkt (BfR 2012, Kapitel 3.2.1, Seite 10, Paragraph 5). Darüber hinaus werden Veränderungen des Glukose-Metabolismus, ein erhöhtes Risiko für die Entstehung eines Diabetes mellitus sowie bei exponierten Arbeitern Effekte auf den Atemtrakt und Irritationen der Schleimhaut berichtet (BfR 2012, Kapitel 3.2.1, Seite 10, Paragraph 6).

Arsen ist plazentagängig. In Regionen mit hohen Arsenkonzentrationen im Trinkwasser wurden erhöhte Risiken bezüglich Spontanabort, Frühgeburt, Totgeburt sowie Assoziationen mit geringeren Geburtsgewichten sowie Kopf- und Brustumfängen der Neugeborenen berichtet. Es gibt zunehmend Hinweise, dass erhöhte pränatale und postnatale Expositionen das Wachstum des Fötus und Säuglings negativ beeinflussen und im späteren Leben zu chronischen Krankheiten führen können (BfR 2012, Kapitel 3.2.1, Seite 10, Paragraph 3).

- Eine chronische Aufnahme niedriger Arsendosen kann das Zentralnervensystem beeinträchtigen und zur Verschlechterung der kognitiven Funktionen, des Lernens, der Hand-Augen-Koordination und der Aufmerksamkeit führen. Einige Studien berichten intellektuelle Defizite bei Kindern, die mit Arsengehalten im Trinkwasser über 50 µg/l assoziiert waren, bzw. die in der Nähe von entsprechenden Hüttenwerken lebten. Dauerhafte neurotoxische Effekte wurden in einer Follow-up Untersuchung einer Kohorte, die 1955 in Japan, als Kleinkinder durch mit Arsen kontaminierte Milch exponiert waren, berichtet. 15 Jahre und auch 50 Jahre später wurden irreversible und ernste neurologische Veränderungen wie Epilepsie und mentale Verzögerungen festgestellt (BfR 2012, Kapitel 3.2.1, Seite 10, Paragraph 4).

9.4 Gesundheitsbasierter Referenzwert

Ein paar Referenzwerte wurden durch internationale Gremien hergeleitet:

- JECFA hatte 1989 auf der Basis der damals vorliegenden Trinkwasserstudien einen PTWI (provisional tolerable weekly intake) von 15 µg/kg KG pro Woche (entspricht 2 µg kg KG/Tag) abgeleitet, der für Hautkrebs als kritischer Effekt auf einem LOAEL von 100 µg Arsen/L Trinkwasser und einer täglichen Wasseraufnahme von 1.5 L beruhte (FAO/WHO 1989).
- ATSDR (2007) leitete einen wesentlich niedrigeren Wert für die chronische orale Arsenaufnahme ab. Der MRL (Minimal Risk level, vergleichbar mit dem TDI) von 0.3 µg/kg KG/Tag beruht auf epidemiologischen Studien zu peripheren Durchblutungsstörungen (Blackfoot disease), Hyperkeratose und Hyperpigmentierung als kritische Effekte, einem NOAEL von 0.8 µg/kg KG/Tag und einem Faktor von 3 für die Intraspeziesvariabilität.
- Die US EPA bestätigte den Wert der ATSDR von 0.3 µg/kg KG/Tag in Form einer chronischen oralen Referenzdosis (RfD) (USEPA 1991; BfR 2012, Kapitel 3.2.1, Seite 10, Paragraph 7).
- Auch die EFSA kommt in ihrer Bewertung (2009) zu der Schlussfolgerung, dass der PTWI-Wert von JECFA von 15 µg/kg KG pro Woche (entspricht 2 µg kg KG/Tag) nach heutigem Kenntnisstand deutlich zu hoch ist, da adverse kanzerogene Effekte auch unterhalb der von JECFA berücksichtigten Exposition belegt sind. Auf der Basis epidemiologischer Studien für die kritischen Effekte Lungen-, Blasen- und Hautkrebs sowie Hautläsionen hat die EFSA einen Bereich von $BMDL_{01}$-Werten (tägliche Aufnahmedosis, bei der ein 1%-iges Risiko für verschiedene toxikologische Endpunkte einschliesslich der Krebserkrankungen besteht) abgeleitet, der zwischen 0.3 und 8 µg/kg KG und Tag liegt (EFSA 2009, Kapitel 8.4.1.6, Seite 139 ff und Seite 141 Tabelle 43; siehe **Tabelle 9-1**). Aufgrund der Unsicherheiten bei den Dosis-Wirkungsbeziehungen kann nach Ansicht der EFSA keine tolerable Aufnahmedosis in Form von TDI- oder PTWI-Werten festgelegt werden (EFSA 2009).

Tabelle 9-1: Zusammenfassung der Referenzwerte für verschiedene toxikologische Endpunkte
(Quelle: EFSA 2009, Seite 141, Tabelle 43)

Endpoint	Population	Reference point µg/L water	Reference point µg/kg b.w. per day
Dermal lesions	Bangladesh (Ahsan et al., 2006)	$BMCL_{01}$: 23[a]	$BMDL_{01}$: 2.2-5.7[b]
Dermal lesions	Mongolia (Xia et al., 2009)	$BMCL_{01}$: 0.3[a]	$BMDL_{01}$: 0.93-3.7[b]
Lung cancer	Chile (Ferreccio et al., 2000)	$BMCL_{01}$: 14 (NRC, 2001)	$BMDL_{01}$: 0.34-0.69[c]
Bladder cancer	North East Taiwan (Chiou et al., 2001)	$BMCL_{01}$: 42 (NRC, 2001)	$BMDL_{01}$: 3.2-7.5[b]
Skin cancer	USA (New Hampshire) (Karagas et al., 2002)	Change point[d]: 1-2	Change point: 0.16-0.31[c]
Bladder cancer	USA (New Hampshire) (Karagas et al., 2004)	Change point: *ca.* 50	Change point: 0.9-1.7[c]

b.w.: body weight; $BMCL_{01}$: 95 % lower confidence limit of the benchmark concentration of 1 % extra risk; $BMDL_{01}$: 95 % lower confidence limit of the benchmark dose of 1 % extra risk
(a): Calculated by CONTAM Panel for this opinion
(b): Extrapolated from the $BMCL_{01}$ assuming 3-5 L water and 50-200 µg/day inorganic arsenic in food per day, 55 kg b.w. (see Section 8.4.1.1)
(c): Extrapolated from the $BMCL_{01}$ assuming 1-2 L water and 10-20 µg/day inorganic arsenic in food consumed per day, 70 kg b.w. (see Section 8.4.1.1)
(d): The maximum likelihood change point before the trend becomes significant, which provides an indication of a no effect level rather than a BMDL (see Section 8.3.3.1)

9.5 Exposition

9.5.1 Äussere Exposition

Die EFSA hat zuletzt 2014 die ernährungsbedingte Exposition gegenüber Arsen abgeschätzt, wobei die Schätzwerte niedriger waren als 2009. Die orale Aufnahme von Arsen erfolgt im Wesentlichen über die Nahrung einschliesslich Trinkwasser. Die Hauptaufnahmequellen für Kinder zwischen 1 und 3 Jahren sind Milch und Milchprodukte, gefolgt von Trinkwasser und Getreideprodukten (EFSA 2014, Kapitel 3.3.1, Seite 42, Paragraph 5).

- So wurde für erwachsene Normalverzehrer eine tägliche Aufnahmemenge von 0.09 bis 0.38 µg anorganisches Arsen/kg KG ermittelt, während die Aufnahme bei Vielverzehrern (95-Perzentil) bei Werten zwischen 0.14 und 0.64 µg/kg KG liegt.

- Für Kinder ist die Arsenaufnahme bezogen auf das Körpergewicht deutlich höher. Für die mittleren Verzehrmengen werden Werte zwischen 0.20 und 1.37 µg anorganisches Arsen/kg KG/d erreicht, für die Vielverzehrer sogar 0.36 bis 2.09 µg/kg KG/Tag (EFSA 2014, Abstract, Seite 1 und Kapitel 3.2, Tabelle 24) (siehe **Tabelle 9-2**).

Tabelle 9.-2: Chronische Exposition gegenüber anorganischem Arsen über die Nahrung

(Quelle: EFSA 2014, Kapitel 3.2, Seite 41, Tabelle 24)

	Mean dietary exposure (µg/kg b.w. per day)								
	Lower bound (LB)			Middle bound (UB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max	Min	Median	Max
Infants (2 surveys)	0.24	-[a]	0.43	0.56	-[a]	0.87	0.88	-[a]	1.37
Toddlers (9 surveys)	0.32	0.39	0.45	0.59	0.68	0.81	0.91	1.00	1.17
Other children (17 surveys)	0.20	0.30	0.36	0.33	0.51	0.61	0.47	0.71	0.87
Adolescents (12 surveys)	0.12	0.18	0.23	0.22	0.29	0.36	0.31	0.42	0.48
Adults (15 surveys)	0.11	0.13	0.17	0.18	0.23	0.28	0.24	0.33	0.38
Elderly (7 surveys)	0.09	0.11	0.15	0.16	0.20	0.24	0.24	0.29	0.34
Very Elderly (6 surveys)	0.09	0.12	0.16	0.17	0.20	0.26	0.25	0.28	0.36
	95th dietary exposure (µg/kg b.w. per day)								
	Lower bound (LB)			Middle bound (UB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max	Min	Median	Max
Infants (2 surveys)	0.54	-[c]	-[c]	1.07	-[c]	-[c]	1.66	-[c]	-[c]
Toddlers (9 surveys)	0.61	0.86	1.04	1.03	1.38	1.42	1.48	1.82	2.09
Other children (17 surveys)	0.36	0.53	0.63	0.59	0.83	1.00	0.81	1.15	1.41
Adolescents (12 surveys)	0.23	0.31	0.43	0.39	0.51	0.61	0.52	0.68	0.84
Adults (15 surveys)	0.18	0.22	0.32	0.31	0.39	0.47	0.44	0.54	0.64
Elderly (7 surveys)	0.14	0.17	0.26	0.25	0.31	0.39	0.35	0.45	0.53
Very Elderly (6 surveys)	0.16	0.24	0.29	0.26	0.35	0.40	0.37	0.47	0.54

(a): Not calculated since estimates were only available from two dietary surveys.
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.
(c): Not calculated since estimates were only available from one dietary survey.

⇒ Nach diesen aktuellen Schätzwerten liegt die ernährungsbedingte tägliche Arsenaufnahme von Kleinkindern (Toddlers) somit im unteren Bereich der von der EFSA abgeleiteten $BMDL_{01}$-Werte von 0.3 bis 8 µg/kg KG/Tag.

Auch in der Luft kommt Arsen vor, hier bevorzugt als anorganisches As_2O_3 (arsenic trioxide), so dass auch eine inhalative Aufnahme zur Hintergrundexposition beiträgt. Die Konzentrationen liegen meist

im Bereich von 0.001 bis 0.003 µg/m^3, können in Städten aber auch Werte bis zu 0.1 µg/m^3 erreichen. Für einen Erwachsenen errechnen sich hieraus tägliche inhalative Aufnahmedosen von etwa 0.001 µg/kg KG bis zu 0.03 µg/kg KG in belasteten städtischen Regionen. Aufgrund der höheren Atemfrequenz und des geringeren Körpergewichts beträgt die tägliche inhalative Aufnahme bei kleineren Kindern mit Werten im Bereich von 0.002 bis 0.06 µg/kg KG (in belasteten städtischen Regionen) etwa das Doppelte. Auch Rauchen führt zu einer Exposition gegenüber Arsen. Allerdings werden keine Angaben zur inhalativen Aufnahme über das Passivrauchen, das für Kinder relevant sein könnte, berichtet (BfR 2012, Kapitel 3.2.2, Seite 11, Paragraph 4).

Die Arsenbelastung der Böden kann von natürlichen und anthropogenen Quellen stammen. Luftverschmutzung und das Ausbringen von Phosphatdüngern sind die Hauptquellen für Arsenablagerungen in landwirtschaftlichen Böden. Allgemein ist die atmosphärische Deposition von Arsen auf den Boden in den letzten 20 Jahren in Europa zurückgegangen.

- Die Hintergrundbelastung des Gesamtarsengehalts im Oberboden in der Schweiz beträgt 1.5 - 9.5 mg/kg (NABO 1999). Die menschliche Exposition gegenüber Arsen aus dem Boden kann relevant sein für Kinder die in kontaminierten Bereichen leben.

Nach den aktuellen Schätzwerten zur Hintergrundbelastung der Böden in der Schweiz liegt die maximale direkte Arsenaufnahme über den Boden bei Kleinkindern (Toddlers) mit 0.015 – 0.1 µg/kg KG/Tag deutlich unter dem von der EFSA abgeleiteten $BMDL_{01}$-Wertebereich von 0.3 bis 8 µg/kg KG/Tag (siehe **Tabelle 9-3**).

Tabelle 9-3: **Schätzwerte für die tägliche Exposition (µg/kg KG/Tag) gegenüber anorganischem Arsen im Vergleich zum $BMDL_{01}$.**

Exposition $As_{anorg.}$	**Zielgruppe**	**Normale Belastung $As_{anorg.}$ (µg/kg KG/Tag)**	**Starke Belastung $As_{anorg.}$ (µg/kg KG/Tag)**
Oral	Erwachsene	0.09 – 0.38	0.14 – 0.64
	Kleinkinder (1 - 3 Jahre)	**0.32 – 1.17**	**0.61 – 2.09**
Inhalativ	Erwachsene	0.001	0.03
	Kinder	**0.002 – 0.06**	**0.004 – 0.12**
Boden mit Hintergrundbelastung	**Kinder**	**0.015**[1]	**0.1**[2]
Gesamtexposition	**Kinder**	**0.3235 – 1.33**	**0.6155 – 2.31**
$BMDL_{01}$		**0.3 – 8**	**0.3 – 8**

[1] Basierend auf einer Hintergrundbelastung von 1.5 mg/kg Boden und KG = 12.5 kg und 50% „Relative Bioavailability“
[2] Basierend auf einer Hintergrundbelastung von 9.5 mg/kg Boden und KG = 12.5 kg und 50% „Relative Bioavailability“

9.5.2 Innere Exposition

For arsenic, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

The absolute oral bioavailability of arsenic from soil is not directly available for humans. Arsenic absorption rate is not well characterized in humans (section 9.5.2.1), in particular in food which sugegst 33-86% bioavailability vs > 80-95% in drinking water. SCAHT therefore recommends the use of a conservative 100% value for the oral bioavailability from food and water. No studies on arsenic bioavailability from ingested soil have been conducted in humans (9.5.2.2), but data are available in experimental animals (9.5.2.3).

The Relative Oral Adjustment Factor (RAF) approach can be used to estimate the absolute oral bioavailability from soil (section 9.5.2.4). Animal oral relative bioavailability from soil data woud support the use of a lower default RAF value i.e. 30%, rather than the medium specific RAF of 50%. However, SCAHT considers the latter as a conservative upper value for its risk assesssment, constituting a realistic worst case approach.

Therefore, for its assessment, SCAHT estimates the absolute oral bioavailabilty of arsenic from soil to be 50%, assuming a conservative 100% oral bioavailability from dietary sources/drinking water, and considering that soluble forms of arsenic would account for max 50% of this value.

9.5.2.1 Oral bioavailability from food and/or water from dietary studies

The absorption of ingested inorganic arsenic varies, depending on the chemical speciation, the solubility of the arsenical compounds (the more water soluble the compound, the greater its absorption), the presence of other food constituents and nutrients in the gastrointestinal tract, and the food matrix itself (EFSA 2009, EFSA 2014). Other estimates by Batelle and Exponent (2000) indicate a bioavailability from soluble forms of arsenic of > 80%. Bioavailability data from foodstuffs are scarce but suggest absorption rate between 33-86% (Juhasz et al., 2006, 2008). There are no data to suggest that absorption of arsenic from the gut in children differs from that in adults (ATSDR 2007).

- Studies in humans indicate that arsenite and arsenate present in drinking water are rapidly and nearly completely (about 95 %) absorbed after ingestion, which is well supported by several studies in experimental animals, in particular rats and mice (ATSDR, 2007).
- In a juvenile swine model, Juhasz et al. (2006, 2008) conducted a serie of experiments to investigate the impact of arsenic in food on the oral arsenic bioavailability. They showed that the speciation of arsenic has a large impact on the amount of arsenic absorbed after consumption of arsenic-contaminated rice (Juhasz et al., 2006): for rice (from the supermarket) cooked with arsenic contaminated water, arsenic was present entirely in the inorganic form, and bioavailability was high (89%); however, for a greenhouse-grown rice (using irrigation water contaminated with sodium arsenate), 86% of total arsenic was present as dimethylarsinate (organic arsenic) resulting in the absorption of only 33% of the total rice-bound arsenic. Juhasz et al. (2008) demonstrated further that bioavailability from arsenic contaminated foodstuffs was 100% for mung beans but only 50% for lettuce and chard.

⇒ **Based on these data, SCAHT assumes a conservative oral bioavailability from the diet of 100% for its assesssment.**

9.5.2.2 Oral bioavailability from in vivo soil ingestion studies in humans

No studies could be identified in the literature that investigated the oral absorption of arsenic in humans following soil ingestion. According to Battelle and Exponent (2000, chapter 3.1.2, page 3-2,

first paragraph), it has been estimated to be between 10-50% lower as the bioavailability form soluble arsenic compounds.

9.5.2.3 Oral bioavailability from in vivo soil ingestion studies in experimental animals

There are many studies that studies in experimental animals that have evaluated the impact of the ingestion of arsenic contaminated soil on arsenic bioavailability. Most notably, the USEPA has compiled and reviewed data on relative bioavailability of arsenic in soil (USEPA 2012):

- Key studies consist of 64 relative bioavailability (RBA) estimates based on bioassays in juvenile swine (Basta et al., 2007; Casteel and SRC, 2005, 2009a,b,c, 2010a,b,c; Juhasz et al., 2007; Rodriguez et al., 1999; U.S. EPA, 1996, 2010, as cited by USEPA 2012), 24 RBA estimates based on bioassays in monkeys (Freeman et al., 1995; Roberts et al., 2002, 2007; U.S. EPA, 2009, as cited by USEPA 2012), and 15 RBA estimates based on bioassays in mice (Bradham et al., 2011, 2012, as cited by USEPA 2012).

➢ **For the entire data set (n=103), RBA estimates ranged from 4.1 to 78%, with an arithmetic mean of 31% (±16, SD, 5th-95th percentile range: 7–57%) (as cited).**

Some relative bioavailability data from soil ingestion studies have also been reviewed recently by Ng et al. (2015):

- USEPA (1996) reported mean relative bioavailability value from soil of 78%, following oral gavage in immature swine during 6 days. Studies with the New Zeland white rabbit showed mean relative bioavailability values of 50% ± 5.7% and 70% following ingestion (oral gavage) of smelter impacted soil during 5 days (Freeman 1993a, 1993b as cited). In monkeys, Freeman et al. (1993b, 1995 as cited) showed mean relative bioavailability values between 10-44%, following oral gavage of smelter impacted soil during 5-7 days. In rats, studies with various contaminated soils reported mean relative bioavailability value from soil between 4-92%, following oral gavage with soluble arsenic salts during 4 days (Ng and Moore, 1996 as cited).
- These results are in good agreement with Ruby et al. (1999) who reported that studies of relative arsenic bioavailability from (residential) soils of 48% in rabbits, 20% in monkeys and values between 15-62% (mean 36%) in juvenile swine. DEPA (2003) reported that studies of arsenic in soils gave relative bioavailabilities of 7-58% (6 soils).

9.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of arsen from soil compared to food or water, is to use the **Relative Oral Adjustment Factor** (RAF) approach proposed by the USEPA, as outlined in the methodology section (TIER 2 approach).

A default oral Relative Adjustment Factor of 0.5 (50%) has been proposed by the US. Michigan State Department of Environmental Quality to account for reduced oral bioavailability from arsenic in soil (NRC 2003, Table 2.1 p.70). However, the justification for this value is not made explicit in the NRC report (personnal communication).

- Relative bioavailability values from soil of 80% and 42% based on in vivo studies in swine, and 18% in monkey, respectively, have been used for human health risk assessment by USEPA Region 10 and 8 (NRC 2003, Table 2.4 pp.86-87).
- According to the Danish EPA (DEPA 2003), it has been suggested that a range of arsenic bioavailability from soils of 8-30% would be more appropriate than the default 50% RAF (or RBA) value.

➢ **This view is in line with the recent estimate by USEPA (2012) which estimated a collective**

RBA arithmetic mean of 31% (±16, SD, 5th-95th percentile range: 7-57%). However, US EPA evaluated literature relevant to estimating a relative bioavailability (RBA) value of arsenic in soil and reached the following conclusions: (1) Currently available research information suggests that an RBA of arsenic in soils can be expected to be less than 100%; (2) the upper percentile of U.S. data [SCAHT notes: Superfund Sites data] gives a default RBA arsenic in soil value of 60%; and (3) the default RBA for arsenic in soils should be used only if site-specific assessments for arsenic RBA are not feasible (USEPA 2016).

⇒ **The 50% RAF constitutes a realistic worst case approach, which is used by SCAHT as a conservative upper value for its risk assesssment**

⇒ **For its risk assessment, SCAHT estimates the absolute oral bioavailabilty of arsenic from soil to be 50%, assuming a conservative 100% oral bioavailability from dietary sources/drinking water, and considering that soluble forms of arsenic would account for max 50% of this value.**

9.5.2.5 Summary of the in vitro bioaccessibility information

Arsenite and arsenate are the most abundant forms found in the environment. In soil, it is expected that under oxidizing conditions and low pH inorganic arsenic is predominatly found in the pentavalent state. The availability/bioaccessibility of arsenic in soils is usually driven by multiple factors: the presence of Fe-oxides and/or phosphorus, (co)precipitation in salts, pH, organic matter, clay content, rainfall amount, etc. (Moreno-Jiménez et al., 2012). Depending on the soil type chemistry, arsenic may be strongly embedded in the matrix of poorly soluble minerals (e.g. sulfide or silica) and have a poor bioaccessibility. For example, sandy soils are known to have a strong arsenic retention capacity (ATSDR 2007).

Many *in vitro* studies have evaluated the bioaccessibility of arsenic from soil using various test systems (e.g. SBET, PBET, IVG, DIN, UBM). DEPA (2003, Appendix) and Ng et al. (2015) have reviewed several studies (1996-2007), which collectively showed a broad range of bioaccessiblity values (<1-89%).

- Studies with residential soils using PBET (intestinal) have found bioaccessibility values between 39-66% (Carrizales et al 2006) or PBET (gastric) values between 34-54% (Ruby et al., 1996).
- Wilson et al. (2013) found that arsenic oral bioaccessibility as measured by SBET was <7 % for total arsenic in two soils.
- Li et al. (2014) reported that arsenic bioaccessibility values from soil were mostly less than 30%, with average bioaccessibility values 2.13 ± 2.55% for the SBET extraction; 6.62 ± 6.37% for the PBET (gastric) extraction; and 2.40 ± 2.01% for the PBET (intestinal) extraction, respectively.

➢ According to ATSDR (2007), estimates of the soluble, or bioaccessible, arsenic fraction have ranged from 3 to 50% for various soils and mining and smelter waste materials (Pouschat and Zagury 2006; Rodriguez et al. 1999; Ruby et al. 1996). ATSDR (2007) further notes that these estimates are similar to in vivo estimates of the relative bioavailability of arsenic in these same materials (Ruby et al. 1999).

Indeed, some studies (e.g. Denys et al., 2012; Juhasz et al., 2007, 2009; Rodriguez et al., 1999) have attempted to establish a relationship between arsenic bioaccessibility in vitro and arsenic

bioavailability in vivo, i.e. to demonstrate that in vitro bioaccessibility data may be a good predictor of its bioavailability in vivo. While correspondence or linear correlation between bioaccessibility and bioavailability has been reported, the data available however clearly demonstrate that the correspondence or correlation is not obtained with all soils and tests (DEPA 2003, Ng et al., 2015). However, Denys et al. (2012) reported a good correlation for arsenic between bioaccessibility data as produced with the Unified BARGE Method test compared with bioavailability measurements in the juvenile swine model.

9.6 Risikoabschätzung

Die EFSA geht davon aus, dass in der Regel innerhalb der EU die Arsenexposition über den Boden im Vergleich zu der täglichen alimentären Arsenaufnahme wahrscheinlich gering ist (EFSA 2009), macht aber keine expliziten Angaben zur Bioverfügbarkeit des Arsens nach direkter Bodenaufnahme. Die Annahme der EFSA wird auch durch Untersuchungen in einer ehemaligen deutschen Bergbauregion mit hohen Arsengehalten im Boden belegt. Dort wurden keine erhöhten Arsenkonzentrationen im Urin und im Haar von Kindern gefunden. Die EFSA schlussfolgert, dass die Exposition gegenüber Arsen über den Boden offenbar für Kinder in Europa keinen relevanten Aufnahmeweg darstellt (BfR 2012, Kapitel 3.2.2, Seite 11, Paragraph 5).

Ein Vergleich des von der EFSA abgeleiteten Bereichs der $BMDL_{01}$-Werte zwischen 0.3 bis 8 µg/kg KG/Tag mit den aktuellen Schätzwerten für die tägliche Exposition gegenüber anorganischem Arsen (siehe Tabelle 9.3) zeigt, dass für Kinder die tägliche Arsenaufnahme über Lebensmittel und Trinkwasser im Bereich der unteren Grenze dieses BMDL-Wertebereiches liegt. Dieser Wertebereich ist aber bereits risikobehaftet, weil er eine tägliche Aufnahmedosis charakterisiert, bei der ein 1%-iges Risiko für verschiedene toxikologische Endpunkte besteht. Die zugrunde gelegten gesundheitlichen Effekte (Hautläsionen, Haut-, Lungen- und Blasenkrebs) sind dabei besonders schwerwiegend. Zwischen den Arsen-Aufnahmemengen und den Dosen, ab denen Arsen Gesundheitsbeeinträchtigungen verursachen kann, besteht daher kein Sicherheitsabstand. Daher können alleine durch die Arsenaufnahme über Nahrung und Trinkwasser gesundheitliche Risiken nicht ausgeschlossen werden (BfR 2012, Kapitel 3.2.3, Seite 12, Paragraph 3). Jede zusätzliche Arsenbelastung durch das Verschlucken kontaminierter Böden könnte das Risiko gesundheitlicher Beeinträchtigungen erhöhen. Deshalb sollte für die Festlegung des Sanierungswerts das ALARA-Prinzip zur Anwendung kommen.

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten) festgelegte Sanierungswert für Arsen für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, ist auf 50 mg As/kg Boden festgelegt. Ein 12.5 kg schweres Kind, das täglich 250 mg Boden verschluckt, nimmt unter der Annahme einer 50% absolute orale Bioverfügbarkeit des Arsens aus dem Boden zusätzlich 0.5 µg/kg KG/Tag auf.

Aufgrund der Streuung des $BMDL_{01}$-Wertebereiches von 0.3 bis 8 µg/kg KG/Tag ist das zusätzliche Gesundheitsrisiko durch die Aufnahme von Arsen über den Boden in Höhe von 0.5 µg/kg KG/Tag schwer abzuschätzen. Im vorliegenden Szenario liegt die tägliche Exposition gegenüber anorganischem Arsen aus dem Boden im unteren Bereich der mittleren täglichen Arsenaufnahme über Lebensmittel und Trinkwasser von 0.32 - 2.09 µg/kg KG/Tag und im Bereich der unteren Grenze des $BMDL_{01}$-Wertebereiches von 0.3 bis 8 µg/kg KG/Tag, der mit einem kleinen zusätzlichen Gesundheitsrisiko verbunden ist. Obwohl nach Meinung des SCAHT das zusätzliche Gesundheitsrisiko durch die direkte Arsenaufnahme über den Boden eher gering ist, stellt die Exposition über den Boden einen Hauptaufnahmepfad in der gleichen Grössenordnung wie die diätische Exposition dar. Obwohl standardmässig für die Festlegung des Sanierungswerts das ALARA-Prinzip zur Anwendung kommen sollte, ist es sinnvoll die Wirksamkeit einer Reduzierung des Sanierungswertes für Arsen im Boden im Zusammenhang mit anderen möglichen Risikominimierungsmassnahmen abzugleichen.

9.7 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften in Europa, USA und Kanada (z. B. Carlon, 2007; Provoost et al., 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden (siehe Anhang 1).

BE: 110; CZ: 70; NL: 55; D: 50; A, **CH: 50**; F: 37; E: 30; I, UK: 20; S: 15; USA: 19; CAN: 12 (mg/kg dm).

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10 Chromium (VI)

10.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 100 mg Cr(VI)/kg Boden sollte reduziert werden, weil bereits alleine das Verschlucken von kontaminiertem Boden einen Hauptexpositionspfad für Cr(VI) darstellt und zu einer Exposition führt, die den von der EFSA geforderten Mindest-MOE für neoplastische Befunde unterschreitet.
Gefährdungspotential	Hoch	Humankanzerogen
Kanzerogen	Ja	Im Menschen Tumore in der Lunge und Nasennebenhöhle nach Inhalation hoher Dosen am Arbeitsplatz. Im Tier Magen-Darm-Krebs.
Mutagen	Ja	DNA-Schäden im Menschen: Durch die intrazelluläre Reduktion von Cr(VI) zu Cr(III) entstehen reaktive Sauerstoffspezies, die DNA-Addukte bilden und die Struktur schädigen können. Wenn die Reduktion nicht in direkter Nähe der DNA stattfindet werden die Sauerstoffspezies durch Reaktionen mit anderen intrazellulären Liganden abgefangen und detoxifiziert. Positive in vitro-tests: Die Relevanz der in vitro Tests für die orale Exposition des Menschen ist unklar, weil die Tests die physiologischen Abwehrmechanismen des Menschen umgehen die Cr(VI) zum weniger toxischen Cr(III) reduzieren.
Reprotoxisch	Ja	Entwicklungstoxisch in Tierstudien. Im Menschen gibt es keine Hinweise auf Reproduktionstoxizität.Chrom ist plazentagängig liegt aber aufgrund der reduzierenden Bedingungen im Organismus in der Muttermilch im Wesentlichen als Cr(III) vor. Cr(III) ist ein wichtiger Nährstoff zur Aufrechterhaltung des Glukosestoffwechsels. Aufgrund der schlechten Bioverfügbarkeit von Chrom führen auch hohe Dosen nicht zu einer Überversorgung des Säuglings.
Neurotoxisch	Nein	
Andere	Ja	Intestinale Hyperplasie und Hämatotoxizität beim Menschen

Gesundheitsbasierter Referenzwert		$BMDL_{10}$ von 1.0 mg Cr (VI)/kg KG/Tag (Adenomen und Karzinomen im Dünndarm von Versuchstieren) $BMDL_{10}$ von 0.11 mg Cr (VI)/kg KG/Tag (Intestinale Hyperplasie in vivo) $BMDL_{05}$ von 0.2 mg Cr (VI)/kg KG/Tag (Hämatotoxizität, Hämatokrit in vivo)
Exposition		
Äussere Exposition Boden (250 mg)		100 mg Cr(VI)/kg Boden = 25 µg Cr(VI)/250 mg Boden = 2 µg Cr(VI)/kg KG/Tag (KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 10% oraler Bioverfügbarkeit: 2 µg Cr(VI)/kg KG/Tag (KG: 12.5kg) = 0.2 µg Cr(VI)/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Die Allgemeinbevölkerung nimmt i.d.R. mehr als 90% des Gesamtchromgehalts über Lebensmittel auf. In der festen Nahrung findet sich hauptsächlich Cr (III), im Trinkwasser hauptsächlich Cr (VI). EFSA-Studie zur Exposition gegenüber Trinkwasser: 96.6 - 239.3 ng Cr(VI)/kg KG/Tag (Kleinkinder) Zulässige Exposition gemäss FIV: 1600 ng Cr(VI)/kg KG/Tag (Kleinkinder)
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Möglich	Die geschätzte tägliche Cr(VI)-Aufnahme durch das Trinkwasser für stark belastete Kleinkinder unterschreitet den geforderten Mindest-MOE für neoplastische Befunde von > 10000. Auch das Verschlucken von kontaminiertem Boden unterschreitet den MOE. Eine zusätzliche Gesundheitsgefährdung ist möglich. Trinkwasser EFSA mittel: MOE = 10352 Trinkwasser EFSA hoch: MOE = 4179 Trinkwasser FIV: MOE = 625 Boden: MOE = 5000
Grenzwert im Vergleich		USA: 210; **CH: 100**; NL: 78; E: 10; S: 5; I: 2; CAN: 0.4 (mg **Cr(VI)**/kg dm)
Datenlage	Zufriedenstellend	Es gibt keine Studien zur Bioverfügbarkeit von Chromium aus dem Boden im Mensch, und nur wenige Tierstudien. Epidemiologische Daten zur Humankanzerogenität nach oraler Exposition im Menschen lassen keine eindeutigen Schlüsse zu.

10.2 Zusammenfassung

Der in der Schweizer Altlasten-Verordnung (Verordnung über die Sanierung von belasteten Standorten)[1], festgelegte Sanierungswert für sechwertiges Chrom (Cr VI) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen, in Höhe von 100 mg Cr(VI)/kg Boden soll nach Meinung des SCAHT reduziert werden, weil der von der EFSA geforderte Mindest-Margin of Exposure (MOE) von >10000 für neoplastische Läsionen durch die Gesamtexposition gegenüber Cr (VI) aus Trinkwasser und direkter Bodenaufnahme unterschritten wird. Der Mindest-MOE für neoplastische Läsionen von > 10000 bezieht sich auf die niedrigste Dosis, die in chronischen Trinkwasserstudien in Versuchstieren zu einer 10% Erhöhung von Adenomen und Karzinomen geführt hat.

Die Allgemeinbevölkerung nimmt i.d.R. mehr als 90% des Gesamtchromgehalts über Lebensmittel auf (EFSA 2014). In der festen Nahrung findet sich hauptsächlich dreiwertiges Cr (III), im Trinkwasser hauptsächlich Cr (VI). Im Menschen werden weniger als 10% des über die Nahrung eingenommenen Chroms in den Körper aufgenommen. Die Bioverfügbarkeit ist abhängig von der Oxidationsstufe und der Art der Liganden. Die geringe Bioverfügbarkeit des Cr (III) (<0.5%) gegenüber dem Cr (VI) (<10%) geht einher mit einer geringeren oralen Toxizität.

Im Gegensatz zu Cr (III) ist Cr (VI) genotoxisch und kanzerogen. Für den Menschen ist ein Zusammenhang zwischen der Exposition gegenüber Cr (VI) und dem Auftreten von Tumoren allerdings ausschliesslich für Tumoren der Lunge und seltener der Nasenhöhle und nur nach hoher inhalativer Exposition am Arbeitsplatz belegt. Befunde zu anderen Krebserkrankungen, die gelegentlich in einigen epidemiologischen Studien beschrieben wurden (Prostatakrebs, Lymphome, Leukämie, sowie Tumore der Knochen, des Magens, des Gehirns, der Nieren und der Hoden), waren fast ausnahmslos nicht statistisch signifikant, und inkonsistent (De Flora 2000).

Bei oraler Exposition wird Cr (VI) wirksam durch Speichel, Magensaft und Darmbakterien zu Cr (III) reduziert und damit entgiftet. Ist die Reduktion unvollständig kann Cr (VI) aus dem Darm absorbiert werden und mit dem Blut in die Leber gelangen. Durch die effiziente Aufnahme und Reduktion von Cr (VI) zu Cr (III) sowohl in den roten Blutkörperchen als auch in der Leber kann weiteres Cr (VI) effizient reduziert und detoxifiziert werden. Diese Mechanismen erklären die mangelnde Genotoxizität, Karzinogenität und Induktion von anderen langfristigen Auswirkungen auf die menschliche Gesundheit nach oraler Exposition gegenüber Cr (VI).

Tierversuche mit Cr (VI)-Verbindungen zeigen kanzerogene Effekte. Am kritischsten werden Karzinome des Dünndarms eingeschätzt. Viele dieser positiven Tierstudien sind aber nicht relevant für den Menschen, weil keine orale Exposition stattgefunden hat und somit die oben beschriebenen physiologischen Abwehrmechanismen des menschlichen Organismus umgangen werden (De Flora 2000). Das gilt auch für zahlreiche *in vitro* Studien, die eine genotoxische Wirkung des Cr (VI) belegen. Typischerweise wurden im Tierversuch Tumore nur bei der höchsten getesteten Dosis gefunden und die Tumoren waren lokal auf die Applikationsstelle der Testsubstanz begrenzt.

⇒ Obwohl es derzeit nicht genügend wissenschaftliche Daten gibt, die eine humankanzerogene Wirkung von Cr (VI) nach oraler Exposition belegen, betrachtet das SCAHT den von der EFSA festgelegten Mindest-MOE für neoplastische Läsionen von grösser als 10000 als relevant für

[1] AltlV 1998, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

die vorliegende Risikobeurteilung. Das SCAHT ist der Meinung, dass eine mögliche kanzerogene Wirkung des Cr (VI) nach oraler Exposition nicht völlig ausgeschlossen werden kann. Dass in epidemiologischen Studien kein Zusammenhang zwischen hohen Cr (VI)-Belastung durch das Trinkwasser und einem erhöhten Krebsrisiko identifiziert werden konnte, könnte an den bekannten Unzulänglichkeiten epidemiologischer Studien liegen. Ausserdem basiert die Herleitung von BMDL-Werten durch die EFSA auf chronischen Trinkwasserstudien in Versuchstieren, die die physiologischen Abwehrmechanismen des Menschen hinreichend simulieren sollten.

Das Ausmass der Risikominimierungsmassnahmen um die Belastung des Menschen gegenüber Cr (VI) zu reduzieren, hängt entscheidend davon ab, welche Expositionsschätzungen zur Hintergrundbelastung zu Grunde gelegt werden.

⇒ Das SCAHT hat acht verschiedene Szenarien (S1 – S8) aufgestellt, um diese Frage zu beantworten. Die geschätzte Hintergrundbelastung über das Trinkwasser laut EFSA (S3 und S4: 96.6 - 239 ng/kg KG/Tag) ist wesentlich geringer als die berechnete Belastung über das Trinkwasser die laut Schweizer FIV zulässig wäre (S5: 1600 ng/kg KG/Tag). Dem Verschlucken von Boden kommt in den EFSA-Szenarien eine wesentlich grössere Bedeutung zu. Die Szenarioplanung zeigt, dasss die Belastung durch das Verschlucken von belastetem Boden bei Kleinkindern zu einer Exposition führt (S1: 200 ng/kg KG/Tag), die etwa doppelt so hoch ist wie die von der EFSA geschätzte mittlere Exposition über das Trinkwasser (S3: 96.6 ng/kg KG/Tag) und die etwa gleich gross ist, wie die von der EFSA geschätzte hohe diätische Exposition gegenüber Trinkwasser (S4: 239 ng/kg KG/Tag).

- Im letzteren Fall argumentiert die EFSA, dass ein Krebsrisiko rein rechnerisch wahrscheinlich ist, weil der geforderte Mindest-MOE von >10000 für neoplastische Läsionen bei hoher Exposition nicht mehr eingehalten wird, aber aufgrund der breiten Streuung der zugrundeliegenden Expositionsabschätzungen (vergleiche Tabelle 4) nur für eine kleine Gruppe relevant sein dürfte und wenig Anlass zur Besorgnis besteht (EFSA 2014). Auch die zusätzliche Aufnahme von 200 ng Cr(VI)/kg KG/Tag über den Boden ist mit grossen Unsicherheiten behaftet, so dass man bei der Gesamtexposition aus Trinkwasser und Boden in ähnlicherweise argumentieren könnte.

⇒ Das SCAHT ist aber der Meinung, das zur Berechnung der Gesamtexposition aus dem Verschlucken von Boden und dem Trinkwasserkonsum die zulässige Hintergrundbelastung über das Trinkwasser gemäss Schweizer FIV (S5: 1600 ng/kg KG/Tag) berücksichtigt werden muss. Legt man den Grenzwert aus der FIV zugrunde, wird sogar der geforderte Mindest-MOE für die sensitivste nicht-neoplastischen Läsion von > 100 unterschritten (S8: MOE = 67). Da das Trinkwasser in diesem Szenario den Hauptexpositionspfad darstellt, kann ein MOE >100 nur durch eine Reduktion des FIV-Wertes erreicht werden.

10.3 Gefährdungspotential

Chrom und seine Salze werden beim Gerben von Leder, zur Herstellung von Katalysatoren, Pigmenten, Anstrichfarben und Fungiziden/Pflanzenschutzmittel, in der Keramik- und Glasindustrie, bei der Herstellung von synthetischen Rubinen und Tonbänder sowie in der Fotografie und als Laborreagenzien verwendet.

Chrom tritt in verschiedenen Wertigkeitsstufen von -2 bis +6 auf, wobei dreiwertiges Chrom (Cr (III)) und sechswertiges Chrom (Cr (VI) die stabilsten und biologisch relevantesten Oxidationsstufen sind. Cr (III) ist ein natürlicher Nahrungsbestandteil in einer Vielzahl von Lebensmitteln und auch in Nahrungsergänzungsmitteln. Das toxischere Cr (VI) stellt eine Kontamination durch anthropogene Aktivitäten dar (EFSA 2014, Summary, page 2, paragraph 2).

Im allgemeinen sind Cr (VI)-Verbindungen deutlich toxischer als Cr (III)-Verbindungen, weil sie besser von der Zelle aufgenommen werden. Die inhalative Exposition von Cr (VI)-Verbindungen ist toxischer als die orale Exposition, weil eine rasche Detoxifizierung von Cr (VI) zu Cr (III), wie sie unter den reduzierenden Bedingungen des sauren Milieus im Verdauungstrakts stattfindet in der Lunge nicht stattfindet.

- **Inhalative Exposition**

  Die inhalative Exposition ist für die Allgemeinbevölkerung wenig relevant. Die berufsbedingt inhalative Exposition gegenüber Cr (VI)-Verbindungen führt zu Irritationen der Atemwege und Augen. Geschwüre und Perforationen der Nasenscheidewand, Krebserkrankungen der Atemwege und Asthma können die Folge sein.

- **Orale Exposition**

  Die orale Exposition gegenüber hohen Dosen von Cr (VI) Verbindungen führt zu schweren Atemwegserkrankungen, Herz-Kreislauf, Magen-Darm-, Blut-, Leber-, Nieren- und neurologische Erkrankungen.

- **Dermale Exposition**

  Die berufsbedingte dermale Exposition kann zu Hautgeschwüren führen. Cr (VI) ist eine häufige Ursache für allergische Kontaktdermatitis (WHO 2013, Seite 5, rechte Spalte, Paragraph 5).

10.3.1 Toxikologische relevante Endpunkte

10.3.1.1 Kanzerogenität

Im Gegensatz zu Cr (III) ist Cr (VI) genotoxisch und kanzerogen. Für den Menschen ist ein Zusammenhang zwischen der Exposition gegenüber Cr (VI) und dem Auftreten von Tumoren allerdings ausschliesslich für Tumoren der Lunge und seltener der Nasenhöhle, und nur nach hoher inhalativer Exposition am Arbeitsplatz belegt. Befunde zu anderer Krebserkrankungen, die gelegentlich in einigen epidemiologischen Studien beschrieben wurden (Prostatakrebs, Lymphome, Leukämie, sowie Tumore der Knochen, des Magens, des Gehirns, der Nieren und der Hoden), waren fast ausnahmslos nicht statistisch signifikant, und inkonsistent (De Flora 2000). Ein Zusammenhang zwischen der oralen Exposition von Cr (VI) im Trinkwasser und Krebs beim Menschen ist unklar (WHO 2013, Seite 6, rechte Spalte, Paragraph 2-4).

Bei oraler Exposition wird Cr (VI) wirksam durch Speichel, Magensaft und Darmbakterien zu Cr (III) reduziert und damit entgiftet. Ist die Reduktion unvollständig kann Cr (VI) aus dem Darm absorbiert

werden und mit dem Blut in die Leber gelangen. Durch die effiziente Aufnahme und Reduktion von Cr (VI) zu Cr (III) sowohl in den roten Blutkörperchen als auch in der Leber kann weiteres Cr(VI) effizient reduziert und detoxifiziert werden. Diese Mechanismen erklären die mangelnde Genotoxizität, Karzinogenität und Induktion von anderen langfristigen Auswirkungen auf die menschliche Gesundheit nach oraler Exposition gegenüber Cr (VI) und das auf die Applikationsstelle der Testsubstanz begrenzte Auftreten von Tumoren im Tierversuch.

Die orale Exposition gegenüber Cr (VI)-Verbindungen löste bei Versuchstieren Magen-Darm-Krebs aus. In einem Teil der *in vivo* Studien (30 von 70, d.h. 42,9%) wurden kanzerogene Effekte von Cr (VI)-Verbindungen berichtet.

Viele dieser positiven Studien sind nicht relevant für den Menschen, weil die Expositionspfade nicht relevant sind und somit die physiologischen Abwehrmechanismen des menschlichen Organismus umgangen werden (De Flora 2000). Das gilt auch für zahlreiche *in vitro* Studien, die eine genotoxische Wirkung des Cr (VI) belegen. Typischerweise wurden im Tierversuch Tumore nur bei der höchsten getesteten Dosis gefunden und die Tumoren waren lokal auf die Applikationsstelle der Testsubstanz begrenzt.

Zur Herleitung eines BMDL-Wertes durch die EFSA wurde allerdings eine chronische orale Studie an Ratten herangezogen, die ebenfalls neoplastische Läsionen zeigte (EFSA 2014). Diese Studie ist relevant für die Risikoabschätzung, weil aufgrund der oralen Aufnahme die physiologischen Abwehrmechanismen des menschlichen Organismus hinreichend berücksichtigt sein sollten.

10.3.1.2 Genotoxizität

Chromosomenaberrationen und DNA-Schäden wurden in einigen Arbeitern, die Cr (VI) ausgesetzt waren beobachtet. Cr (VI) ist auch genotoxisch in *in vivo* (oral Ratte, Maus) und *in vitro* Tests. Im Körper wird Cr (VI) in der Regel zu dem weniger toxischen Cr (III) reduziert. Dadurch entsteht ein oxidativer Stress, der für die Toxizität von Cr (VI)-Verbindungen verantwortlich gemacht wird. Die Bildung von Cr-DNA-Addukten kann zu strukturellen DNA-Schäden führen, allerdings bindet Cr (III) stärker an die DNA als Cr (VI) (De Flora 2000; WHO 2013, Seite 5, rechte Spalte, Paragraph 3; WHO 2013, Seite 6, linke Spalte, Paragraph 3).

In diesem Zusammenhang wird diskutiert, ob die Reduktion von Cr (VI) zum weniger toxischen Cr (III) überhaupt als Detoxifizierung bezeichnet werden kann. Die Kontrahenten kamen zu der Übereinkunft, dass die intrazelluläre Reduktion des Cr (VI) zu Cr (III) als Toxifizierung betrachtet werden kann, wenn sie in unmittelbarer Nähe der DNA abläuft. Ansonsten ist die Reduktion als Detoxifizerung zu betrachten, weil die reaktiven Sauerstoffspezies die bei der Reduktion von Cr(VI) zu Cr(III) entstehen durch eine Reihe intrazellulärer Liganden, Nukleophile und Antioxidantien abgefangen werden, bevor sie an die DNA binden können (De Flora 2000, Seite 537, linke Spalte, Paragraph 2).

10.3.1.3 Kinder

Es gibt nur begrenzte Informationen über die Toxizität von Chrom in Kindern. Die meisten Angaben stammen von tödlichen Vergiftungsfällen. Die Effekte sind dabei ähnlich wie bei Erwachsenen, die letalen Dosen eingenommen haben (ATSDR 2012, Seite 285-289).

In Tierstudien konnte gezeigt werden, dass insbesondere Cr (VI) entwicklungstoxisch ist. Chrom ist plazentagängig und kann über die Muttermilch auf Säuglinge übertragen werden. Unter den reduzierenden Bedingungen im Organismus kann davon ausgegangen werden, dass der Grossteil des Chroms in der Muttermilch als Cr (III) vorliegt. Cr (III) ist ein wichtiger Nährstoff für die Aufrechterhaltung des normalen Glukosestoffwechsels (EFSA 2012, Seite 22-23). Es ist anzunehmen, dass selbst hohe Konzentrationen in der Muttermilch, aufgrund der geringen Bioverfügbarkeit von Chrom nicht zu einer Überexposition des Säuglings führen.

10.4 Gesundheitsbasierter Referenzwert

- Für **neoplastische Wirkungen des Cr (VI)** hat das CONTAM-Gremium einen "Benchmark Dosis Level-10%" ($BMDL_{10}$) von 1,0 mg Cr (VI)/kg KG/Tag abgeleitet aufgrund von diffuser Hyperplasie der Epithelzellen des Zwölffingerdarm in weiblichen Mäusen in einer chronischen Trinkwasserstudie. Dieser $BMDL_{10}$ wurde anschliessend für Margin of Exposure (MOE) Berechnungen für neoplastische Effekte ausgewählt (EFSA 2014, Kapitel 7.6, Seite 114, Absatz 3).
- Für **nicht-neoplastischen Effekte wurden zwei BMDL-Werte abgeleitet**. Zu einen wurde ein $BMDL_{10}$ von 0,11 mg Cr (VI)/kg KG/Tag für diffuse epitheliale Hyperplasie des Duodenum bei weiblichen Mäusen abgeleitet (in der gleichen chronischen Trinkwasserstudie). Dieser $BMDL_{10}$ wurde anschliessend für Margin of Exposure (MOE) Berechnungen für nicht-neoplastischen Effekte ausgewählt (EFSA 2014, Kapitel 7.6, Seite 115, Ende Absatz 1).

  Desweiteren wurde ein zweiter BMDL-Wert für nicht-neoplastischen Effekte, ein $BMDL_{05}$ von 0,2 mg Cr (VI)/kg KG/Tag für die Abnahme des Hämatokritwertes bei männlichen Ratten als Referenzpunkt für die MOE Schätzung der hämatotoxischen Effekte des Cr (VI) ausgewählt (EFSA 2014, Kapitel 7.6, Seite 115, Ende Absatz 1).

⇒ Das CONTAM-Gremium hat für nicht-neoplastischen Wirkung von Cr (III) einen tolerierbare tägliche Aufnahme (tolerable daily intake, TDI) von 0,3 mg/kg Körpergewicht (KG) pro Tag abgeleitet basierend auf dem niedrigsten NOAEL in einer chronischen oralen Toxizitätsstudie an Ratten und einem Sicherheitsfaktor von 1000. In diesem Fall wurde zusätzlich zum Standardsicherheitsfaktor von 100 wurde ein Sicherheitsfaktor von 10 angewandt, weil in der Studie keine ausreichenden Daten zur Reproduktions- und Entwicklungstoxizität vorlagen (EFSA 2014, Kapitel 7.6, Seite 114, Absatz 2).

Die Referenzwerte für neoplastische und nicht-neoplastische Effekte von Cr (III) und Cr (VI) sind in **Tabelle 10-1** dargestellt:

Tabelle 10-1: Übersicht der gesundheitsbasierten Referenzwerte für neoplastische und nicht-neoplastische Effekte von Cr(III) und Cr(VI).

(Quelle: EFSA 2014, Seite 114-115)

Chrom	Neoplastische Effekte	Nicht-neoplastische Effekte
Cr(III)	Keine Effekte	TDI von 0.3 mg Cr (III)/kg KG/Tag (NOAEL 2yr-rat, Safety factor: 1000)
Cr(VI)	$BMDL_{10}$ von 1.0 mg Cr (VI)/kg KG/Tag (Adenome und Karzinome im Dünndarm von Versuchstieren)	$BMDL_{10}$ von 0.11 mg Cr (VI)/kg KG/Tag (Intestinale Hyperplasie)
		$BMDL_{05}$ von 0.2 mg Cr (VI)/kg KG/Tag (Hämatotoxizität, Hämatokrit)

10.5 Exposition

10.5.1 Äussere Exposition

Die Allgemeinbevölkerung nimmt mehr als 90% des Gesamtchromgehalts über Lebensmittel auf (EFSA 2014, Kapitel 1, Seite 11, Paragraph 1). In der festen Nahrung findet sich hauptsächlich Cr (III), im Trinkwasser hauptsächlich Cr (VI). Über den Cr (VI)-Gehalt in der festen Nahrung gibt es nur mangelhafte Daten.

- Das CONTAM-Gremium geht in seiner Risikobewertung davon aus, dass der Gesamtgehalt an Chrom in Lebensmitteln als Cr (III) vorliegt, weil organische Substanzen in Lebensmittel ein reduzierendes Medium darstellen und eine Oxidation von Cr (III) zu Cr (VI) daher unwahrscheinlich ist. Ausserdem begünstigt das saure Milieu im Verdauungstrakt die Reduktion von Cr (VI) zu Cr (III).
- Weiterhin nimmt das CONTAM-Gremium an, dass im Trinkwasser Chrom ausschliesslich als Cr (VI) ("worst case") vorliegt. Zum einen hat sich gezeigt, dass das durchschnittliche Verhältnis Cr (VI) zu Gesamtchrom 0,97 beträgt, zum anderen werden in der Wasseraufbereitung Oxidationsmittel eingesetzt, die die Bildung von Cr (VI) gegenüber Cr (III) begünstigen (EFSA 2014, Kapitel 4.2.2.2, Seite 40, letzter Paragraph).

Das CONTAM-Gremium hat den Cr (VI)-Gehalt in den verschiedenen Trinkwasserarten abgeschätzt (siehe **Tabelle 10-2**) und anhand von Verbraucherstudien die Exposition des Menschen gegenüber Cr (VI) berechnet. Dabei wurde entweder der Konsum aller Trinkwasserarten berücksichtigt (siehe **Tabelle 10-3**) oder nur der Konsum von abgefülltem Trinkwasser (siehe **Tabelle 10-4**).

Tabelle 10-2: Chrom-Konzentrationen (µg/L) in den verschiedenen Arten von Trinkwasser

(Quelle: EFSA 2014, Seite 46 , Tabelle 7)

			N	LC	Concentration (µg/L)					
					LB/UB	Mean	P25	P50	P75	P95[(a)]
Drinking water	Bottle water	Bottled water (unspecified)	1 617	84	LB	0.9	0.0	0.0	0.0	6.7
					UB	3.4	1.0	4.0	5.0	6.77
		Carbonated mineral water	7 839	94	LB	0.3	0.0	0.0	0.0	1.2
					UB	2.8	2.0	2.0	3.0	10.0
		Still mineral water	3 706	88	LB	0.7	0.0	0.0	0.0	4.0
					UB	3.2	2.0	2.0	5.0	7.0
		Drinking water (unspecified)	3 174	55	LB	2.0	0.0	0.0	1.8	9.3
					UB	2.2	0.3	0.5	2.0	9.3
		Tap water	27 971	96	LB	0.2	0.0	0.0	0.0	0.0
					UB	1.9	1.0	1.0	2.0	5.0
		Water ice (for consumption)	21	95	LB	0.1	0.0	0.0	0.0	-
					UB	2.4	0.3	0.3	5.0	-
		Well water	1 818	86	LB	1.0	0.0	0.0	0.0	4.0
					UB	3.9	2.0	5.0	5.0	5.0

N: number of samples; LC: left-censored; LB: lower bound; UB: upper bound; P25/50/75/95: 25th/50th/75th/95th percentile.
(a): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

Aus der **Tabelle 10-3** geht hervor, dass Säuglinge und Kleinkinder durch den Konsum von Trinkwasser am stärksten gegenüber Cr (VI) exponiert sind. Die mittlere chronische Exposition von Kleinkindern (Toddlers) gegenüber Cr (VI) durch den Konsum aller Trinkwasserarten reichte von 7,5 (Minimum LB - mean exposure) bis 239,2 ng/kg KG/Tag (Maximum UB - 95% exposure).

Tabelle 10-3: Chronische Exposition (ng/kg KG/Tag) für Cr (VI) in den europäischen Ernährungserhebungen durch den Verbrauch von Leitungswasser und abgefülltem Mineralwasser.

(Quelle: EFSA 2014, Seite 57, Tabelle 9)

Mean exposure (ng/kg b.w. per day)						
	Lower bound (LB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max
Infants	14.2	-[a]	33.2	106.2	-[a]	159.1
Toddlers	7.5	15.3	39.6	34.8	82.2	96.6
Other children[d]	0.7	7.9	26.6	7.4	49.0	60.8
Adolescents[d]	0.9	4.0	10.2	8.8	26.9	44.2
Adults[d]	1.4	4.9	10.9	9.5	24.8	43.7
Elderly[d]	1.9	4.0	8.4	21.0	23.3	33.4
Very Elderly[d]	1.3	4.8	7.4	15.3	26.2	33.0
95th percentile exposure[b] (ng/kg b.w per day)						
	Lower bound (LB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max
Infants	49.8	-[c]	-[c]	-[c]	-[c]	320.2
Toddlers	16.1	101.3	113.3	126.5	185.4	239.3
Other children[d]	2.8	22.2	76.0	28.1	108.9	150.9
Adolescents[d]	2.9	11.5	29.7	28.5	64.1	110.3
Adults[d]	4.3	13.7	29.3	32.3	60.2	108.3
Elderly[d]	4.8	11.6	24.1	50.7	59.4	89.8
Very Elderly[d]	10.5	13.8	21.0	51.8	64.1	87.4

b.w.: body weight; LB: lower bound; UB: upper bound; P95: 95th percentile.
(a): Not calculated since estimates were only available from two dietary surveys;
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.
(c): Not calculated since estimates were only available from one dietary survey.
(d): Surveys from Greece (age class 'Other children'), Cyprus (age class 'Adolescents'), Latvia (age classes 'Other children', 'Adolescents' and 'Adults') and Hungary (age classes 'Adults', 'Elderly' and 'Very elderly' were excluded (see Table G2 in appendix)

Dies konnte durch Studien bestätigt werden in denen nur der Konsum von abgefülltem Wasser separat erfasst wurde (Tabelle 4). Hier reichte die Bandbreite der mittleren chronischen Exposition von Kleinkindern von <0,1 (Minimum LB – mean exposure) bis zu 149.7 ng/ kg KG/Tag (Maximum UB - 95% exposure).

Tabelle 10-4: Chronische Exposition (ng/kg KG/Tag) für Cr (VI) in den europäischen Ernährungserhebungen durch den Verbrauch von abgefülltem Mineralwasser.

(Quelle: EFSA 2014, Seite 58, Tabelle 10)

Mean exposure (ng/kg b.w per day)						
	Lower bound (LB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max
Infants	7.3	-[a]	32.4	28.2	-[a]	149.8
Toddlers	< 0.1	6.9	13.5	< 0.1	26.4	62.5
Other children	< 0.1	4.1	11.6	< 0.1	16.2	44.8
Adolescents	< 0.1	1.4	9.6	< 0.1	6.3	35.7
Adults	< 0.1	0.7	10.1	< 0.1	2.8	37.8
Elderly	< 0.1	3.4	7.8	< 0.1	15.7	28.9
Very Elderly	0.1	3.6	6.6	0.5	17.4	24.6
95th percentile exposure[b] (ng/kg b.w per day)						
	Lower bound (LB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max
Infants	38.3	-[c]	-[c]	-[c]	-[c]	143.8
Toddlers	0.0	27.6	39.9	0.0	109.8	148.7
Other children	0.0	20.0	33.0	0.0	76.9	126.4
Adolescents	0.0	10.3	29.0	0.0	38.2	107.9
Adults	0.0	4.0	28.5	0.0	16.3	106.3
Elderly	0.6	10.2	23.7	5.4	47.0	88.1
Very Elderly	5.1	10.6	19.7	18.8	49.7	75.8

(a): Not calculated since estimates were only available from two dietary surveys;
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.
(c): Not calculated since estimates were only available from one dietary survey.

Berücksichtigt man in einem "worst-case" Scenario zusätzlich Wasser das zur Zubereitung von Lebensmitteln (Kaffee, Tee, Baby- und Kindernahrung, Instant-Suppen, Trockenmilch und entwässerten Fruchtsäften) verwendet wurde, könnte sich die Exposition gegenüber Cr (VI) verdoppeln. Hierbei geht man davon aus, dass der Cr (VI)-Gehalt des verwendeten Wassers nicht zu Cr (III) reduziert wird, wenn die Nahrung gleich nach der Zubereitung verzehrt wird (ohne Tabelle). In ihren Risikoabschätzungen hat die EFSA solche Szenarien allerdings nicht berücksichtigt, weil es keine verlässlichen Methoden zur Bestimmung des Cr (VI)-Gehalts in der Nahrung gibt.

Die Relevanz der inhalativen und dermalen Exposition der Allgemeinbevölkerung gegenüber Chromverbindungen ist weniger gut charakterisiert.

- Das Einatmen von Chromverbindungen insbesondere im Zigarettenrauch kann zur Gesamtexposition beitragen, allerdings ist weder die Höhe der Exposition noch die Absorptionsraten verschiedener Chromverbindungen über die Lunge ausreichend charakterisiert.
- Durch Hautkontakt mit chromhaltigen Verbraucherprodukten (behandeltes Holz, Düngemittel, gegerbtes Leder) ist die Bevölkerung ebenfalls gegenüber Cr (VI) exponiert (ATSDR 2012; EFSA 2014). Auch hier lassen die vorhandenen Daten keine Quantifizierung zu.
- Die berufliche Exposition gegenüber Chrom kann zwei Größenordnungen höher sein als die Exposition der Allgemeinbevölkerung. Exponiert sind vor allem Arbeiter in der Chromat- und der Edelstahlproduktion, beim Schweißen und Verchromen, bei der Herstellung von Ferrochrom-Legierungen und der Chrompigmentproduktion sowie Arbeiter in der Gerberei-Industrie.

10.5.2 Innere Exposition

For chromium, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

The absolute oral bioavailability of chromium from soil is not directly available for humans. Since Chromium absorption rate is fairly well characterized in humans (at least from water sources) and below 10% (section 10.5.2.1), therefore it can be combined with the Relative Oral Adjustment Factor (RAF) approach to estimate the absolute oral bioavailability from soil.

However, given the lack of oral bioavailability information from soil ingestion in humans (section 10.5.2.2) and the limited data available in experimental animals (section 10.5.2.3), the proposed default value of 50% for inorganics is associated with a high degree of uncertainty, and a conservative approach to the RAF-value is applied (100%), which is in line with USEPA recommendations (USEPA 2007) for such situations (section 10.5.2.4).

This decision is further supported by the general lack of information related to speciation, and the quality of the in vitro studies (bioaccessbility) database, which in the present case cannot be used as supporting information to derive a more realistic bioavailability estimate (section 10.5.2.5).

In conclusion, SCAHT estimates the absolute oral bioavailability from ingested soil to be 10% for chromium.

10.5.2.1 Oral bioavailability from food and/or water from dietary studies

Die orale Bioverfügbarkeit ("Bioavailability") ist abhängig von der Oxidationsstufe und der Art der Liganden. Cr (III) hat über alle Expositionswege eine niedrigere Bioverfügbarkeit (<0.5%) als Cr (VI) (2-8%), weil es die Zellmembran nicht so leicht passieren kann (EFSA 2014). Im Menschen werden weniger als 10% des über die Nahrung aufgenommenen Chroms absorbiert (EFSA 2014, Kapitel 1, Seite 11, Paragraph 2; EFSA 2014, Kapitel 7.1.2, Seite 66). Die inhalative und dermale Bioverfügbarkeit wird auf 1% geschätzt.

Studies in humans studies suggest that the absorbed fraction of soluble Cr(VI) compounds (e.g. K2Cr2O7) is higher than insoluble forms; and soluble Cr(VI) compounds are absorbed to a greater extent than soluble Cr(III) compounds (e.g., CrCl3). Absorption of Cr(III) and Cr(VI), following ingestion by human volunteers of either single or multiple drinking water doses, were evaluated in a series of studies, based suually on urinary measurements; these studies have been summarized by NEPI (2000) and USEPA (2010).

USEPA (2010) noted that a considerable variability across the human volunteers was observed in the reviwed studies, which may reflect interindividual differences influencing gastric reduction (such as time since last meal or volume of the contaminated water ingested), but may also reflect different genetic capacities for Cr(VI) reduction (USEPA 2010, page 41).

- Donaldson and Barreras (1966) dosed six volunteers with either Cr(III) as chromium trichloride or Cr(VI) as sodium chromate and observed 0.5 and 2.1% absorption for Cr(III) and Cr(VI), respectively.
- Bunker et al. (1984) administered 0.35 μg Cr/kg-day as dietary Cr(III) and measured ca. 2.5% absorption in elderly humans, based on urinary chromium measurements.
- Kerger et al. (1996) estimated human oral bioavailability of Cr(III) as CrCl3 in drinking water to be 0.13%, of potassium dichromate (VI) reduced with orange juice to be 0.60%, and of Cr(VI) as K2Cr2O7 in drinking water to be 6.9%.
- Paustenbach et al. (1996) estimated oral bioavailability of Cr(VI) as K2Cr2O4 via drinking water consumed daily (5x 400 ml) for 17 days in a male Caucasian volunteer (age 44 years) to be 2%. Both plasma and red blood cells chromium concentrations returned rapidly to

background levels within a few days, again suggesting that concentrations of 10 mg Cr(VI)/L or less in drinking water of humans appears to be completely reduced to Cr(III) prior to systemic distribution.

- Kerger et al. (1997) found total chromium oral bioavailybility between 1.7-5.7% in five adult volunteers, using either bolus (5 or 10 mg) or multiple doses (15 or 30 mg) of Cr(VI) as K2Cr2O7 or K2CrO4, respectively via drinking water.

⇒ **In conclusion, oral bioavailability in humans from water sources are ca. in the range 0.5-3% for Cr(III) and 2-7% Cr(VI) (NEPI 2000; USEPA 2010; EFSA 2014). Based on these data, SCAHT assumes a max conservative 10% oral bioavailability from dietary sources (drinking water). Arsenic absorption data from foodstuffs were not located, but it is assumed that the bioavailability of soluble chromium compounds will not exceeed that of drinking water.**

10.5.2.2 Oral bioavailability from in vivo soil ingestion studies in humans

Only one study could be identified that investigated the impact of soil ingestion on the oral bioavailability of chromium (Gargas et al, 1994).

- Adult volunteers ingested a single daily bolus of a mixture of soil and chromite ore processing residue, for 3 consecutive days with chromium excretion monitored in the urine. The soil contained 103 mg total Cr/kg soil [81% as Cr(III) and 9% as Cr(VI)], and was sieved to <500 µm particle size. No significant increases in urinary chromium were found when comparing the individual baseline values with the post-dose samples. Because no positive control (i.e., pure chromium compounds without soil) was included in the study, relative bioavailability cannot be estimated from this study. Although not a formal bioavailability study, this study does provide evidence of very limited absorption of chromium from these samples (as cited by NEPI 2000, Kapitel 4.3.3.2, S. 4-20 und 4-21).

10.5.2.3 Oral bioavailability from in vivo soil ingestion studies in experimental animals

There are only limited in vivo studies in animals that investigated the impact of soil ingestion on the oral bioavailability of chromium (e.g. studies in rats by Witmer et al., 1989, 1991). Unfortunately, no reliable quantitative estimates of the relative bioavailability of soil chromium were generated by these studies (NEPI 2000, Kapitel 4.3.3.2, S. 4-20 und 4-21).

10.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of chromium from soil compared to food or water, is to use the Relative Oral Adjustment Factor (RAF) approach proposed by the USEPA, as outlined in the methodology section (TIER 2 approach).

- A default medium-specific oral relative absorption factor of 0.5 (50%) for inorganics has been proposed by the Michigan Department of Environmental Quality (NRC 2003, table 2.1, page 69). However, the justification for this value is not made explicit in the NRC report (personnal communication)

⇒ **However, the in vivo database is considered to be largely insufficient to support the use of the proposed default RAF factor of 50%. Therefore SCAHT applies a default RAF-value of 100%. This is in line with USEPA (2007) recommendations in such a case.**

⇒ **Es liegen keine Daten zur relativen Bioverfügbarkeit von Chrom aus dem Boden im Vergleich zur Nahrung vor. Deshalb geht das SCAHT in seiner Risikobeurteilung von einer absolute orale Bioverfügbarkeit des Chroms aus dem Boden in Höhe von 10% aus unter der**

Annahme dass die Bioverfügbarkeit des Chroms aus dem Boden nicht höher ist als die Bioverfügbarkeit aus der Nahrung. Im Menschen werden weniger als 10% des über die Nahrung aufgenommenen Chroms absorbiert.

10.5.2.5 Summary of the in vitro bioaccessibility information

Die Bioverfügbarkeit von Chrom aus dem Boden (= "bioaccessibility") wird ebenso wie die Spezifikation des Chroms und die Sorptionskapazität durch die physikalisch-chemischen Eigenschaften des Bodens, insbesondere dem pH-Wert, dem Gehalt an organischer Bodensubstanz, dem Tongehalt und der Menge an Eisenoxiden beeinflusst. Es hat sich gezeigt, dass die Cr (VI)-Sorption und damit die Bioverfügbarkeit aus dem Boden für den Menschen, je nach Bodenqualität variiert (z.B. im Bereich von 50 bis 750 mg Cr (VI) / kg Boden nach Jardine et al 2013) und dass die Sorption umso stärker ist, je höher der Gehalt an organischem Material und je niedriger der pH-Wert des Bodens (Broadway et al 2010; Jardine et al 2013).

Einige Studien haben die Bioverfügbarkeit von Chrom aus dem Boden (i.e. "bioaccessibility") auf Basis von Modellen abgeschätzt, die in vitro die Verdauungsprozesse im Magen und/oder Darm simulieren (e.g. SBET, PBET, UBM, siehe Methodik). Diese in vitro-Daten deuten tendenziell auf eine niedrige Absorptionsrate hin (im Mittel 2-10%, Broadway et al 2010; De Miguel et al 2012; Jardine et al 2013) (siehe **Tabelle 10-5**). Broadway et al (2010) untersuchte 27 städtischen Böden in Glasgow, Schottland, und fanden eine mittlere Bioverfügbarleit von 5% (Bereich: 1-31%). Die Daten ähnlich den Erhebungen von Ljung et al. (2007) auf städtischen Spielplätzen in Schweden (Mittel: 4,2%) oder De Miguel et al (2012) in Madrid, Spanien (Mittel: 6,4%). Ljung et al. (2007) zeigten, dass Chrom im Vergleich mit anderen Metallen, die niedrigste Bioverfügbarkeit aus dem Boden hat, vergleichbar mit Nickel, aber niedriger als Blei und niedriger als Arsen und Cadmium (Cr = Ni <Pb <As = Cd). Dies steht im Einklang mit Resultaten von De Miguel et al (2012), die zeigten, dass die Bioverfügbarkeit für Chrom aus den obersten Bodenschicht (1-2 cm) von Spielplätzen in Madrid, Spanien, am geringsten waren für Chrom (Cr <Ni <Co <Zn = Pb = Cu = As).

Tabelle 10-5: Overview of selected Cr bioaccessibility values published in the literature

(Quelle: De Miguel et al. 2012, page 682-683, Table 4; DEPA 2003, Appendix, page 101)

Soil type, source	In vitro Test	Type of phase in the in vitro model	Bioaccessibility mean value	Range (SD)	Reference
Waste and urban impact	DIN	gastric gastric+intestinal	17% 0.6%	- -	Barkowski et al. 1999
Mountain soil, mine waste	DIN	gastric gastric+intestinal	1.5% < LOD	- -	Barkowski et al. 1999
Soil, unspecified	DIN	gastric+intestinal	-	4-54%	Hack et al. 2002
Soil + chromium choride (III)	PBET	gastric	-	37-72%	Skowronski et al. 2001
Soil + dichromate (VI)	PBET	gastric	-	18-46%	Skowronski et al. 2001
Aged soil + chromium choride (III)	SBET	gastric	-	1.5-35%	Stewart et al. 2002
Urban	SBET	gastric	9.0	4-16	Madrid et al. 2008
Playground	SBET	gastric	6.4	(±4.2)	De Miguel et al. 2012
Urban	SBET	gastric	2.6	1-6	Madrid et al. 2008
Residential	PBET	gastric+intestinal	34	(±14)	Hamel et al. 1999
Playground	RIVM	gastric+intestinal	4.2	-	Ljung et al. 2007
Playground	PBET	gastric+intestinal	7.7	(±4.1)	De Miguel et al. 2012

10.6 Risikoabschätzung

Chrom (VI)-Verbindungen sind genotoxisch und kanzerogen. Die EFSA hat für die kritischsten toxikologischen Endpunkte eine Cr (VI)-Exposition berechnet, die das zusätzliche Gesundheitsrisiko für den Menschen begrenzen soll (sog. BMDL). Aus dem Verhältnis der Dosis, bei der man eine kleine, jedoch messbare negative Auswirkung erstmalig feststellt (BMDL), und dem tatsächlichen Expositionsniveau hat man den sog. MOE berechnet.

Ist der MOE für nicht-neoplastischen Effekte grösser als 100 und für neoplastischen Effekte grösser als 10000 geht das CONTAM-Gremium davon aus, dass die aktuelle Belastung mit Cr (VI) über das Trinkwasser nicht von Belang für die öffentliche Gesundheit ist.

Tabelle 10-6 listet die MOEs auf, wie sie von der EFSA aufgrund verschiedener europäischen Ernährungserhebungen berechnet wurden. Obwohl die MOEs für die verschiedenen Altersgruppen in den verschiedenen europäischen Ernährungserhebungen erheblich variieren zeigen sie, dass die Exposition gegenüber Cr (VI) aus dem Trinkwasser wenig Anlass zur Besorgnis gibt (EFSA 2014). Allerdings sind Säuglinge und Kinder grundsätzlich eher gefährdet als Erwachsene. Der geforderte Mindest-MOE von >100 für nicht-neoplastische Läsionen wird bei allen Altersgruppen deutlich überschritten. **Für neoplastische Läsionen wird der geforderte Mindest-MOE von >10000 bei einer mittleren Exposition nur bei Säuglingen unterschritten. Bei einer sehr hohen Exposition (95% Maximum UB) wird der geforderte MOE zwar von fast allen Altersgruppen unterschritten, allerdings erwartet man aufgrund der breiten Streuung der Werte, dass diese Unterschreitung nur für eine kleine Gruppe relevant sein dürfte.**

Tabelle 10-6: Margin of Exposure (MOE) für Cr (VI) berechnet aus verschiedenen europäischen Ernährungsstudien anhand des Trinkwasserverbrauchs (Leitungswasser und abgepacktes Mineralwasser).

(Quelle: EFSA 2014, Seite 116, Tabelle 24)

	Mean exposure[a]		95th percentile exposure[a]	
	MOE (min LB-max UB)	Dietary surveys with MOE below 10 000/Total surveys[b]	MOE (min LB-max UB)	Dietary surveys with MOE below 10 000/Total surveys[b]
Infants[c]	71 000 - 6300	2/2	21 000 - 3100	1/1
Toddlers	130 000 - 11 000	0/9	62 000 - 4200	6/6
Other children	1 400 000 - 16 000	0/15	360 000 - 6600	9/15
Adolescents	1 200 000 - 23 000	0/10	350 000 - 9100	1/10
Adults	710 000 - 23 000	0/13	230 000 - 9200	1/13
Elderly	540 000 - 29 000	0/6	210 000 - 11 000	0/6
Very elderly	740 000 - 29 000	0/4	95 000 - 11 000	0/3

(a): Dietary surveys with less than 50 % consumers were not considered (surveys from Greece (age class 'Other children'), Cyprus (age class 'Adolescents'), Latvia (age classes 'Other children', 'Adolescents' and 'Adults') and Hungary (age classes 'Adults', 'Elderly' and 'Very elderly', see Table G2 in appendix);
(b): Number of surveys with a MOE lower than 10000 at the UB;
(c): Estimate only available from two dietary surveys for the mean and only one for the 95th percentiles;

In **Tabelle 10-7** sind jeweils drei MOEs für acht verschiedene Expositionsszenarien berechnet. Der jeweilige MOE-Wert für neoplastische Befunde (Krebs) und die zwei unterschiedlichen nicht-neoplastischen Befunde (intestinale Hyperplasie und Hämatotoxizität) ergeben sich, indem man den jeweiligen BMDL-Wert für die drei unterschiedlichen toxikologischen Endpunkte durch spezifische Exposition dividiert, die für das jeweilige Szenario abgeschätzte wurde.

Rote Felder zeigen für welches Szenario der geforderte Mindest-MOE von >10000 für neoplastische Läsionen oder die geforderten Mindest-MOEs von >100 für nicht-neoplastische Läsionen nicht eingehalten werden und ein Gesundheitsrisiko wahrscheinlich ist. Grüne Felder zeigen wo die geforderten Mindest-MOEs eingehalten werden und ein Gesundheitsrisiko unwahrscheinlich ist.

10.6.1 Szenario 1

Verschlucken von Boden; Annahme Bioaccessibility Cr (VI) = 10%
Das tägliche Verschlucken von 250 mg Boden der mit 100 mg Cr (VI)/kg Boden belastet ist, führt zu einer externen Exposition von 25 µg Cr (VI)/Tag. Unter der Annahme einer oralen Absorption von 10% nach direkter Bodenaufnahme reduziert sich die bioverfügbare Dosis auf 2.5 µg Cr (VI)/Tag. Die zusätzliche Cr (VI)-Belastung für ein 12.5 kg schweres Kind liegt somit bei 0.2 µg Cr (VI)/kg KG/Tag (200 ng Cr (VI)/kg KG/Tag).

Bei diesem Expositionsszenario wird der geforderte Mindest-MOEs von >10000 für neoplastische Läsionen nicht eingehalten und ein zusätzliches Krebsrisiko ist wahrscheinlich.

Der geforderte Mindest-MOEs von >100 für nicht-neoplastische Läsionen wird eingehalten und ein zusätzliches Gesundheitsrisiko durch nicht neoplastische Befunde ist unwahrscheinlich.

10.6.2 Szenario 2: Verschlucken von Boden; Annahme Bioaccessibility Cr (VI) = 100%

Unter der Annahme eines worst-case Szenario mit 100% oraler Bioverfügbarkeit des Cr (VI) nach direkter Bodenaufnahme beträgt die zusätzliche Cr (VI)-Belastung für ein 12.5 kg schweres Kind 2 µg Cr (VI)/kg KG/Tag (2000 ng Cr (VI)/kg KG/Tag).

Hier werden die geforderten Mindest-MOEs sowohl für neoplastische und den sensitivsten nicht neoplastische Endpunkt unterschritten und ein Gesundheitsrisiko ist wahrscheinlich.

Allerdings ist dieses worst-case Szenario angesichts der zu erwartenden niedrigen Bioverfügbarkeit von Cr (VI) nicht realistisch. Zur Berechnung der MOEs aus der Gesamtexposition gegenüber Trinkwasser und kontaminiertem Boden wird dieses Szenario nicht berücksichtigt.

10.6.3 Szenario 3: Mittlere Exposition durch Trinkwasser laut EFSA

Legt man das mittlere Expositionszenario der EFSA zur Cr(VI)-Aufnahme über das Trinkwasser zugrunde, liegt die Exposition über das Trinkwasser bei 96.6 ng Cr(VI)/kg KG/Tag und alle geforderten Mindest-MOE werden eingehalten. Ein Gesundheitsrisiko ist unwahrscheinlich.

10.6.4 Szenario 4: Hohe Exposition durch Trinkwasser laut EFSA

Legt man das hohe Expositionszenario der EFSA zur Cr(VI)-Aufnahme über das Trinkwasser zugrunde, liegt die Exposition über das Trinkwasser bei 239.3 ng Cr(VI)/kg KG/Tag und der geforderte Mindest-MOE von >10000 für neoplastische Läsionen wird nicht eingehalten (MOE= 4179). Ein Krebsrisiko ist rein rechnerisch wahrscheinlich. EFSA erwartet allerdings, dass aufgrund der breiten Streuung der zugrundeliegenden Expositionsabschätzungen (vergleiche Tabelle 4), diese Unterschreitung des Mindest-MOE nur für eine kleine Gruppe relevant sein dürfte und wenig Anlass zur Besorgnis besteht (EFSA 2014).

10.6.5 Szenario 5: Exposition durch Trinkwasser laut Schweizer FIV

Dieses Szenario beschreibt, wieviel Cr(VI) ein 12.5 kg schweres Kind aufnehmen würde, das täglich 1 l

Wasser trinkt, dessen Cr(VI)-Gehalt der zulässigen Höchstgrenze an Cr (VI) im Trinkwasser (0.02 mg/L) laut Schweizer FIV (2014) entspricht.

In diesem Fall würde die Exposition 1600 ng/kg Körpergewicht/Tag betragen und der Minimal-MOE für neoplastische Läsionen deutlich unterschritten. Ein Krebsrisiko wäre demnach wahrscheinlich.

Auffällig ist, dass diese Exposition um das 7 bis 17-fache höher ist, als die Cr(VI)-Exposition, die die EFSA für den Genuss von Trinkwasser geschätzt hat.

NB: Seit dem 1. Januar 2014 ist eine neue Version der Fremd- und Inhaltsstoffverordnung (FIV, SR 817.021.23) in Kraft (FIV 2014). Eine wesentliche Änderung ist die Differenzierung zwischen Trinkwasser und natürlichem Mineralwasser. Darin ist ein Grenzwert von 0.02 mg/kg für Cr (VI) und 0.05 mg/kg für den Gesamtchromgehalt im Trinkwasser festgelegt. Der Grenzwert für den Gesamtchromgehalt im natürlichen Mineralwasser liegt bei 0.05 mg/kg, ein Grenzwert für Cr (VI)-Gehalt existiert hier nicht. In der FIV (2014) sind keine Höchstgehalte für Chrom (VI) in Lebensmitteln festgelegt.

10.6.6 Szenario 6: Mittlere kombinierte Gesamtexposition aus Boden (S1) und Trinkwasser (S3)

Im Vergleich zu den von der EFSA aufgelisteten Expositionsabschätzungen von Kleinkindern über das Trinkwasser in Höhe von 96.6 ng Cr (VI)/kg KG/Tag (Maximum UB – mean exposure) bzw 239.3 ng/kgKG/Tag (Maximum UB – 95% exposure) (S3 und S4) stellt die zusätzliche Aufnahme von 200 ng Cr (VI)/kg KG/Tag (S1) durch das Verschlucken von kontaminiertem Boden einen relevanten Expositionspfad dar.

Bei einer kombinierten Gesamtexposition aus Trinkwasser (laut S3-EFSA Mittel) und dem Verschlucken von Boden (laut S1-SCAHT Mittel) wird der geforderte MOE für neoplastische Endpunkte von > 10000 unterschritten (MOE= 3372).

Wie unter Szenario 4 bereits aufgeführt argumentiert die EFSA in einem ähnlichen Fall (MOE = 4179), dass aufgrund der breiten Streuung der zugrundeliegenden Expositionsabschätzungen, die Unterschreitung des MOE nur für eine kleine Gruppe relevant sein dürfte und wenig Anlass zur Besorgnis besteht. In gleicher Weise könnte man beim vorliegenden Kombinationsszenario den MOE = 3372 interpretieren.

10.6.7 Szenario 7 : Hohe kombinierte Gesamtexposition aus Boden (S1) und Trinkwasser (S4)

Für dieses Expositionsszenario wird der Mindest-MOE für neoplastische Läsionen deutlich unterschritten. Die beiden Mindest-MOE für verschiedenen nicht-neoplastische Befunde werden eingehalten.

10.6.8 Szenario 8: Höchste kombinierte Gesamtexposition aus Boden (S1) und Trinkwasser (S5)

Für dieses Expositionsszenario wird der Mindest-MOE für neoplastische Läsionen deutlich unterschritten (MOE = 555) und auch der Mindest-MOE für die sensitivste nicht-neoplastische Läsion wird unterschritten (MOE = 61). Das Trinkwasser ist in diesem Szenario die Hauptexpositionsquelle. Der Boden trägt 11% zur Gesamtbelastung bei.

Tabelle 10-7: Vergleich der Exposition von Kleinkindern (ng/kg KG/Tag) gegenüber Cr (VI) durch das Verschlucken von kontaminiertem Boden mit der unvermeidbaren Hintergrundbelastung durch das Trinkwasser und der daraus resultierenden MOEs.

Rote Felder zeigen wo der geforderte Mindest-MOE nicht eingehalten wird und ein Gesundheitsrisiko wahrscheinlich ist. Grüne Felder zeigen wo der geforderte Mindest-MOE eingehalten wird und ein Gesundheitsrisiko unwahrscheinlich ist.

Szenario Nr.:	**S 1**	**S 2**	**S 3**	**S 4**	**S 5**	**S 6** S1 + S3	**S 7** S1 + S4	**S 8** S1+S5
Expositions-Szenarien	**SCAHT Boden**[1] Mittlere Exposition Bioaccessibility: 10%	**SCAHT Boden**[1] Hohe Exposition Bioaccessibility: 100%	**EFSA Wasser**[2] **(vgl. Tabelle 3)** Mittlere diätische Exposition	**EFSA Wasser**[2] **(vgl. Tabelle 3)** Hohe diätische Exposition	**FIV Wasser**[3]	**Kombination**[4] **SCAHT Boden und EFSA Wasser**	**Kombination**[5] **SCAHT Boden und EFSA Wasser**	**Kombination**[6] **SCAHT Boden und FIV Wasser**
Exposition (ng/kg KG/Tag)	200.0	2000	96.6	239.3	1600	296.6	439.3	1800
MOE[7] neoplastische Läsionen Ideal: MOE > 10000 $BMDL_{10}$: 1 mg/kg KG/Tag	**5000**	**500**	10352	**4179**	**625**	**3372**	**2276**	**555**
MOE[8] intestinale Hyperplasie (nicht neoplastische Läsion) Ideal: MOE > 100 $BMDL_{10}$: 0.11 mg/kg KG/Tag	550	**55**	1139	460	690	371	250	**61**
MOE[9] Hämatotoxizität (nicht neoplastische Läsion) Ideal: MOE > 100 $BMDL_{05}$: 0.2 mg/kg KG/Tag	1000	100	2070	836	125	674	455	111

[1] Boden kontaminiert mit 100 mg Cr (VI)/kg Boden.
[2] Exposition durch Wasserkonsum laut CONTAM-Panel der EFSA.
[3] Exposition durch Wasserkonsum mit max. Belastung laut FIV mit Cr (VI) = 0.02mg/L; Annahme: Wasserkonsum = 1L /Tag.
[4] Kombination der mittleren Exposition durch das Verschlucken von Boden (laut SCAHT) mit der mittleren diätischen Exposition durch das Trinkwasser (laut EFSA 2014).
[5] Kombination der mittleren Exposition durch das Verschlucken von Boden (laut SCAHT) mit der hohen diätischen Exposition durch das Trinkwasser (laut EFSA 2014).
[6] Kombination der mittleren Exposition durch das Verschlucken von Boden (laut SCAHT) mit der Exposition durch das Trinkwasser (laut FIV 2014).
[7, 8, 9] MOE = BMDL/Exposition.

10.7 Schlussfolgerung

Mit Ausnahme von S3 besteht bei allen Szenarien rein rechnerisch ein erhöhtes Krebsrisiko und bei S2 und S8 ein zusätzliches Risiko für intestinale Hyperplasie. Ob eine Reduktion des Sanierungswertes für Böden in Betracht gezogen werden soll, hängt im Wesentlichen von zwei Überlegungen ab.

1) Geht man davon aus, dass erhöhte Cr (VI)-Werte nach oraler Exposition im Menschen Krebs auslösen und möchte deshalb den Mindest-MOE von >10000 für neoplastische Läsionen erreichen, um das Krebsrisiko möglichst klein zu halten, dann muss die Exposition gegenüber Cr(VI) reduziert werden. Geht man aber davon aus, dass Cr(VI) im Menschen nur nach inhalativer Exposition Krebs induziert, wäre der geforderte Mindest-MOE von >10000 für neoplastische Läsionen irrelevant für die Risikobetrachtung beim Verschlucken des Bodens und es müssten nur die die geforderten Mindest-MOEs von >100 für die nicht-neoplastischen Läsionen eingehalten werden. In diesem Fall bestünde kaum Handlungsbedarf.

Tatsächlich ist ein Zusammenhang zwischen der Exposition mit Cr (VI) in Trinkwasser und Krebs beim Menschen unklar (WHO 2013, Seite 6, rechte Spalte, Paragraph 2-4). Die IARC hat Cr (VI)-Verbindungen als krebserzeugend für den Menschen (Gruppe 1) klassifiziert, weil Chrom in der Lunge akkumuliert und die berufsbedingte inhalative Exposition zu Lungen-, Nasen- und Nasennebenhöhlenkrebs führen kann (EFSA 2014, Summary, page 2, paragraph 5; WHO 2013, Seite 6, linke Spalte Paragraph 2-4; De Flora 2000, Seite 534 rechte Spalte, letzter Paragraph – Seite 535 linke Spalte).

Ausserdem ist nach Schätzungen der EFSA der Mindest-MOE für neoplastische Läsionen für die meisten Altersgruppen, die einer hohen Cr (VI)-Belastung durch das Trinkwasser ausgesetzt sind, bereits unterschritten (Tabelle 6) und trotzdem konnte kein erhöhtes Krebsrisiko identifiziert werden.

Eine mögliche Erklärung die von Wissenschaftlern vorgebracht wird ist, dass Chrom (VI) nach oraler Exposition durch Speichel, Magensaft, Darmbakterien, rote Blutkörperchen und die Leber wirksam zu Cr(III) entgiftet wird und viele der Tierstudien mit Cr(VI) die Krebsbefunde zeigen für den Menschen nicht relevant sind, weil die gewählten Expositionspfade, diese physiologischen Entgiftungsmechanismen des menschlichen Organismus umgehen.

⇒ **Das SCAHT ist der Meinung, dass eine mögliche kanzerogene Wirkung des Cr(VI) nach oraler Exposition nicht ausgeschlossen werden kann. Dass in epidemiologischen Studien kein Zusammenhang zwischen hohen Cr (VI)-Belastung durch das Trinkwasser und einem erhöhten Krebsrisiko identifiziert werden konnte, könnte an den bekannten Unzulänglichkeiten epidemiologischer Studien liegen. Ausserdem basiert die Herleitung von BMDL-Werten durch die EFSA auf chronischen Trinkwasserstudien, die die physiologischen Abwehrmechanismen des Menschen hinreichend simulieren sollten. Nach Meinung des SCAHT ist der geforderte Mindest-MOE für neoplastische Läsionen von > 10000 bei der vorliegenden Risikobewertung zu berücksichtigen.**

2) Das Ausmass der Risikominimierungsmassnahmen um die Belastung des Menschen gegenüber Cr(VI) zu reduzieren, hängt entscheidend davon ab, welche Expositionsschätzungen zur Hintergrundbelastung zu Grunde gelegt werden. Die geschätzte Hintergrundbelastung über das Trinkwasser laut EFSA (S3 und S4: 96.6 - 239 ng/kg KG/Tag) ist wesentlich geringer als die berechnete Belastung über das Trinkwasser die laut Schweizer FIV zulässig wäre (S5: 1600 ng/kg KG/Tag). Dem Verschlucken von Boden kommt in den EFSA-Szenarien eine wesentlich grössere Bedeutung zu. Die

Szenarioplanung zeigt, dasss die Belastung durch das Verschlucken von belastetem Boden bei Kleinkindern zu einer Exposition führt (S1: 200 ng/kg KG/Tag), die etwa doppelt so hoch ist wie die von der EFSA geschätzte mittlere Exposition über das Trinkwasser (S3: 96.6 ng/kg KG/Tag) und die etwa gleich gross ist, wie die von der EFSA geschätzte hohe diätische Exposition gegenüber Trinkwasser (S4: 239 ng/kg KG/Tag).

Im letzteren Fall argumentiert die EFSA, dass ein Krebsrisiko rein rechnerisch wahrscheinlich ist, weil der geforderte Mindest-MOE von >10000 für neoplastische Läsionen bei hoher Exposition nicht mehr eingehalten wird, aber aufgrund der breiten Streuung der zugrundeliegenden Expositionsabschätzungen (vergleiche Tabelle 4) nur für eine kleine Gruppe relevant sein dürfte und wenig Anlass zur Besorgnis besteht (EFSA 2014). Auch die zusätzliche Aufnahme von 200 ng Cr(VI)/kg KG/Tag über den Boden ist mit grossen Unsicherheiten behaftet, so dass man bei der Gesamtexposition aus Trinkwasser und Boden in ähnlicherweise argumentieren könnte.

⇒ **Das SCAHT ist aber der Meinung, das zur Berechnung der Gesamtexposition aus dem Verschlucken von Boden und dem Trinkwasserkonsum die zulässige Hintergrundbelastung über das Trinkwasser gemäss Schweizer FIV (S5: 1600 ng/kg KG/Tag) berücksichtigt werden muss. Legt man den Grenzwert aus der FIV zugrunde, wird sogar der geforderte Mindest-MOE für die sensitivste nicht-neoplastischen Läsion von > 100 unterschritten (S8: MOE = 67). Da das Trinkwasser in diesem Szenario den Hauptexpositionspfad darstellt, kann ein MOE >100 nur durch eine Reduktion des FIV-Wertes erreicht werden.**

10.8 Grenzwerte im internationalen Vergleich

Durch eine Zusammenstellung der wissenschaftlichen und regulatorischen Literatur, insbesondere der nationalen Bodensanierungsvorschriften oder Richtlinien in Europa, USA und Kanada (z.B. Carlon 2007; Provoost et al. 2006), kann der Schweizer Sanierungswert im internationalen Umfeld verglichen werden:

USA: 210; **CH: 100**; NL: 78; E: 10; S: 5; I: 2; CAN: 0.4 (mg **Cr(VI)**/kg dm)

Chrom wird in den nationalen Bodensanierungsvorschriften oder Richtlinien verschiedener Ländern unterschiedlich reguliert. Manche Länder haben nur einen Grenzwert für den Gesamtchromgehalt (A, CZ, D, F), während Belgien und das Vereinigte Königreich nur Cr (III) regulieren und die Schweiz das einzige Land unter den betrachteten ist, das nur Cr (VI) reguliert. Italien und Kanada haben ein Grenzwert für den Gesamtchromgehalt und Cr (III) festgelegt, während viele Länder explizit den Cr (III) und Cr (VI)-Gehalt regulieren (E, NL, S, USA in bestimmten Staaten) (Siehe **Tabelle 10-8** und **Anhang 1**).

Tabelle 10-8: Vergleich den nationalen Bodensanierungsvorschriften oder Richtlinien verschiedener Ländern bezüglich des Chromgehalts (Siehe Anhang 1).

Contaminant (mg/kg dm)	Austria	Belgium	Czech Republic	Netherlands	Germany	Italy	France	Spain	Sweden	UK	Canada	USA	Switzerland
Chromium total	250	-	500	-	400	150	130	-	-	-	64	-	-
Chromium III	-	300	-	180	-	-	-	1000	120	130/ 200	-	110000	-
Chromium VI	-	-	-	78	-	2	-	10	5	-	0.4	210	100

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11 Nickel

11.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 1000 mg Ni/kg, sollte auf 100 mg Ni/kg reduziert werden.
Gefährdungspotential	Hoch	Humankanzerogen nach Inhalation.
Kanzerogen	Ja	Humankanzerogen nach Inhalation.
Mutagen	Ja	Ja *in vivo*, Befunde nach arbeitsbedingter Exposition unschlüssig.
Reprotoxisch	Ja	Ja *in vivo*, aber Daten sind widersprüchlich. Die Relevanz der positiven Resultate aus Tierstudien für den Menschen ist unklar.
Neurotoxisch	Nein	
Andere	Ja	Immunotoxizität. Allergische Kontaktdermatitis (Sensibilisierung nach Hautkontakt). Systemisches Nickelallergie Syndrom (Sensibilisierung nach oraler und inhalativer Exposition).
Gesundheitsbasierter Referenzwert		Chronische Effekte (Repro- und Entwicklungstoxizität): TDI = 2.8 µg/kg KG/Tag. Akute Effekte (Sensibilisierung): Referenzwert = 0.11 µg/kg KG/Tag.
Exposition		
Äussere Exposition Boden (250 mg)		1000 mg Ni/kg Boden = 250 µg Ni/250 mg Boden = 20 µg Ni/kg KG/Tag (KG: 12.5kg).
Innere Exposition Boden „Bioavailability“		Bei 15% absolute Bioverfügbarkeit aus dem Boden: 20 µg Ni/kg KG/Tag (KG: 12.5kg) = 3.0 µg Ni/kg KG/Tag (KG: 12.5kg).
Hintergrundexposition Nahrung, Wasser, Luft		Die Allgemeinbevölkerung nimmt 95% des Nickels über die Nahrung auf. Für Kleinkinder (1-3 Jahre): 5.3 - 20.1 µg Ni/kg KG/Tag.
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Wahrscheinlich	Die geschätzte tägliche Nickelaufnahme durch die Nahrung überschreitet bereits leicht die tolerierbare tägliche Aufnahmemenge. Die Aufnahme von Nickel durch das Verschlucken von kontaminiertem Boden entspricht 57% der unvermeidbaren Hintergrundbelastung von Kleinkindern die wenig belastet sind und stellt somit einen Hauptexpositionspfad dar. Tolerierbare Aufnahmemenge: 2.8 µg Ni/kg KG/Tag (Kinder 1 - 3 Jahre)

		Nickelaufnahme über die Nahrung: 5.3 – 20.1 µg Ni/kg KG/Tag (Kinder 1 - 3 Jahre) Nickelaufnahme durch direkte Bodenaufnahme: 3.0. µg Ni/kg KG/Tag (15% Bioaccessibility)
Grenzwert im Vergleich		USA: 1600; **CH: 1000**; E: 470; B: 470; CZ: 250; NL: 210; A: 140; F: 140; G: 140; I:120; N:50; UK: 50/75; CAN: 50; S:35 (mg/kg dm)
Datenlage	Zufriedenstellend	Es gibt keine Studien zur Bioverfügbarkeit von Nickel aus dem Boden im Mensch und nur wenige Tierstudien. Die Relevanz der positiven Befunde aus Repro- und Entwicklungstoxizitätsstudien für den Menschen ist unklar. Die Daten dienen aber als Referenz zur Herleitung der Grenzwerte.

11.2 Zusammenfassung

The Swiss Contaminated Sites Ordinance (CSO)[1] clean up value of 1000 mg nickel (Ni)/kg soil for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly, should be reduced to 100 mg Ni/kg soil.

Nickel is a human genotoxic carcinogen after inhalation exposure. Typically for such toxicants no risk free threshold level can be set. Therefore it is recommeded to reduce the clean up value based on the ALARA-principle ("as low as reasonably achievable").

In a recent EFSA dietary risk assessment of Ni in food and drinking water (EFSA 2015), the CONTAM Panel considered it unlikely that dietary exposure to Ni results in cancer in humans, which is further supported by the fact that no tumours have been found in oral carcinogenicity studies in experimental animals. The Panel identified reproductive and developmental toxicity as the most sensitive critical effects for the risk characterization of chronic oral exposure to Ni and derived a TDI of 2.8 µg Ni/kg bw/day.

⇒ **The SCAHT uses this TDI to derive its recommendation to reduce the current soil clean up value to 100 mg Ni/kg soil. This would reduce additional Ni exposure from soil ingestion to 0.27 µg/kg bw/day (assuming a 13.5% absolute oral bioavailability from soil), which is <10% of the TDI. Under these conditions, SCAHT considers that soil ingestion would no longer be a major exposure pathway and that an additional health risk is unlikely**.

It is generally acknowledged that the TDI of 2.8 µg Ni/kg bw/day may not be sufficiently protective of individuals sensitized to Ni and consequently the SCAHT derived soil clean up value may neither.

Exposure through skin or by inhalation may lead to Ni sensitization. Allergic contact dermatitis (a type IV hypersensitivity, also termed Systemic Contact Dermatitis, SCD) is the most prevalent effect of Ni in the general population (due to e.g. jewellery). It has been reported that individuals sensitised to Ni through dermal contact and who have allergic contact dermatitis may develop hand eczema from oral exposure to Ni salts. This eczematous flare-up reaction is referred to as systemic Ni contact dermatitis or haematogenous contact eczema.

Whereas SCD is the most frequent clinical pattern in Ni-sensitized individuals, many other clinical elements may demonstrate that the systemic absorption of Ni, e.g. by the oral route, is able to elicit gastrointestinal (e.g. abdominal pain, diarrhoea and/or constipation, nausea and/or vomiting), atypical systemic manifestations (e.g. headache, chronic fatigue) and chronic dermatological symptoms (e.g. urticaria-angioedema), that are called Systemic Nickel Allergy Syndrome (SNAS). The occurrence of SNAS as a systemic reaction to the Ni concentrations normally present in the daily diet is very controversial.

To protect people from systemic hypersensitivity reactions such as SCD and SNAS, EFSA derived an acute reference point of 1.1 µg Ni/kg bw/day which is lower than the TDI.

⇒ However, the SCAHT does not base its recommendation on this lower acute reference point for acute/hypersensitivity reactions for individuals sensitized to Ni. The SCAHT assumes that the severity of the chronic effects is more relevant. Furthermore SCAHT does not consider soil ingestion as a major driver for Ni sensitization in humans nor does it consider that soil ingestion is the most relevant driver for development of hypersensitivity reactions in already

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen.

Ni-sensitized individuals.

The SCAHT supports a reduction of the clean up value based on the ALARA-principle. Overall the SCAHT still acknowledges that this is a conservative approach to risk assessment because the toxicological relevance of chronic oral exposure to Ni in humans is not clear. In particular there is a need for mechanistic studies to assess the human relevance of the effects on reproduction and development observed in experimental animals. There is also a need for additional studies on human absorption of Ni from food.

11.3 Gefährdungspotential

Nickel (Ni) is a widespread and naturally occurring component of the Earth's surface, and predominates in the most stable divalent state (2+) in the environment, where it forms often strong and highly stable complexes, including in aqueous media. Nickel is widely used in the production of many varieties of iron-Ni alloys, in countless industrial and consumer products, in electroplating, in pigments and colours for ceramics and glassware, in marine anti-fouling agents, and in alloys with aluminium, cobalt, chromium, copper, gold, lead, silver, and titanium. Nickel is an essential micronutrient for higher plants and some animal species but there are no data proving that it is essential for humans (ATSDR 2005; EFSA 2015).

Epidemiological/occupational studies show that the toxicity of Ni is dependent on the route of exposure and the solubility of the Ni compound.

- **Inhalation exposure**

  The respiratory tract and the skin are the major routes of exposure for Ni-induced toxicity in the occupationally exposed population. **Nickel compounds are carcinogenic to humans after inhalation** causing cancers of the lung, nasal cavity and paranasal sinuses.

- **Dermal exposure**

  Allergic contact dermatitis (ACD) is the most prevalent effect of Ni in the general population.

- **Oral exposure**

  Observations in humans showed toxicity of Ni in humans at very high doses following accidental, intended oral or occupational exposure, or other type of intoxication. However, epidemiological data from well conducted studies on human dietary exposure to Ni have been rare and were negative or inconclusive (EFSA 2015).

11.3.1 Toxicological endpoints

In experimental animals the major effects observed in repeated dose toxicity studies in rats were decreases in body weihgts (bw), effects on organ weights (liver and kidneys), hepatotoxicity, nephrotoxicity, and irritation of gastrointestinal tract at high doses. In a 180-day study in mice, the primary toxic effects were observed in the myeloid system. The CONTAM Panel identified **reproductive and developmental toxicity as the critical effect for the risk characterization of chronic oral exposure to Ni** (EFSA 2015, page 3, paragraph 7). The Panel concluded that the lowest NOAEL for long-term exposure to Ni is 2.2 mg Ni/kg b.w. per day from a 2-year rat study (EFSA 2015, page 64, chapter 7.2.2.1).

11.3.1.1 Genotoxicity

- In animal studies and *in vitro* tests soluble Ni compounds induce DNA damage. Various types of DNA damage have been reported including DNA SSBs (single strand breaks), oxidative base damage and DNA protein crosslinks. The genotoxicity of Ni is likely to be caused by indirect mechanisms. The formation of hydroxyl radicals by Ni is strongly suggested as the first step in the formation of all types of Ni-induced DNA lesions and the inhibition of DNA repair (caused by Ni compounds) may account for their persistence (EFSA 2015, page 82, chapter 7.2.4.4). Dysregulation of signaling pathways and alteration of the epigenetic landscape are other predominant mechanisms.
- In humans DNA damage and chromosomal alterations have been analysed in cells from Ni-exposed workers but findings are inconsistent. Co-exposure is often uncertain; some positive association between Ni levels and the rate of oxidative DNA lesions has been found but

occupational exposure was not always associated with an increase in micronuclei frequency.

11.3.1.2 Carcinogenicity

Nickel and Ni compounds have been classified by IARC (2012) as human carcinogens causing cancers of the lung, nasal cavity and paranasal sinuses after inhalation (evidence is based on data in humans and experimental animals) (EFSA 2015, page 3, paragraph 5).

- The CONTAM Panel considered it **unlikely that dietary exposure to Ni results in cancer in humans** (EFSA 2015, page 3, paragraph 5)**.** From the epidemiological data there is currently no consistency to suggest that Ni compounds cause cancer at additional sites other than the lung, nasal cavity and paranasal sinuses or by additional routes other than inhalation. Moreover, no tumours have been found in the oral carcinogenicity studies in experimental animals.
- Other routes of administration that were shown to produce tumours in animal studies include intramuscular and subcutaneous administration and intraperitoneal, intrarenal, intratesticular and intraocular injection. However, no tumours were found in animals that received soluble Ni compounds by oral administration (EFSA 2015, page 82, chapter 7.2.5).

11.3.1.3 Reproductive and developmental toxicity

11.3.1.3.1 Animal studies

Reproductive toxicity studies of Ni following oral exposure to mice and rats have found conflicting results (EFSA 2015, page 65, chapter 7.2.3.1, first paragraph):

- In **mice**, Sobti and Gill (1989, cited by EFSA 2015) reported increases in sperm head abnormalities in epididymes in mice receiving a single gavage dose of 23, 28 or 43 mg Ni/kg bw as Ni nitrate, Ni sulphate or Ni chloride, respectively (study poorly reported). Effects on male sex organs weights, histopathological changes in these organs, altered seminiferous structures, disturbed spermatogenesis, decreased sperm motility, sperm damages and overall reduced fertiliy have been reported in two studies after oral exposure by gavage during 35 days to doses ≥ 1.1 - 5 mg Ni/kg bw/day (EFSA 2015, page 64-65, chapter 7.2.3.1, citing Pandey et al. 1999, Pandey and Srivastava 2000). Because of existing flaws and limitations in these studies, the CONTAM Panel considered they could not be used for establishment of a reference point. More recently, Toman et al (2012, cited by EFSA 2015) reported Toman et al. (2012) demonstrated adverse effect of 10 mg Ni chloride on mouse testis structure after 3-12 weeks dietary eyposure.
- Negative results were also reported by several reproductive toxicity studies and repeated dose toxicity studies in **rats**. Oral administration of soluble Ni compounds did not induce alterations in reproductive tissues and showed no adverse effects on fertility (e.g. alterations in sperm count, concentration, motility, or morphology) or reproductive performances were reported (EFSA 2015, page 66, chapter 7.2.3.1), i.e. rats exposed to 20 mg Ni/kg bw/day as Ni sulphate in drinking water for 90 days (Obone et al. 1999), rats exposed to 2.2 mg Ni/kg bw/day as Ni sulphate hexahydrate administered via gavage for 18 weeks (2-GEN study, SLI 2000b), rats exposed to 125 mg Ni/kg bw/day as Ni sulphate in the diet for 2 years (Ambrose et al. 1976), or dogs exposed to 45 mg Ni/kg bw/day as Ni sulphate in the diet for 2 years (Ambrose et al. 1976). No alterations in sperm count, concentration, motility, or morphology were observed in the F0 or F1 rats administered 2.2 mg Ni/kg b.w. per day as Ni sulphate via gavage for 18 weeks (SLI, 2000b) (all studies cited by EFSA 2015).

⇒ **The CONTAM Panel concluded that the lowest no-observed-adverse-effect-level (NOAEL) for adverse fertility effects after long-term exposure to Ni is 2.2 mg Ni/kg bw/day from a 2-**

year rat study (EFSA 2015, page 64, chapter 7.2.2.1).

Developmental toxicity in animal studies have shown that Ni is a developmental toxicant inducing fetotoxicity, embryotoxicity and teratogenicity (EFSA 2015, pages 73-74, chapter 7.2.3.3).

- Ni is able to cross the placental barrier, affecting directly the developing embryo or fetus. There is consistent evidence of increased pup mortality (pre- or post- implantation/perinatal mortality) after oral exposure of rats to Ni chloride or sulphate in several reproductive toxicity studies at doses ≥ 1.3 mg/kg bw/day (EFSA 2015, pages 73-74, chapter 7.2.3.3).
- Decreases in foetuses or pups weights were observed at higher doses. In mice exposed to Ni chloride, malformations, reduced ossification and increased incidence of skeletal anomalies were observed at doses ≥ 92 mg Ni/kg bw/day in the presence of maternal toxicity. However, microphthalmia was observed at 46 mg Ni/kg bw/day in the absence of maternal toxicity. (EFSA 2015, pages 73-74, chapter 7.2.3.3).

⇒ **The CONTAM Panel decided to apply a benchmark dose approach on the data from a range-finding reproductive toxicity study and a 2-generation reproductive toxicity study to derive a reference point on the dose-response curve for the incidence of litters with post-implantation loss per treatment group (EFSA 2015, pages 73-74, chapter 7.2.3.3).**

11.3.1.3.2 Epidemiological/occupational studies in humans

In humans, there is evidence that Ni is actively transferred across the blood-placental barrier into the fetus because Ni has been detected in human milk at concentrations ranging from 0.79 to 43.9 µg/L, indicating that Ni excretion can occur to some extent via this pathway; there are no human or animal data however for age-related differences in ADME parameters, in particular regarding absorption rate (ATSDR 2005; EFSA 2015).

Reproductive and developmental effects in humans following exposure to Ni compounds have been reviewed by EFSA (2015), based on epidemiological data of occupationally exposed workers. Although the data were mostly related to Ni inhalation, a partial exposure by ingestion could not be excluded. Some of these studies showed conflicting results in term of pregnancy outcomes (e.g. spontaneous abortions, structural malformations, birth parameters of the newborn, gender ratio) and advere effects on male fertility (reduced sperm concentrations, altered spermatozoa motiliy and morphology) or presented flaws in the study designs and reporting, potential confounders and other limitations.

- In a Russian cohort of female metalworkers, Chashschin et al. (1994) reported a statistically significant increase of spontaneous abortions and structural malformations among offspring, compared to the control population. Exposure was primarily via inhalation but oral exposure could not be excluded. This study was criticized at several instances as of being inconclusive due to flaws in the study design, potential confounders and reporting (i.a. EU RAR 2008).
- In a follow-up register-based cohort study in Russia, Vaktskjold and colleagues investigated pregnancy outcomes in Ni-exposed female workers, based on inhalation data or urinary concentrations. No adverse effects of maternal exposure to water-soluble Ni were reported for genital malformation or undescended testicles in the newborn (Vaktskjold et al. 2006; statistically not significant) or for newborn small for gestational age (statistically significant). In a case control study in the same area, Vaktskjold et al. (2008a) found no association between maternal occupational exposure to water-soluble Ni in early pregnancy and the risk of self-reported spontaneous abortion, although the findings would not exclude the possibility of a weak excess risk, or a risk in the first weeks of pregnancy.

- Danadevi et al. (2003) reported altered semen quality in a cohort of Indian metalworkers with reduced sperm concentrations, sperm motility and vitality (all statistically significant), as well as several sperm defects (morphology, head and mid segment). However, the study suffers from several limitations (low study power, selection bias, analytical bias).
- Figá-Talamanca and Petrelli (2000) reported a statistically significantly reduced portion of male children in Italian founders suggesting Ni exposure could affect the gender ratio, whereas Bonde et al. (1992) found no change in the gender ratio in a large cohort of Danish metalworkers exposed to Ni and Chromium.

⇒ **The CONTAM Panel concluded that the currently available epidemiological data do not support the existence of an association between dietary exposure to Ni and reproductive and developmental effects, incl. muskuloskelettal defects in humans (EFSA 2015, page 88, paragraph 2).**

11.3.1.4 Immunotoxicology, hypersensitivity reactions

- *Allergic contact dermatitis (ACD), systemic contact dermatitis (SCD)*

  Exposure through skin or by inhalation may lead to Ni sensitization. Allergic contact dermatitis (ACD, type IV hypersensitivity) is the most prevalent effect of Ni in the general population (due to e.g. jewellery). Whereas oral exposure to Ni is not known to lead to sensitization, it has been reported that individuals sensitised to Ni through dermal contact and who have allergic contact dermatitis may develop hand eczema from oral exposure to Ni salts. This eczematous flare-up reaction is referred to as systemic Ni contact dermatitis or haematogenous contact eczema (EFSA 2015, page 3, paragraph 6). Nielsen et al. (1999) established a low-observed-adverse-effect-level (LOAEL) of 12 µg Ni/kg bw for sensitisation after provocation in 20 Ni-allergic eczema patients, a study which was used by the WHO to derive its guideline value for Ni in drinking water (WHO 2007). Occupational exposure to Ni can cause allergic asthma (type I allergic reactions).

- *Systemic Nickel Allergy Syndrome (SNAS)*

  Whereas contact allergy is the most frequent clinical pattern in Ni-sensitized individuals, and resistance to infections may be influenced, many other clinical elements may demonstrate that the systemic absorption of Ni, e.g. by the oral route, is able to elicit gastrointestinal (e.g. abdominal pain, diarrhoea and/or constipation, nausea and/or vomiting), atypical systemic manifestations (e.g. headache, chronic fatigue) and chronic dermatological symptoms (e.g. urticaria-angioedema), that are called Systemic Nickel Allergy Syndrome (SNAS). The occurrence of SCD as a systemic reaction to the Ni normally assumed in the daily diet is very controversial. The current information that is available about SNAS and its relationship with oral Ni exposure does not allow to draw final conclusions and further and broader studies, more rigorously conducted, are needed (EFSA 2015).

11.3.1.5 Other non-carcinogenic health effects

In experimental animals, oral ingestion of soluble Ni salts has resulted in a wide range of adverse effects including nephrotoxicity/hepatotoxicity and metabolic effects.

In humans, other non-carcinogenic health effects of oral exposure to Ni include effects on the gastrointestinal effects (vomiting, cramps, and diarrhea) and neurological symptoms (giddiness, headache, and weariness), which were the most reported effects after acute exposure, but also haematological effects. No human data were identified on respiratory, endocrine, metabolic, ocular, neurological, and carcinogenic effects after oral exposure (EFSA 2015, page 86, chapter 7.3.1, paragraph 2).

11.4 Gesundheitsbasierter Referenzwert

In 2015, EFSA's CONTAM Panel has performed a dietary risk assessment on the presence of Ni in food and drinking water (EFSA, 2015).

Considering the evidence from previous risk assessments on Ni from major regulatory bodies at international level (see **Table 11-1**), EFSA derived new health-based guidance values based on Ni critical effects in term of chronicity and acute/hypersensitivity reactions (see **Table 11-2**):

⇒ For the risk characterization of **chronic oral** exposure to Ni, the **reproductive and developmental toxicity** in experimental animals was selected as the critical effect.

⇒ For the risk characterization of **acute/hypersensitivity effects**, **systemic contact dermatitis** (SCD) elicited in Ni-sensitive humans after oral exposure to Ni was selected as the critical endpoint.

11.4.1 EFSA's assessment of chronic effects of Ni based on experimental animal studies

- The risk characterization of chronic oral exposure to Ni was based on reproductive and developmental toxicity effects observed in experimental animals.
- Benchmark dose (BMD) modelling was performed on a dose range finding 1-generation study, on a subsequent full 2-generation study and on the combination of the data from the two studies. The CONTAM Panel noted that the use of combined data from the dose range finding and 2-generation studies provided the most robust results and decided to use the results from this dataset for the selection of the reference point (EFSA 2015, page 3, paragraph 7, second half).
- The Panel derived a **tolerable daily intake (TDI) of 2.8 µg Ni/kg bw** from a lower 95 % confidence limit for a benchmark dose at 10 % extra risk (**$BMDL_{10}$**) of **0.28 mg Ni/kg bw** as calculated from the dose response analysis of the incidence of litters with post-implantation loss in rats, applying the default uncertainty factor of 100 to account for interspecies differences and human variability. The CONTAM Panel noted considerable model uncertainty due to the complexity of the developmental toxicity data and the choice of the critical endpoint (EFSA 2015, chapter 7.6.1, page 98-99).

11.4.2 EFSA's assessment of acute effects of Ni based on clinical human studies

- It has been reported that individuals sensitised to nickel through dermal contact and who have allergic contact dermatitis (estimated prevalence in the general population to be up to 15 %, but frequently remaining undiagnosed) may develop eczematous flare-up reactions in the skin (systemic contact dermatitis, SCD) from oral exposure to nickel salts. **Since the TDI of 2.8 µg Ni/kg bw/day may not be sufficiently protective for Ni-sensitized individuals, SCD was therefore selected as the critical effect for the assessment of acute oral exposure to Ni.**
- Three studies analysing SCD elicited in Ni-sensitive humans after acute oral exposure to Ni were identified as suitable for dose-response analysis using the BMD approach. From the dose-response analysis of these studies, the CONTAM Panel selected the **lowest $BMDL_{10}$ of 1.1 µg Ni/kg bw** for the incidence of SCD following oral exposure to Ni of human volunteers as an acute reference point and adopted a Margin of Exposure (MOE) approach for risk characterization (EFSA 2015, page 4, paragraph 3).
- The selected reference point is calculated on data obtained in a highly sensitive study group of fasted individuals given Ni sulphate in lactose capsules (human volunteer study by Jensen et al. (2003), EFSA 2015, page 103, first sentence). Since absorption is assumed to be

considerably higher than from food, the selected reference point could be conservative for the characterisation of the acute risks. Considering the large inter-individual variability in the immune response that might not be covered by the limited number of individuals in the selected studies, the Panel therefore decided that **a MOE of 10 or higher would be indicative of a low health concern** (EFSA 2015, page 4, paragraph 4).

- EFSA (2015) noted that the derived acute reference point is lower than that derived by other institutional bodies using the same studies (see table 1); this was attributed to the fact that BMD modelling was applied for the first time to the dose response analysis of the complete data sets of studies instead of using a NOAEL-approach.
- The MOEs calculated considering the estimated mean and the 95th percentile dietary acute exposure levels were considerably below 10 for all age groups. Due to the approach followed for the derivation of the acute RP, it cannot be predicted whether all sensitized individuals will actually develop adverse reactions, nor what percentage eventually will develop such reactions at the estimated levels of Ni intake (EFSA 2015, page 4, paragraph 5).
- Finally, even in this study, at the intake levels that still produced eczematous flare-up reactions in sensitized individuals, not all individuals in fact developed such reactions. Taking into account these elements in the MOE interpretation, it cannot be predicted that all sensitized individuals will actually develop adverse reactions, nor what percentage eventually will develop such reactions at the estimated levels of Ni intake. Overall, the CONTAM Panel concluded that, at the current levels of acute dietary exposure to Ni, there is a concern that Ni-sensitized individuals may develop eczematous flare-up skin reactions.

⇒ **Overall, the CONTAM Panel concluded that, at the current levels of acute dietary exposure to Ni, there is a concern that Ni-sensitized individuals may develop eczematous flare-up skin reactions. The CONTAM Panel noted the need for mechanistic studies to assess the human relevance of the effects on reproduction and development observed in experimental animals and for additional studies on human absorption of Ni from food, for example in combination with duplicate diet studies (EFSA 2015, page 4, paragraph 6).**

Table 11-1: Overview of health-based guidance values established for Ni by various institutional bodies.

(Source: EFSA 2015, page 22-23, table 3)

Organisation	Limit type	Health-based guidance value (µg/kg b.w. per day)	Species	Reference point (mg/kg b.w. per day)	Critical effect	Reference	UF
FSCJ (2012)	TDI	4	Fasted human	LOAEL 0.012	Eczematous reaction	Nielsen et al. (1990)	3
OEHHA (2011)	REL	11	Rat	NOAEL	Increased pup mortality	SLI (2000b)	10
WHO (2005)	TDI	12	Fasted human	LOAEL 0.012	Eczematous reaction	Nielsen et al. (1990)	1[(a)]
RIVM (2001)	TDI	50	Rat	NOAEL	Decreased organ and body weight	Ambrose et al. (1976)	100
TERA (1999)	RfD	8	Rat	LOAEL 8	Increased kidney weight	Vyskocil et al (1994)	1 000
Health Canada (1994)	TI Ni sulphate	50	Rat	NOAEL 5	Decreased organ and body weight	Ambrose et al. (1976)	100
	TI Ni chloride	1.3	Rat	LOAEL 1.3	Increased pup mortality	George et al. (1989) Smith et al. (1993)	1 000
US EPA (1996)	RfD	20 (soluble Ni salts)	Rat	NOAEL 5	Decreased organ and body weight	Ambrose et al. (1976)	300

b.w.: body weight; LOAEL: lowest-observed-adverse-effect level; NOAEL: no-observed-adverse-effect level; REL: reference exposure level; RfD: reference dose; TI: tolerable intake; TDI: tolerable daily intake; UF: uncertainty factor.
(a): No uncertainty factor applied.

Table 11-2: Overview of health-based reference values established by EFSA (2015) for acute and chronic effects following oral exposure to Ni.

Type of effects	Acute effects	Chronic effects
Selected toxicity endpoint	Systemic contact dermatitis (SCD)	Repro- and developmental toxicity
Reference point	$BMDL_{10}$ of 1.1 µg Ni/kg bw/day	$BMDL_{10}$ of 0.28 mg Ni /kg bw/day
Derived health-based reference value	Value of 0.11 µg Ni/kg kg bw/day The $BMDL_{10}$ for SCD is used as a reference point; A MOE > 10 indicates a low health concern	TDI of 2.8 µg Ni/kg kg bw/day Including a default uncertainty factor of 100
Protection level	Protective of individuals sensitized to nickel	Not protective of individuals sensitized to nickel

11.5 Exposition

11.5.1 Äussere Exposition

- *Oral exposure*

  The general population is primarily exposed to Ni via food and to a lesser extent via drinking water, and it is generally considered that dietary exposure accounts for > 95% of the total exposure (EU RAR 2008; EFSA 2015, page 54, chapter 6.4.2).

  In the second French Total Diet Study, Arnich et al. (2012) reported that drinking water could account for up to 8% of the overall Ni exposure.

  Migration from food contact material and Ni-containing cookware and tableware may in certain cases represent an additional source of Ni in food and drinking water, but usually it has little or no relevance compared to the dietary exposure (EFSA 2015).

- *Inhalation exposure*

  Exposure to Ni through inhalation of ambient air is considered to be only a minor contributor to the overall exposure for the non occupationally exposed population.

  However, for local communities living in the proximities of Ni refining or stainless steel manufacturing plants, exposure by inhalation has been shown to contribute up to 65 % and 43 % in children to the overall exposure, respectively.

  Additional exposure for smokers (e.g. according to EU RAR 2008, a heavy smoker consuming 30 cigarettes per day would be approximately exposed to a systemic dose ranging from 7 to 160 ng Ni/kg bw/day through cigarette smoke) is expected to represent a minor to negligible contribution to the daily overall exposure (EFSA 2015, page 3, paragraph 4).

- *Dermal exposure*

  Percutaneous absorption of Ni is low and dermal exposure is generally a minor source of exposure in comparison to dietary exposure for the non occupationnally exposed population.

11.5.1.1 Dietary exposure assessment

In a recent dietary exposure assessment, EFSA assessed the risk to human health from the presence of nickel (Ni) in food, particularly in vegetables, and in water intended for human consumption and natural mineral waters (EFSA 2015) (N.B: the potential leaching of Ni into food from food contact material was not covered).

- *Assessment of mean and high chronic dietary exposure to nickel (EFSA 2015)*

  Mean chronic dietary exposure to Ni across the different dietary surveys and age classes ranged from 2.0 µg/kg bw/day (minimum LB, 'Elderly') to 13.1 µg/kg bw/day (maximum UB, 'Toddlers'). The 95th percentile dietary exposure ranged from 3.6 µg/kg bw/day (minimum LB, 'Elderly') to 20.1 µg/kg bw/day (maximum UB, 'Toddlers'). The highest dietary exposure to Ni was observed in the age classes 'Toddlers' and 'Other children'. The adult population showed, in general, lower exposure than the young population (EFSA 2015, page 43, chapter 6.2.1, paragraph 4). These reuslts are shown in **Table 11-3** below:

Table 11-3: Mean and high chronic dietary exposure to Nickel for different age groups.

(Source: EFSA 2015, page 44, table 9).

Mean dietary exposure (µg/kg b.w. per day)						
	Lower bound (LB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max
Infants	3.3	-[a]	4.1	5.6	-[a]	6.3
Toddlers	5.3	7.4	11.0	7.3	10.3	13.1
Other children	4.9	6.7	8.2	5.9	8.6	9.9
Adolescents	2.7	3.5	4.9	3.4	4.1	5.9
Adults	2.2	2.7	3.0	2.7	3.4	3.6
Elderly	2.0	2.5	2.5	2.6	3.0	3.2
Very Elderly	2.2	2.4	2.7	2.8	3.1	3.2
95th percentile dietary exposure[b] (µg/kg b.w. per day)						
	Lower bound (LB)			Upper bound (UB)		
	Min	Median	Max	Min	Median	Max
Infants	8.0	-[c]	-[c]	-[c]	-[c]	12.3
Toddlers	8.7	-[a]	14.7	10.8	-[a]	20.1
Other children	9.1	12.3	16.5	11.3	14.7	18.2
Adolescents	5.6	7.3	10.7	5.9	8.0	12.3
Adults	3.7	5.1	6.1	4.7	5.8	6.9
Elderly	3.6	4.3	4.8	4.4	5.3	5.8
Very Elderly	4.0	-[a]	4.8	4.9	-[a]	5.7

b.w.: body weight; LB: lower bound; UB: upper bound
(a): Not calculated since estimates were only available from less than six dietary surveys.
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.
(c): Not calculated since estimates were only available from one dietary survey.

- *Assessment of mean and high acute dietary exposure to nickel (EFSA 2015)*

  Minimum, median and maximum exposure estimates for acute dietary exposure across dietary surveys and age groups are reported in **Table 11-4** below. The highest levels for mean and acute dietary exposure to Ni were observed in the category 'Toddlers', followed by 'Other children'.

  For toddlers, mean dietary exposure to Ni was 7.5-14.3 µg/kg bw/day and 95th percentile exposure was 16.6-35.0 µg/kg bw/day (EFSA 2015, page 52, chapter 6.3.1). Mean dietary acute exposure in the young population ('Infants', 'Toddlers', 'Other children' and 'Adolescents') ranged from 3.4µg/kg bw in one survey for 'Adolescents' to 14.3 µg/kg bw in one survey for 'Toddlers'. The 95th percentile ranged from 8.6 µg/kg bw in one survey for 'Adolescents' to 35.0 µg/kg. in one survey for 'Toddlers' (EFSA 2015, page 52, chapter 6.3.1).

Table 11-4: Mean and high acute dietary exposure to Ni for different age groups across EU dietary surveys.

The 95 % confidence intervals are reported in brackets, the mean and high (95per%ile) acute dietary exposure as min. and max. UB.

(Source: EFSA 2015, page 53, table 11)

Age class	Mean acute dietary exposure[a] (µg/kg b.w. per day)		95th percentile acute dietary exposure[a] (µg/kg b.w. per day)	
	Min	Max	Min	Max
Infants	5.6 (5.4-6.0)	6.4 (5.0-7.7)	15.1 (14.3-15.9)	- (b)
Toddlers	7.5 (7.0-8.1)	14.3 (13.2-15.5)	16.6 (15.0-18.8)	35.0 (26.8-47.2)
Other children	6.0 (5.5-6.8)	10.8 (98-12.6)	15.5 (13.5-18.2)	29.7 (27.8-31.8)
Adolescents	3.4 (3.1-3.7)	7.2 (6.7-7.8)	8.6 (8.0-9.1)	16.1 (15.0-17.7)
Adults	2.7 (2.6-2.9)	5.1 (4.8-5.7)	6.4 (6.2-6.6)	11.8 (10.6-13.8)
Elderly	2.5 (2.2-2.9)	4.0 (3.5-5.2)	5.5 (5.1-6.0)	9.1 (7.9-10.7)
Very elderly	2.7 (2.4-3.1)	4.0 (3.2-6.6)	6.5 (5.9-7.3)	8.7 (6.6-11.3)

b.w.: body weight.
(a): Estimates were rounded up to one decimal place.
(b): One of the surveys contains less than 60 consuming days and the 95th percentile estimates obtained in this dietary survey/age class may not be statistically robust (EFSA, 2011b). These estimates were not included in this table.

Alltogether, these values for children were higher in comparison with previously reported EU exposure assessments (2003-2012) reviewed by EFSA (EFSA 2015, chapter 6.1, page 42-43):

- Wittsiepe et al (2009) reported a mean and high (95 per%ile) nickel dietary exposure of German children aged 48-63 mo of 5.59 µg/kg bw/day and 12.0 µg/kg bw/day, respectively.
- Rose et al. (2010) reported a mean and high (97.5 per%ile) nickel dietary exposure of UK children aged 1.5-4.5 yr old ("toddlers") of 4.17 (LB)-4.87 (UB) µg/kg bw/day and 7.34 (LB)-8.32 (UB) µg/kg bw/day, respectively.
- Arnich et al (2012) reported a mean and a high (97.5 per%ile) nickel dietary exposure of French children aged 3-17 yr old of 3.83 µg/kg bw/day and 7.44 µg/kg bw/day, respectively.

11.5.2 Innere Exposition

For nickel, SCAHT applies the TIER 2-strategy as outlined in the methodology section.

Many data gaps exist for antimony. The absolute oral bioavailability of nickel from soil is not directly available for humans. Data on nickel absorption rate are fairly well characterized in humans (1-40%) (section 11.5.2.1), and SCAHT proposes to use a 30% consevative estimate, in accordance with the EU RAR (2008), to account for fasted state consditions.

There are no data following ingestion of soil in humans (section 11.5.2.2) and in vivo data in experimental animals are limited (section 11.5.2.3). Notwithstanding the limitations of the database, the Relative Oral Adjustment Factor (RAF) approach can be used to estimate the absolute oral bioavailability from soil (section 11.5.2.4), and information from the in vitro bioaccessibility studies (section 11.5.2.5) is used to support the use of the proposed defaut RAF of 50% for inorganics.

In conclusion, based on a human oral bioavailability of 30% from drinking water in the fasted state, and a relative adjustment factor (RAF) of 50%, SCAHT calculates a 15% oral absolute bioavailability of nickel from soil.

11.5.2.1 Oral bioavailability from food and/or water from dietary studies

In humans, it was shown that the oral absorption of nickel is dependent on nickel chemical form, the diet composition and fasting status, and animal studies showed that the gastrointestinal absorption of nickel correlates directly with the solubility of the metal (NEPI 2000, chapter 4.6.3.1, page 4-36 and chapter 4.6.3.2, page 4-37). According to EFSA, nickel absorption from the gastrointestinal tract in humans can vary significantly between 1-40%; intestinal absorption is much higher when nickel is ingested on an empty stomach in drinking water than when ingested with food (ATSDR 2005, page 135; EFSA 2015, page 55, 107). WHO considers that the absorption of nickel from drinking water on an empty stomach is 10 to 40 fold higher than the absorption from food (EU RAR, 2008).

- In human volunteers, Sunderman et al. (1989) estimated that nickel absorption from the gastrointestinal tract was 27 ± 17% (mean ± SD) in fasting subjects when ingested with water, but only 0.7 ± 0.4% (mean ± SD) (a 40-fold difference) when nickel was ingested with food.

  Patriarca et al. (1997) reported an oral absorbed fraction of 33.1 ± 4.9% in four fasted human volunteers following ingestion of 10 µg radiolabelled Ni/kg bw in drinking water.

  Nielsen et al. (1999) estimated absorption of nickel when mixed with scramble eggs to be 2.5%.

- In experimental animals, studies in rats and dogs have shown that nickel administered in the diet resulted in a 1-3% absorption as measured by urinary Ni excretion (NEPI 2000, chapter 4.6.3.1, page 4-36). EFSA (2015) reported oral absortion values of 1-2% for dogs; for rats, most studies showed values between <<1%-11% with various nickel salts, with up to 33% for nickel nitrate. These values are similar to the bioavailability of 1-3% for dogs and rats given nickel in the diet (Ambrose et al., 1976).

⇒ **In its Risk Assessment Report on nickel compounds, the European Union used an oral bioavailability of 30% for exposure via drinking water (assuming fasting conditions) and 5% for exposure via food (assuming non-fasting conditions) (EU RAR 2008). This latter value (5%) is also applied for soil ingestion. The absolute absorption factor of 30 % for fasting (and not 5 % in cases where water is mixed with food) was chosen as a conservative approach, and because it may be possible that ingestion of soil/dust particles is preceded by a fasting period (EU RAR 2008, Annex 12, page 202; HERAG 2007, page 10).**

⇒ **While the value of 30% may be overconservative for the non-fasted state, it is difficult to estimate a semi-fasted value between meals, which may be more realistic for children. The toxicity profile of nickel further support this approach, as well as the lack of information related to possible age-related differences in the toxicokinetics of nickel between adults and children, whose absorption rates may be higher than for adults (as shown for lead).**

⇒ **Therefore, SCAHT uses a conservative human oral bioavailability of 30% in its risk assessment approach to account for the fasted state, as proposed by the EU RAR (2008), and based on the Sunderman and Patriarca studies.**

11.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

No *in vivo* study could be located in the literature that have investigated human nickel bioavailability from direct soil exposure.

11.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

The oral bioavailability of nickel in soil is not well characterized. Only a few in vivo studies on the impact of ingested soil on the bioavailability of nickel have been conducted (SCAHT notes: primary data could not be accessed).

- A study by Griffin et al (1990) reported mean *absolute bioavailabilities* of 1.5% and 3% in rats following administration of clay- and sandy-loam slurries containing nickel *chloride*, respectively. Griffin et al (1990) calculated an oral relative bioavailability of 34% and 63% for clay- and sandy-loam slurries, respectively, as measured by nickel in blood, compared to nickel chloride aministered in drinking water (NEPI 2000, chapter 4.6.3.3, page 4-37, first paragraph; Batelle and Exponent 2000, page 3-16).
- Maximum relative absorption factors in rats of 3.9 % for three soils were also reported by the EU RAR (2008, Annex 12, page 202, citing unpublished results by Conrad et al. corresp. to Jacques Whitford Ltd. 2005). In that study, Ni was administered to male rats at doses of +/- 50 mg Ni/kg body weight, either under the form of salts (NiSO4) or under the form of soil suspensions of 3 Port Colborne soils (wetland clay, organic soil, or fill soil). The relative oral bioavailability factors for nickel were 3.9 %, 3.2% and 2.1% for the wetland clay soil, the organic soil and the fill soil.

11.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of nickel in soil compared to food or water, is to use the RAF approach proposed by the USEPA, as outlined in the Methodology section. A default medium-specific RAF value of 0.5 (50%) has been proposed for inorganics by the US Michigan State Department of Environmental Quality (NRC 2003, Table 2.1 pp.69-70), which could be theoretically applied to nickel to adjust exposure for reduced bioavailability from soil-borne nickel. However, the justification for this value is not made explicit in the NRC report (personnal communication).

- VITO (De Brouwere et al., 2012) used the EU RAR (2008) estimates of relative gastrointestinal absorption of nickel from water (30%), solid matrices such as food (5%) or soil (5%). Considering the relative bioavailability value of 5% set be the EU RAR as a worst case estimate for absorption of nickel from soil/dust, VITO reported an intake of 3.0-9.4 µg Ni/day via soil and dust for children, based on child-specific soil+dust ingestion rates of 100 mg/day (US EPA, 2008); they estimated that the nickel intake via soil and dust ingestion for children ranged between 3-10% compared to nickel dietary intake for the regional scale. Similarly, EU RAR (2008) estimated that the the soil/dust ingestion pathway contributes 6.6 % to the total absorbed systemic nickel dose for the typical regional scenario for children (1-2 years).

⇒ **In vivo data are limited, but suggest a poor oral bioavailability of nickel from soil. While the use of a RAF of 5% is not well supported given the quality of the database, a RAF of 100% may be overconservative in this case. Therefore, the proposed RAF of 50% is a more suitable compromise, which is further supported by in vitro bioaccessibility studies, which collectively demonstrate that nickel is released only in small amounts from the soil matrix in extraction tests (see section 11.5.2.5).**

11.5.2.5 Summary of the in vitro bioaccessibility information

Nickel is relatively strongly adsorbed by soil, For exemple, the amount of adsorbed nickel ranged from 13% in subsoil to 95% in soil high in organic matter. Soil physicochemical characteristics, pH, soil organic matter and to a lesser extent clay content and the amount of hydrous iron and manganese oxides, most influence nickel sorption to soil particles (ATSDR 2005, chapter 6.3.1, page 223-225).

Several in vitro bioaccessibility studies are available from the literature and have been summarized by de Miguel et al. (2012). **Table 11-5** shows in particuular the studies which have investigated the bioaccessiblity of nickel from urban soils based on *in vitro* digestion models simulating gastric (e.g. PBET) or gastric and intestinal (e.g. SBET) dissolution processes. Collectively, the data sumarized by de Miguel. show consistently that nickel has among the lowest bioaccessibility in comparison to other metals.

- Ljung et al (2007) showed that nickel bioaccessiblity from playground soils in Uppsala, Sweden, was the lowest in comparison with other metals (Ni=Cr<Pb<Cd=As).
- Similar results were obtained by Saikat et al (2007) when comparing interlaboratory results for nickel bioaccessibility values in comparison to lead and arsenic in three UK contaminated soils (Ni<As<<Pb), reported median value of 2 μg Ni/g for soil no 2.
- These results are also consistent with de Miguel et al (2012) who showed that nickel bioaccessibility from surficial soils (1-2cm top layer) of playground areas in Madrid, Spain, was among the lowest in comparison with other metals (Cr<Ni<Co<Zn<Pb=Cu=As), as well as Rasmussen et al. (2008) who showed bioaccessibility values for garden soils in the range Ni<Cu<Zn (ratio 1:3:9, i.e. with a bioaccessibility of 2 μg Ni/g soil).

Table 11-5: Overview of selected nickel bioaccessibility values published in the literature

(Source: De Miguel et al. 2012, page 682-683, Table 4)

Soil type, source	In vitro Test	Type of phase in the in vitro model	Bioaccessibility mean value (%)	Range (SD) (%)	Reference
Urban, <50 μm	SBET	gastric	12	8-14	Madrid et al. 2008
Urban, <2000 μm	PBET	gastric	16	(±2)	Poggio et al. 2009
Urban, <150 μm	EN-71[a]	gastric	17	(±7)	Rasmussen et al. 2008
Playground, <100 μm	SBET	gastric	20	(±7.5)	De Miguel et al. 2012
Playground, <100 μm	HCl	gastric	20	(±11)	De Miguel et al. 2012
Urban, <50 μm	SBET	gastric	60	(34-86)	Madrid et al. 2008
Playground, <50 μm	RIVM	gastric+intestinal	3.9	-	Ljung et al. 2007
Urban, <2000 μm	PBET	gastric+intestinal	27[a]	(±6.7)	Poggio et al. 2009

[a] The Toy Safety protocol (EN-71, 1995) is a simulated stomach acid extraction in which the sample is mixed with a dilute HCl solution (pH 1.5) for 2 h at 37◦ C.

[b] the sum of the median human bioaccessible concentrations 1st phase and 2nd phase for residential soils divided by the pseudototal gives a bioaccessibility of 27% for nickel.

⇒ **Based on the evidence from the in vitro studies, SCAHT considers that the proposed RAF of 0.5 (50%) can be used for the present assessment.**

⇒ **In conclusion, based on a human oral bioavailability of 30% from drinking water in the fasted state, and a relative adjustment factor (RAF) of 50%, SCAHT calculates a 15% oral absolute bioavailability of nickel from soil.**

11.6 Risikoabschätzung

For the general population there is concern for adverse effects on reproduction and development from chronic dietary exposure to Nickel.

- The CONTAM Panel concluded that the current chronic dietary exposure to Ni is of concern for the general population because the mean chronic dietary exposure to Ni, across the different dietary surveys and age classes, is above the TDI of 2.8 µg/kg bw/day for all the young age classes and close to it for adults. The 95th percentile dietary exposure exceeds the TDI for all age classes (see **Table 11-2**).
- The Swiss Contaminated Sites Ordinance (CSO)[1] sets a clean up value of 1000 mg Ni/kg soil for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly. According to SCAHT accidental ingested soil scenario, a daily direct ingestion of 250 mg soil that is contaminated with 1000 mg Ni/kg soil represents an **additional external exposure** of 20 µg/kg bw/day for a 12.5 kg heavy child. Taking into account an absolute oral bioavailability from soil (in the fasted state) of 15%, this translates into an oral exposure of 3.0 µg/kg bw/day.

⇒ **SCAHT shows that at the current clean up level, the resulting additional exposure from direct soil ingestion would be 3.0 µg/kg bw/day, which is slightly above the TDI-level (2.8 µg/kg bw/day) but accounts for 57% of the dietary background exposure for toddlers (5.3 µg/kg bw/day).**

⇒ **Soil ingestion therefore represents a significant exposure pathway for Ni.**

The toxicological relevance of chronic oral exposure to Ni in humans is not clear.

- Observations in humans showed toxicity of Ni in humans at very high doses resulting after accidental or intended oral, occupational or other intoxication. However, epidemiological data from well conducted studies on human dietary exposure to Ni have been rare and were negative or inconclusive. This is in contrast to studies on humans who were primarily exposed to Ni via inhalation during occupation which could be used to classify Ni as carcinogenic to humans causing cancer of the lung and nasal cavity.

⇒ The CONTAM Panel noted the **need for mechanistic studies to assess the human relevance** of the **effects on reproduction and development** observed in experimental animals and for **additional studies on human absorption of Ni from food**.

For some individuals sensitized to nickel there is health concern from acute dietary exposure to Nickel at even lower doses.

- The CONTAM Panel concluded that the TDI of 2.8 µg Ni/kg bw/day may **not be sufficiently protective of individuals sensitized to Ni** because they may develop eczematous flare-up skin reactions. The CONTAM Panel derived an acute reference point of 1.1 µg Ni/kg bw and requested a minimal MOE > 10 for hypersensitivity reactions. However this is not met when comparing the reference point and the estimated mean and the 95th percentile acute exposure levels.

⇒ The CONTAM Panel concluded that, at the current levels of acute dietary exposure to Ni, there is a concern that **Ni-sensitized individuals may develop eczematous flare-up skin reactions** (EFSA 2015, page 4, paragraph 6) because the MOEs calculated considering the estimated mean and the 95th percentile dietary acute exposure levels were considerably below 10 for all age groups.

It was acknowledged that **EFSA's risk assessment approach for acute toxic effects was rather conservative**, because the reference point was based on a highly Ni-sensitized population

examined under fasting conditions, in which the Ni absorption is significantly higher than via food (Jensen et al. 2003), resulting in the lowest $BMDL_{10}$ for the derivation of the acute reference point. EFSA noted that even in this study, at the intake levels that still produced eczematous flare-up reactions in sensitized individuals, not all individuals developed such reactions. Therefore it cannot be predicted that all sensitized individuals will actually develop adverse reactions, nor what percentage eventually will develop such reactions at the estimated levels of Ni intake (EFSA 2015, page 4, paragraph 5).

Therefore, given this background, the SCAHT recommends reducing the soil clean up value for Nickel.

- In its assesssment, the SCAHT considered the critical chronic effects of Ni in terms of adverse effects on reproduction and development after oral exposure but not the acute/hypersensitivity reactions, assuming that the severity of the chronic effects is more relevant.

⇒ SCAHT considers the TDI of 2.8 µg/kg bw/day for the most sensitive adverse effects on reproduction and development as a reference point but does not base its risk assessment on the lower acute reference point for acute/hypersensitivity reactions of 0.11 µg/kg bw/day for individuals sensitized to Ni because:

(i) Despite the lack of evidence of adverse reproductive and developmental effects in humans following oral exposure, SCAHT considers that the derived TDI is sufficiently protective for all non-carcinogenic effects of Ni in individuals not sensitized to Nickel;

(ii) SCAHT does not consider soil ingestion as a major driver for Nickel sensitization in humans, nor does it consider that soil ingestion is the most relevant driver for development of hypersensitivity reactions in sensitized individuals. Therefore other risk mitigation measures are likely to be more efficient to reduce the risk of sensitization.

Typically, in cases where dietary background exposure already exceeds the TDI there is no room for additional exposure from soil, and the ALARA-principle should be applied.

⇒ **The SCAHT recommends reducing the soil clean up value from 1000 mg to 100 mg. This would reduce additional Ni exposure from soil ingestion to 0.3 µg/kg bw/day (assuming 15% absolute oral bioavailability from soil), which is roughly 10% of the TDI.**

⇒ **Under these conditions soil ingestion would no longer be a major exposure pathway and an additional health risk is unlikely.**

⇒ **The SCAHT acknowledges that this is a conservative approach to risk assessment because the toxicological relevance of chronic oral exposure to Ni in humans is not clear.**

In particular there is a need for mechanistic studies to assess the human relevance of the effects on reproduction and development observed in experimental animals. There is also a need for additional studies on human absorption of Ni from food.

11.7 Grenzwerte im internationalen Vergleich

Based on a review of the scientific and regulatory literature of national soil remediation regulations in Europe, USA and Canada (e.g. Carlon 2007; CCME 2010; Provoost et al. 2006), it appears that the clean up value as defined by the Swiss Ordinance on Polluted Soils (ALtlV 1998) is in the higher range in international comparison (refer to Annex 1):

USA: 1600; **CH: 1000**; E: 470; B: 470; CZ: 250; NL: 210; A: 140; F: 140; G: 140; I:120; N:50; UK: 50/75; CAN: 50; S:35 (mg/kg dm)

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12 BTEX inklusive Benzol

12.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 500 mg BTEX/kg Boden sollte durch individuelle Sanierungswerte für T, E und X ersetzt werden. Ohne Definition von kritischen BTEX-Mischungen kann eine Risikoanalyse nicht durchgeführt werden. Aktueller Sanierungswert von 1 mg Benzol/kg Boden kann beibehalten werden
Gefährdungspotential	Hoch	Akute Neurotoxizität bei B, T, E und X Kanzerogenität bei B und E
Kanzerogen	Ja	Benzol: Einstufung: IARC Gruppe 1, krebserregend im Menschen. Benzol ist ein genotoxisches, klastogenes Humankarzinogen ohne Schwellenwert. Bei wiederholter Exposition kann Benzol vor allem das blutbildende System und das Immunsystem schädigen und wirkt krebserzeugend (hauptsächlich Leukämien). Ethylbenzol: Einstufung: IARC Gruppe 2a wahrscheinlich krebserregend in Menschen, Mechanismus unklar.
Mutagen	Nein	Benzol ist genotoxisch, klastogen aber nicht mutagen. Ethylbenzol ist wahrscheinlich nicht genotoxisch.
Reprotoxisch	Unklar	Befunde zur Reprotoxizität von B, T, E sind unklar. X ist nicht reprotoxisch. Entwicklungstoxizität (Fötotoxizität) in vivo bei B, T, E und X.
Neurotoxisch	Ja	Alle vier Substanzen B, T, E und X sind leicht flüchtige organische Verbindungen, die beim Einatmen neurotoxisch sind; akute Vergiftungen treten erst bei relativ hohen Konzentrationen ein. Es kommt zu Schwindelgefühl, Brechreiz, Benommenheit und Apathie. Schwere Vergiftungen kommt es zu Fieber und Sehstörungen bis hin zu vorübergehender Erblindung und Bewusstlosigkeit.
Andere	Ja	Der sensitivste nicht kanzerogene Endpunkt bei Benzolexposition ist die Schädigung der blutbildenden Organe, was sich in Knochenmarks- und Blutbildveränderungen sowie immuntoxischen Effekten äußert und schliesslich zu Leukämie führen kann. Irritationen der Atemwege.

<table>
<tr><td>Gesundheitsbasierter Referenzwert</td><td></td><td>
<table>
<tr><th></th><th>Toxicological endpoint</th><th>Population or animal, reference study</th><th>Reference point (mg/kg/day)</th><th>Drinking water guideline (µg/L)[a]</th><th>Tolerable intake (µg/kg bw/day)</th><th>Reference</th></tr>
<tr><td rowspan="2">B</td><td>Carcinogenicity</td><td>Leukemia in humans after inhalation exposure</td><td>N.A.</td><td>10[b]</td><td>ILCR = 1 x 10^{-5}</td><td>WHO 1993a, 1993b
WHO 2011</td></tr>
<tr><td>Decreased lymphocyte count</td><td>Occupational, inhalation study (Rothman et al. 1996)</td><td>$BMDL_{ADJ}$: 1.2[c]</td><td>N.A.</td><td>RfD = 4</td><td>USEPA 2003a</td></tr>
<tr><td rowspan="2">T</td><td>Hepatotoxicity</td><td>Rats oral subchronic (NTP 1990)</td><td>LOAEL: 312</td><td>700</td><td>TDI = 223</td><td>WHO 1993a</td></tr>
<tr><td>Nephrotoxicity Increased kidney weight</td><td>Rats oral subchronic (NTP 1990)</td><td>$BMDL_{10}$: 238</td><td>N.A.</td><td>RfD = 80</td><td>USEPA 2005</td></tr>
<tr><td rowspan="2">E</td><td>Hepatotoxicity, Nephrotoxicity</td><td>Rats oral subchronic (Wolf et al. 1956)</td><td>NOAEL: 136</td><td>300</td><td>TDI = 97.1</td><td>WHO 1993a</td></tr>
<tr><td>Hepatotoxicity, Nephrotoxicity</td><td>Rats oral subchronic (Wolf et al. 1956)</td><td>NOAEL: 136</td><td>N.A.</td><td>RfD = 100</td><td>USEPA 1991</td></tr>
<tr><td rowspan="2">X</td><td>weight loss, increased mortality</td><td>rats oral chronic (NTP 1986)</td><td>NOAEL: 250</td><td>500</td><td>TDI = 179</td><td>WHO 1993a</td></tr>
<tr><td>weight loss, increased mortality</td><td>rats oral chronic (NTP 1986)</td><td>NOAEL: 250</td><td>N.A.</td><td>RfD = 200</td><td>USEPA 2003b</td></tr>
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</td></tr>
<tr><td>Exposition</td><td></td><td></td></tr>
<tr><td>Äussere Exposition Boden (250 mg)</td><td></td><td>Benzol: 1 mg /kg Boden = 250 ng/250 mg Boden = 20 ng/kg KG/Tag (KG: 12.5kg).
BTEX: 500 mg /kg Boden = 125 µg/250 mg Boden = 10 µg/kg bw/day (KG: 12.5kg).</td></tr>
<tr><td>Innere Exposition Boden</td><td></td><td>Benzol: konservative Annahme 100% orale absolute orale Bioverfügbarkeit aus dem Boden, also innere</td></tr>
</table>

„Bioavailability“		Exposition = 20 ng/kg KG/Tag (KG: 12.5kg) BTEX: konservative Annahme 100% orale absolute orale Bioverfügbarkeit aus dem Boden, also innere Exposition = 20 ng/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte Benzolaufnahme über die Nahrung: 0.056-2.4 µg/kg KG/Tag (Kinder 1 - 3 Jahre) Geschätzte Benzolaufnahme über die Luft: Keine Daten, aber die inhalative Exposition ist der Hauptaufnahmepfad für leichtflüchtige organische Substanzen.
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Unwahrscheinlich	Für Benzol ist ein zusätzliches Risko durch das Verschlucken von kontaminiertem Boden trotz der hohen Giftigkeit des Benzols unwahrscheinlichkeit, weil die zu erwartenede Exposition klein im Vergleich zur Hintergrundbelastung ist. Die zusätzliche Belastung für ein 12.5 kg schweres Kind, das täglich 250 mg kontaminierten Boden verschluckt liegt bei 20 ng/kg KG/Tag das entspricht 8% - 36% der geschätzen Aufnahme über die Nahrung für Erwachsene (0.056-2.4 µg/kg bw/day). Bezogen auf das Körpergewicht ist anzunehmen, dass die Belastung über die Nahrung bei Kindern noch höher liegt und der Beitrag durch das Verschlucken von Boden sich entsprechend reduziert. Wenn man weiterhin davon ausgeht, dass die inhalative Exposition der Hauptaufnahmepfad für Benzol ist (bis zu 99,9%), kann eine zusätliches Gesundheitsrisiko als unwahrscheinlich betrachtet werden. Für BTEX, ohne die Definition von kritischen Mischungen, ist eine Risikobeurteilung nicht möglich.
Grenzwert im Vergleich		BTEX-Mischung: **CH: 500**; A: 6 (mg/kg dm) Benzol: USA: 2; USA: 1.2; **CH**, E, NL: **1**; CZ: 0.8; B, CAN: 0.5; UK: 0.33; I: 0.1; S: 0.06 (mg/kg dm) Toluol: 0.5 (I) – 610 (UK), max: 7500 (USA) (mg/kg dm) Ethylbenzol: 0.5 (I) – 350 (UK), max: 7800 (USA) (mg/kg dm) Xylol: 0.5 (I) – 720 (UK), max: 12000 (USA) (mg/kg dm)
Datenlage	Unzureichend	Es gibt keine Studien zur Bioverfügbarkeit von BTEX aus dem Boden im Mensch oder Tier. Es gibt kaum Studien zur Bioverfügbarkeit des einzelsubstanzen B, T, E oder X aus dem Boden. Ohne die Definition von kritischen BTEX-Mischungen kann keine Risikoanalyse für die quarternären Mischungen vorgenommen werden.

12.2 Zusammenfassung

The Swiss Contaminated Sites Ordinance (CSO)[1] sets a clean up value for benzene at 1 mg/kg soil and for BTEX at 500 mg/kg soil, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

According to SCAHT there are currently no sound scientific data which would support a change in the current clean up value for benzene.

- Benzene is hematotoxic, immunotoxic, carcinogenic and genotoxic but not mutagenic; after prolonged exposure, hematotoxicity may lead to aplastic anemia and leukemia. For genotoxic carcinogens we would typically apply the ALARA principle. However, in this case SCAHT assumes that the oral route of exposure is not the major exposure pathway for benzene and ingestion of soil does not create a significant additional health risk.
- For benzene, the additional exposure from direct ingestion of 250 mg contaminated soil is 20 ng/kg bw/day for a child weighing 12.5 kg. Based on this exposure scenario, the SCAHT assumes that the overall contribution from soil ingestion is small compared to the total background exposure and that an additional health risk from direct soil ingestion of benzene-contaminated soil is small.
- In the SCAHT scenario soil ingestion accounts for 8% - 36% of the estimated dietary exposure for adults (range: 0.056-2.4 µg/kg bw/day). No dietary exposure data could be identified for children but compared to adults children are typically exposed to higher doses based on a body weight basis and the contribution from soil ingestion to the overall dietary exposure should be lower for children.
- WHO has defined drinking water guidelines based on estimated excess lifetime cancer risks using data on leukemia from epidemiological studies. It was calculated that a drinking water concentration of 1 µg/L. was associated with an excess lifetime cancer risk of 10^{-6} (WHO 1996, page 4, paragraph 3). Assuming that a toodler with a body weight of 12.5 kg would consume 1 L. water a day, this would translate into an exposure of 80 ng/kg bw/day. In this case soil ingestion would account for 25% of exposure via drinking water and the related excess lifetime cancer risk.
- Anyhow, dietary exposure and exposure from direct soil ingestion is expected to be small in comparison to inhalative exposure for volatile organic compounds (VOCs) like B.

The SCAHT proposes to drop the BTEX clean up value and to introduce new individual values for T, E and X.

BTEX is the sum parameter of benzene (B), toluene (T), ethylbenzene (E) and (o-, m-, p-) xylenes (X), which combine at varying concentrations to form a vast array of BTEX (quaternary) mixtures of often unknown composition. The absence of well-defined BTEX mixtures to which humans can be exposed precludes the quantitative assessment of a potential additional risk from soil ingestion to the background exposure for the following reasons:

- There is a huge number of possible combinations of different concentrations of the four chemicals to which humans can be exposed. Unless mixtures of concern are defined there is

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen (AltlV 1998).

no way to compare a BTEX clean up value to the given background exposures to assess a potential additional risk.

- Indeed there is no health-based reference value for the quaternary BTEX mixture which could be used as a reference point for risk assessment. However, health-based reference values have been established for the individual B, T, E, X components.

The toxicological database on BTEX is poor, particularly for oral exposure and mixture effects.

No studies are available that directly characterize health hazards of the quaternary BTEX mixtures. For the four individual chemicals the toxicological profile after inhalation (but not oral) exposure is reasonably well characterized but the potential adverse effects of the interactions between B, T, E and X when present simultaneously in a mixture is poorly understood. Physiologically-based Pharmacokinetic (PBPK) models have been developed to simulate toxicological effects for all different kind of mixtures, yet for inhalation exposure only.

- B, T, E and X are highly volatile organic compounds (VOCs) and inhalation is the most common route of exposure. Neurotoxicity, hematotoxicity, immunotoxicity and carcinogenicity are the critical health effects following human exposure to BTEX.
- **Neurotoxicity of B, T, E and X is a direct effect of the parent compound, and the effect is additive when mixing the individual compounds.** All four individual compounds B, T, E and X are neurotoxic even at low doses after acute oral and inhalation exposure.
- **Hematotoxicity, immunotoxicity and leukemia are benzene specific and no additive effects are expected in BTEX mixtures.**
- **However, inhibitory / less than additive effects have been observed in BTEX mixtures.** Toluene for example, decreases the hematotoxicity and carcinogenicity potential of benzene. This can be explained by metabolic saturation. Metabolism of the four B, T, E, X components is dose-dependent. If the four B, T, E, X compounds are present in low concentrations in the mixture, then they are extensively metabolized. As there are only a limited number of metabolizing enzymes available, simultaneous exposure to higher concentrations of BTEX mixtures can cause two or more components to compete for the same enzyme-mediated biotransformation pathway. This results in an inhibition of the metabolism of at least one of the parent chemicals or its metabolites and has an impact on the toxicological profile.

Despite the fact that no quantitative risk assessment can be conducted for the quaternary BTEX mixture, the SCAHT assumes that an additional health risk from direct soil ingestion is low, because a sufficiently high oral exposure to BTEX from direct soil ingestion to cause permanent toxic effects is unlikely for the following reasons:

- Acute neurotoxicity is the most sensitive toxicological endpoint. Dizziness, vertigo and tremors are expected to be transient but would most likely prevent prolonged exposure to BTEX from soil.
- Moreover, BTEX are VOCs and volatilization occurs on a time scale of minutes to hours. Therefore, inhalation of released vapours may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil.
- BTEX that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (= desorption resistant fraction). Benzene in particular, is a VOC that will not usually be found in high concentrations in surface soils due to loss through volatilization; since B is also fairly mobile in soil, it will migrate downwards following water movement, typically remaining in

subsurface soils or may migrate to the groundwater compartment. The degree of vaporization of VOCs from soils varies between freshly added compounds and aged residues. At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures.

The SCAHT review of the scientific and regulatory literature of national soil remediation regulations reveals that besides Switzerland, Austria is the only country that has set up a remediation value for BTEX. However, Austria has not set a clean up value for benzene alone. Most countries reviewed have established individual remediation values for each of the four B, T, E and X compounds. Germany appears to be the only country that does not specify any clean up values for B, T, E or X in the Federal Soil Protection act and Contaminated Sites Ordinance.

12.3 Gefährdungspotential

BTEX is the sum parameter of benzene (B), toluene (T), ethylbenzene (E) and (o-, m-, p-) xylenes (X). These chemicals are single-ring aromatic hydrocarbons which are classified as volatile organic compounds (VOCs). Because of this high volatility inhalation is the most common route of exposure for these compounds.

While BTEX as such occurs as the quaternary mixture of varying concentrations of B, T, E and X, various combinations of the four chemicals exist, such as binary mixtures (e.g. BE, BT, BX, TE, TX, EX) and ternary mixtures (e.g. BTX, TEX). While the toxicological profile after inhalation exposure of the four individual chemicals is reasonably well characterized, the potential adverse effects of the interactions between B, T, E and X when present simultaneously in a mixture is poorly understood.

No studies are available that directly characterize health hazards and dose-response relationships for exposures to the quaternary BTEX mixtures (ATSDR 2004, page ix, paragraph 2) and there is only limited toxicological information for binary and ternary mixtures.

The health effects information for quaternary BTEX mixtures is a proxy derived from toxicological data of the individual BTEX chemicals and from data on binary component mixtures as well as from some toxicokinetic and mechanistic information that is available from an interaction-based PBPK[2] model of this mixture (ASTDR 2004 page 3, paragraph 1).

PBPK models have been developed to simulate toxicological effects for all different kind of mixtures (ATSDR 2004, chapter 2) but for inhalation exposure only. For oral exposure, no such models exist and therefore route-to-route extrapolations would be required, adding another level of complexity and uncertainty to the modelling approaches.

Likewise, there are extremely limited data for oral chronic exposure to B, T, E and X because inhalation is the most common route of exposure for these compounds. Moreover, the high volatility of the compounds leads to a rapid evaporation from the fed-matrix and challenges dose concentration control in oral exposure scenarios.

12.3.1 Toxicological endpoints

Each of the chemicals is well absorbed, extensively metabolized, and does not persist in the body for long periods of time. **Neurotoxicity, hematotoxicity, immunotoxicity, and carcinogenicity are the critical effects** of concern for human exposure to BTEX. Not all individual mixture components show the same toxicological effects.

- All four compounds B, T, E and X are neurotoxic;
- B is the only hematotoxic compound. Following prolonged exposure hematotoxicity leads to leukemia and immunotoxicity;
- E is possible carcinogenic to humans but not to the bone marrow;
- B, T, E and X data on reproductive and developmental toxicity from occupational exposure and animal studies are inconclusive but suggest some effects at high doses.

Table 12-1 summarizes the major toxicological effects of B, T, E and X. For more in-depth information please refer to the subsequent paragraphs.

[2] Physiologically-based Pharmacokinetic (PBPK) modelling is a mathematical modelling technique for predicting the absorption, distribution, metabolism and excretion (ADME) of chemical substances in humans and animal species.

Table 12-1: Overview of toxicological endpoints for the individual BTEX components

Please note that: this overview does not take into account mixture effects; the majority of data is derived from inhalation studies; if not stated otherwise findings have been observed in humans.

	B	T	E	X
Neurotoxicity	+	+	+	+
Hematotoxicity	+	-	?	-
Immunotoxicity	+[1]	-	-	-
Carcinogenicity	+[1,2]	-	?[3] Possible human carcinogen	-
Genotoxicity	+[2]	-	?	-
Reprotoxicity	? Testicular effects - in vivo	?	? Testicular tumors, uterine and hormonal effects - in vivo	-
Developmental toxicity	+ Fetotox in vivo	+ Fetotox in vivo, humans	+ Fetotox in vivo	+ Fetotox in vivo
Liver	-	-	+ in vivo	+ in vivo
Kidney	-	+	+ in vivo	+ in vivo
Others	-	Irritation Respiratory tract	Irritation Respiratory tract , eyes	Irritation Respiratory tract , eyes, skin

\+ Relevance of toxicological effect for human health established
\- No toxicological effect reported
? Relevance of toxicological effect for human health is inconclusive
[1] Secondary to hematotoxicity
[2] In bone marrow cells and lymphocytes
[3] Not in bone marrow but in kidney (rat), testis (rat), lung (mice), liver (mice)

12.3.1.1 Neurotoxicity

Acute inhalation or oral exposure to the individual B, T, E, X compounds can produce neurotoxic effects {dizziness, vertigo, tremors, central nervous system (CNS) depression, narcosis, etc}, which are reversible upon cessation of exposure. Neurotoxicity is the most critical non-cancer effect of concern for BTEX mixtures following acute inhalation exposure, because it is expected to occur at the lowest exposure levels.

Observed effects for all four B, T, E, X compounds have been attributed to their liposolubility and direct action on neuronal membranes. This is similar to the way general anesthetic agents work, i.e. either by a disruption of the lipid environment in which membrane proteins function or by direct interaction with the hydrophobic/hydrophilic conformation of proteins in the membranes. Mechanistic aspects are summarized in **Table 12-2** below (refer to section 12.3.2).

Benzene

- Acute neurological effects of B are presumed to result from a direct effect of the parent B compound on CNS cell membranes unrelated to its metabolites. Human data are mostly associated with overt signs of CNS toxicity, and dose-response data in the lower

concentration range are often lacking in humans (ATSDR 2004, appendix A, chapter A3, page 88, paragraph 1).

Toluene

- Chronic exposure to high concentrations of T brings about structural changes in the brain related to lipid compositional changes. Supporting evidence for this hypothesis includes altered phospholipid composition of brain synaptosomes, decreased phospholipid concentrations in the cerebral cortex, and decreased number of neurons in the hippocampus in T-exposed rats (ATSDR 2004, appendix B, chapter B3, page 101, first paragraph). Neurological impairment (e.g. gait and speech abnormalities) and brain atrophy have been observed in humans in several cases of chronic inhalation abuse to T, as well as occular and ear toxicity following inhalation exposure of T. Mechanistic understanding of direct T-induced hearing loss at the molecular and cellular level is limited; recent evidence suggests that T modifies the response of protective acoustic reflexes to loud noises via anticholinergic effects, potentially resulting in increased noise-induced hearing loss (ATSDR 2015, chapter 3.5.2, page 247, second paragraph). It has been postulated that toluene interference with dopaminergic mechanisms of retinal cells or toxic demyelination of optic nerve fibers may be involved in the vision impairment (ATSDR 2015, chapter 3.5.2, page 248, second paragraph).

Ethylbenzene

- Neurotoxic effects of E have been primarily studied *in vitro*, in particular changes in integrity and functionnality of cell membranes of astrocyte in rodents have been described. Membrane-mediated effects resulted in a dose-dependent inhibition of the enzymatic activity of Na^+, K^+-ATPase, and Mg^{2+}-ATPase, which may disturb the ability of the cells to maintain homeostasis. Experiments with rat synaptosome preparations showed that membrane fluidity was increased after exposure to E. ATPase and acetylcholinesterase activity were also decreased, as seen in the astrocyte preparations. There is yet no direct evidence that the interaction of E with astrocytes *in vivo* is the mechanism of neurological effects following acute exposure to high levels of E in humans or in animals (ATSDR 2004, appendix C, chapter C3, page 116, second paragraph). Similarly to T, direct ototoxicity (loss of outer hair cells in the Corti organ) of E after inhalation exposure in rats has also been described (ATSDR 2010, chapter 3.5.2, page 122, first paragraph).

Xylenes

- Acute inhalation exposure to X can cause impaired short-term memory, impaired reaction time, performance decrements in numerical ability, and alterations in equilibrium and body balance in humans experimental studies; case reports and occupational studies together provide suggestive supportive evidence that acute and chronic inhalation exposure to X or solvent mixtures containing X may also be associated with several neurotoxic effects (ATSDR 2004, appendix D, chapter D2, page 125, first paragraph). Ito et al. (2002) suggested that high concentrations of *m*-xylene in the cerebellum increased may increase $GABA_A$ receptor binding activity, and that the increased inhibitory effect of GABAergic neurotransmission in the cerebellum is consistent with the adverse effect of *m*-xylene on motor coordination (ATSDR 2007, chpater 3.5.2, page 154, first paragraph). It is yet unclear whether these represent direct effects of X mediated (via altered cellular membrane integrity, function and homeostasis) or are secondary changes resulting from non-specific CNS depression. Some authors have also suggested that metabolic intermediates, such as arene oxides or methylbenzaldehyde, may be responsible for the toxic effects of X (ATSDR 2004, appendix D, chapter D2, page 128, first paragraph).

12.3.1.2 Hematotoxicity, immunotoxicity & carcinogenicity

For B (only) there is a causal relationship between the development of non-cancer hematological effects, immunotoxicity and the development of leukemia. Benzene can cause hematological effects, which may ultimately lead to aplastic anemia and acute myelogenous leukemia (AML).

- Hematotoxicity is the most noted and characteristic systemic effect resulting from intermediate and chronic B exposure in humans and animals. All of the major types of blood cells are susceptible (erythrocytes, leukocytes, and platelets). In the less severe cases of toxicity, specific deficiencies occur in individual types of blood elements. A common clinical finding is cytopenia, which is a decrease in various cellular elements manifested as anemia, leukopenia, or thrombocytopenia in humans. Benzene-associated cytopenias vary and can involve a reduction in one (unicellular cytopenias) to all three (pancytopenia) cellular elements of the blood (ATSDR 2004, appendix A, chapter A2, page 85-86).

- Prolonged exposure to B can cause severe damage to the bone marrow involving cellular aplasia in humans and animals. This condition, is known as aplastic anemia, in which the bone marrow and the blood stem cells that reside there are damaged. This causes a deficiency of all three blood cell types (pancytopenia), i.e. red blood cells (anemia), white blood cells (leukopenia), and platelets (thrombocytopenia). The term “aplastic“ refers to the inability of the stem cells to generate the mature blood cells (ATSDR 2004, appendix A, chapter A2, page 86).

  Human studies that provide some estimate of levels of exposure indicate that adverse hematological effects occurred at levels >10 ppm and generally not at levels <1 ppm. Adverse hematological effects begin to appear in animals at B concentrations of 10-100 ppm and above. Oral data are essentially limited to findings in intermediate- and chronic-duration animal studies showing that loss of blood elements occurs following exposure to B in drinking water or by gavage at doses as low as 8-25 mg/kg/day (ATSDR 2004, appendix A, chapter A2, page 86, paragraph 1).

- Benzene-induced aplastic anemia can progress to AML, a fast-growing cancer of the blood and bone marrow. In AML, the bone marrow makes many cancerous cells called leukemic blasts. While normal blasts would normally develop into white blood cells that fight an infection, in AML the leukemic blasts do not develop properly and cannot fight infections. These leukemic blasts grow quickly and crowd out the bone marrow, preventing it from making the normal red blood cells, white blood cells, and platelets that the body needs.

- Other health effects of B include immunological changes in humans and animals, which appear to be largely related to decreases in circulating white blood cells (leukocytes) and the ability of lymphoid tissue to produce the mature lymphocytes (lymphocytes are white blood cells that encompass B-cells, T-cells and natural killer cells) necessary to form antibodies (ATSDR 2004, appendix A, chapter A2, page 86, paragraph 2, first sentence).

12.3.1.3 Carcinogenicity and genotoxicity

Benzene

- Benzene is a non threshold carcinogen. The causal relationship between hematological effects and the development of leukemia is well established as indicated by its consensus classification as a human carcinogen by the National Toxicology Program, U.S. Environmental Protection Agency (USEPA Category A), and International Agency for Research on Cancer (IARC Group 1) (ATSDR 2004, page 2).

- Benzene is genotoxic and clastogenic, but not mutagenic. Chromosomal damage in bone marrow cells and lymphocytes are well documented effects of benzene based on findings in

human occupational studies and *in vivo* studies in animals (ATSDR 2004, appendix A, chapter A2, page 86, second paragraph).

- Reactive metabolites appear to play key roles in the development of the clastogenic and carcinogenic effects of B (see **Table 12-2** for a description of the mechanism of action in section 12.3.2). It is generally believed that B metabolites covalently bind to cellular macromolecules (including DNA, RNA and proteins), thereby leading to dysfunction in the bone marrow (including stem, progenitor, and stromal cells) and other tissues. For example, B and its metabolites may induce oxidative DNA damage or interfere with the incorporation of iron into bone marrow precursors, chelates of iron and hydroquinone or 1,2,4-benzenetriol appear to be potent DNA cleaving agents, and hydroquinone may accumulate in bone marrow to act as substrates for myeloperoxidase, forming benzoquinone which is myelotoxic and clastogenic. The relationships between adduct formation and toxicity is not clear, and multiple metabolic pathways and mechanisms are involved in B toxicity and carcinogenicity (ATSDR 2004, appendix A, chapter A3, page 87, paragraph 3 and 4).

Ethylbenzene

- Ethylbenzene is not hematotoxic but does cause carcinogenic effects in other tissues. Results from an oral rat study and an epidemiological study were inconclusive but there was clear evidence of carcinogenic activity from a chronic inhalation study in rats and mice which revealed carcinogenic activity in kidney and testis (rat) and in lung and liver (mice). Ethylbenzene has been classified as possibly carcinogenic to humans based on a recent assessment by IARC (ATSDR 2004, page 2; Huff et al., 2010). The mechanism of carcinogenicity of E has not been entirely elucidated, but is likely related to the parent compound and/or reactive oxidative metabolites in the 4-ethylphenol pathway, rather than the 1-phenylethanol pathway (ATSDR 2010, chpater 3.5.2, page 123, first paragraph).
- Ethylbenzene was not genotoxic in most studies, although some marginal effects have been reported. Workers exposed to low levels of E in a styrene plant showed no increases in sister chromatid exchanges, DNA adduct formation, micronuclei, or DNA single-strand breaks in the peripheral lymphocytes. Micronucleated peripheral erythrocytes were not increased in mice that were exposed to 750 ppm ethylbenzene for 13 weeks. Ethylbenzene was generally not mutagenic in bacteria or yeast cells *in vitro*, and did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster cells. A weak positive response was observed when E was tested for sister chromatid exchanges in human lymphocytes *in vitro*, but only at a concentration that was toxic to the cells. A positive response also was seen in mouse lymphoma cells when E was tested at a near lethal concentration (ATSDR 2004, appendix C, chapter C2, page 115, third paragraph).

Toluene and xylenes

- Toluene and (o-, m-, p-) xylenes (X) are not carcinogenic and not mutagenic. T and X have been categorized as not classifiable as to human carcinogenicity by both EPA and IARC, reflecting the lack of evidence for the carcinogenicity of these two chemicals (ATSDR 2004, page 2).

12.3.1.4 Reprotoxicity and developmental toxicity

In general, the reproductive and developmental effects of B, T, E and X are often incompletely characterized and studies are often inconclusive due to study limitations including small population size, absence of adequate study design (e.g no multigeneration studies) or multiple-exposure to other substances.

There is suggestive evidence that B, T and possibly E but not X are reprotoxicants in animals. Most of

this information has been derived from inhalation studies; those positive effects were also confirmed by a limited number of oral studies. In humans, while occupational/epidemiological data are very limited and unconclusive for B and X, there is suggestive evidence for reprotoxic effects of T. No data are avaialble for E.

B, T, E and X are developmental toxicants in animals. However, adverse effects on the developing fetus were only observed at high levels of exposure that are maternally toxic. In humans, it has been shown that the abuse of toluene during pregnancy at high dose can be toxic to the developing fetus; no data are available for E, and very limited or inconclusive evidence exist for B and X.

Benzene

- There are no inhalation or oral multigeneration animal studies available but there is suggestive evidence of reproductive toxicity in rodents and rabbits from (sub)chronic inhalation studies which showed effects on male reproductive organs (e.g. atrophy/degeneration of testes, decrease in spermatozoa, increase in abnormal sperm forms, etc), particularly in mice following intermediate duration exposure to 300 ppm (ATSDR 2004, appendix A, chapter A2, page 86, second paragraph). There were no ovarian effects in either the rats or the mice treated for 90 days or in the rats treated for 2 years. Mice treated for 2 years exhibited ovarian lesions ranging from atrophy to neoplasia (USEPA 2002, page 79, chapter 4.2.2.1.1, first paragraph). However, the incidence of non-neoplastic lesions was not dose related, which might be an indication of secondary effects to B carcinogenic potential.

  Some occupational data regarding reproductive effects of B in humans exist (e.g. reproductive dysfunction, dysmenorrhea) but evidence is limited and rather weak due to co-exposure to other chemicals, lack of good exposure monitoring data or missing quantitative dose-response information (USEPA 2002, chapter 4.1.2.3, page 44-46).

- Results of developmental toxicity studies in animals indicate that inhalation exposure to high levels of B is fetotoxic and maternally toxic in several species as shown by decreased fetal weight and/or minor skeletal variants. Fetotoxic effects in rodents occurred at B levels ≥ 47 ppm, although there was evidence of transient hematopoietic anomalies in fetuses and offspring of mice exposed to 5-20 ppm B (ATSDR 2004, appendix A, chapter A2, page 86, second paragraph).

  Results regarding developmental toxicity of B in humans are unconclusive. Most studies consisted of small numbers of subjects, lacked important experimental details, and involved (in almost all cases) concomitant exposure to other chemicals, and did not provide monitoring data or quantitative dose-response information (USEPA 2002, chapter 4.1.2.4, page 47-50).

Toluene

- Reproductive toxicity studies in experimental animals found some decreased sperm count in male rats and ultrastructural changes in ovary follicles of female rats but showed no damage at the histological level to the reproductive organs in rats and mice in (sub)chronic oral studies. Also, no evidence for impaired reproductive performance was found in several assays, including a 2-generation study of rats intermittently exposed to up to 2000 ppm T (ATSDR 2004, appendix B, chapter B2, page 99, first paragraph).

  Adverse reproductive effects of T in humans have been suggested especially with repeated inhalation exposure during pregnancy to concentrations above 200 ppm T. Occupational exposure to increasing concentrations of T (8-111 ppm) has been associated with decreased plasma levels of the luteinizing hormone, follicle stimulating hormone and testosterone levels in males. Increased risks of spontaneous abortions and menstrual function were

observed in women occupationally exposed to T, or wives of men similarly exposed (Lindbohm et al. 1990; Ng et al. 1992a, 1992b). However, interpretation of these results is limited due to many study limitations and potential confounders.

- Developmental toxicity studies in experimental animals have shown that T exerts fetotoxic effects at exposure levels associated with maternal toxicity. Increased fetal mortality, retardation of growth and altered skeletal development were seen following inhalation exposure during gestation in rats (> 2000 ppm) and rabbits (at 267 ppm). Altered neurobehavioural development was seen following inhalation exposure during gestation and lactation in rats (> 1200 ppm) (ATSDR 2004, appendix B, chapter B2, page 99, first and second paragraphs). Oral exposure of pregnant rats to 650 mg T/kg bw/day resulted in decreased bw, delayed ossification, smaller brain volumes, and decreased forebrain myelination of the offspring. In general, no-effect levels following inhalation exposure ranged from about 133-750 ppm T; however, no developmental effects were observed in pregnant mice exposed by gavage to doses ≥ 1800 mg T/kg bw/day.

  In humans, several reports of birth defects in children born to women who abused T or other organic solvents during pregnancy suggest that high-level (4,000–12,000 ppm) exposure to T during pregnancy can be toxic to the developing fetus, including effects such as microcephaly, central nervous system dysfunction, growth deficiency, cranofacial and limb abnormalities, and reversible renal tubular acidosis.

Ethylbenzene

- Reproductive toxicity studies in experimental animals are limited, and no multigeneration studies are available. In inhalation studies, the only observed reproductive effects were increased incidences of testicular tumors in rats. In oral studies, changes in uterine structure, delayed estrus cycle and reduced hormone levels were observed. For the latter, no dose-reponse could be established.

  In humans, no studies were identified regarding reproductive effects following inhalation, oral or dermal exposure to E (ATSDR 2010, chapter 3.2.1.5 page 69; chapter 3.2.2.5, page 83; chapter 3.2.3.5, page 87).

- Developmental toxicity studies in animals indicate that inhalation exposure to E can produce minimal fetotoxic effects at exposure levels that may or may not induce minimal maternal changes. In both rats and mice anomalies of the skeletton and the urinary tract were reported (ATSDR 2004, appendix C, chapter C2, page 115, second paragraph), as well as increased fetal mortality in rats and rabbits.

  In humans, no studies were identified regarding developmental effects following inhalation, oral or dermal exposure to E (ATSDR 2010, chapter 3.1.2.6, page 70; chapter 3.2.2.6, page 84; chapter 3.2.3.6, page 87).

Xylenes

- The limited data available do not suggest reproductive effects of (mixed) X in experimental animals. A one-generation inhalation study in male and female rats with mixed X showed no reproductive effects. A subchronic inhalation study in male rats did not show changes in hormones levels and no structural changes in testes. Similarly, (sub)chronic oral studies in male and female rats and mice reported no effects on reproductive tissues (ATSDR 2004, appendix D, chapter D2, page 127, second paragraph).

  In humans, information on the reproductive toxicity of X is limited to two studies that found an increased incidence of spontaneous abortions following paternal exposure or maternal

exposure. These findings are inconclusive due to study limitations including multiple chemical exposures and small population size.

- Developmental toxicity in experimental animals was shown following inhalation exposure to mixed X or the individual isomers in rats, mice, and rabbits, incl. increased skeletal abnormalities, delayed ossification, fetal loss, hemorrhages in fetal organs, and decreased fetal body weight; these levels were generally associated with maternal toxicity (350-700 ppm)(ATSDR 2004, appendix D, chapter D2, page 126, third paragraph; ATSDR 2007, chapter 3.5.2, page 156, third paragraph). Neurodevelopmental effects (e.g. neuromotor, learning and memory abilities) were reported in rats at lower gestational inhalation exposure levels (200-500 ppm) that did not induce maternal toxicity. An oral study found that mixed X-induced cleft plate and decreased fetal weight in mice exposed to maternally toxic dose, and a dermal study found changes in brain enzymes levels of rat embryos (ATSDR 2004, appendix D, chapter D2, page 126, third paragraph).

  Information on the developmental toxicity of X in humans is limited to a few occupational studies that are inadequate for assessing the relationship between exposure to X and developmental effects due to concurrent exposure to other solvents and small numbers of subjects.

12.3.2 Mechanisms of action of BTEX

Knowledge of the mechanisms of toxicity for the individual BTEX components can help understnand how they might influence each other in mixtures. Modes of action (MoA) are generally well documented for some general (e.g. BTEX neurotoxicity) and specific toxicological endpoints (e.g. B hematotoxicity or X nephrotoxicity).

However, many data gaps still exist, in particular for T and E. For example, the mechanism of carcinogenicity of E has not yet been elucidated, but involves likely the formation of reactive metabolites; mechanistic investigations are being conducted on E-induced lung tumors in mice, including the role of potenially cytotoxic quinine metabolites of E (ATSDR 2010, chapter 3.12.3, page 143, first paragraph).

Table 12-2 summarizes known or postulated mechanisms of toxicity for the toxicological endpoints of each of the four B, T, E, X compounds.

Table 12-2: Overview of known or postulated modes of action for B, T, E and X

(Source: ATSDR 2004, pp. 87-88, 100-101, 116-117, 128-129; ATSDR 2007, pp. 154-157; ATSDR 2010, pp. 240-250; ATSDR 2010, page 122-124; ATSDR 2015, pp. 240-250)

Enpoint	Compound	Mechanism of action
Neurotoxicity	B, T, E, X	Lipophilic parent compound exert direct, narcotic and anaesthetic effects leading to CNS depression and narcosis via changes in: • CNS-cell membrane composition/structure (intercalation into the lipid bilayer) • Membrane integrity (e.g. increased fluidity) • Functionality (barrier, energy transport, matrix for interaction with proteins and enzymes) • Neurotransmitters levels (ACh, GABA, DA)
Carcinogenicity	B	Compensatory proliferative response to anemia via: • Decrease in bone marrow cellularity • Regenerative hyperplasia in the bone marrow, thymus and spleen leading to aplastic anemia and development of AML
Hematotoxicity Clastogenicity	B	Changes in metabolic pathways via: • Covalent binding of reactive metabolites[a] to cellular macromolecules leading to dysfunction • Competition with other chemicals for Cytochrome (CYP) 450 binding sites and subsequent adduct formation • Direct competition between parent compound and metabolites • Induction or inhibition of (Phase II) conjugating enzymes • Synergism between metabolites or GSH-depleting metabolites and oxygen radicals
Pulmonary toxicity	X	Inhibition of pulmonary microsomal enzymes via: • Formation of toxic reactive metabolite (such as methylbenzaldehyde)
Foetal toxicity	X	Decreased progesterone and estradiol levels; Increased microsomal enzyme activity; Increased hormone catabolism
Nephrotoxicity	X, (T?)	Renal tubules and glomeruli injury due to reactive metabolites formation causing: • Irritation • Direct membrane fluidization • Faster cellular turnover (increased urinary levels of β-glucuronidase, albumin, erythrocytes, leukocytes)

[a] known benzene biologically reactive metabolites include: benzene oxide, benzene dihydrodiol, hydroquinone, catechol, benzoquinones, and muconaldehyde.

12.3.3 Mixture effects

As there are no studies available that directly characterize health hazards and dose-response relationships for exposures to quaternary BTEX mixtures (ATSDR 2004, page ix, paragraph 2), PBPK models have been developed to predict ADME characteristics of chemical substances in humans and animal species; those models allow for calculation of human exposure and estimation of the mixture effects of B, T, E and X on human health.

- PBPK analyses from binary exposure studies suggested competitive inhibition of hepatic metabolism as the most plausible mechanism of interaction between individual B, T, E and X compounds (ATSDR, chapter 2.1, page 3).
- The quaternary PBPK model indicates that the competitive inhibitory effect tends to increase with increasing number and concentration of inhibitors (ATSDR, chapter 2.1, page 4). This is illustrated in **Table 12-3** where data from the quaternary mixture PBPK model were compared to blood concentration data of B, T, E and X in rats that have been exposed to mixtures of BTEX at various concentrations: 50 ppm of each BTEX component; 100 ppm of each BTEX component; 100 ppm of B and 50 ppm each of T, E, and X.

- The predicted blood level of B is 39.4% higher from the binary mixture B/T compared to B alone. The addition of the third chemical, E, to the binary mixture resulted in levels of T and B that were increased 26% and 15.7%, respectively, compared to the binary concentrations. Similarly, addition of X to the ternary mixture affected the kinetics of all three chemicals by increasing levels of B, T and E by approximately 7.1%, 5.7% and 9.4%, respectively, compared to the ternary concentrations. The magnitude of the modulation of binary interactions invoked by the addition of another chemical to an existing "network" of binary interactions (i.e., at the binary, ternary, or quaternary level) depends on its inhibition potency and blood concentration.
- With increasing mixture complexity, the blood level of a chemical is increased according to the potency and number of inhibitors, rather than by modification of the inhibition constant for each binary interaction.

Table 12-3: Quaternary PBPK model predictions of hepatic venous blood levels of B, T, E, X

Data were obtained in rat studies after a 4-hour acute inhalation exposure to 100 ppm B alone or combined with 100 ppm of T, E, and/or X.

(Source: ATSDR 2004, page 5, table 2.1)

	Hepatic venous concentration							
	Benzene		Toluene		Ethylbenzene		Xylene	
Mixture components	mg/L	%	mg/L	%	mg/L	%	mg/L	%
B	1.847	—	—	—	—	—	—	—
B + T	2.576	39.4[a]	2.499	—	—	—	—	—
B + T + E	2.981	15.7[b]	3.150	26.0[b]	5.830	—	—	—
B + T + E + X	3.192	7.1[c]	3.328	5.7[c]	6.377	9.4[c]	6.244	—

[a]Percent increase compared to benzene alone
[b]Percent increase compared to binary mixture (B+T)
[c]Percent increase compared to ternary mixture (B+T+E)

12.3.3.1 Toxicokinetics of BTEX mixtures

BTEX compounds distribute easily to lipid-rich and highly vascular tissues such as the brain, bone marrow, liver and kidneys and body fat due to their lipophilicity, are extensively metabolized and are rapidly eliminated from the body, primarily via the urine. Multiple metabolic pathways and mechanisms are involved in B, T, E and X toxicity. Metabolism of the four B, T, E, X components is dose-dependent and generally extensive at dose levels that do not saturate the first metabolic step of each compound, which involves CYP450-dependent mixed function oxidases, predominantly CYP2E1 (but also 2B1, 2B6, 1A2). There can also be competition for the available CYP450 sites amongst the parent compounds and their metabolites. Elimination occurs by e.g. exhalation for the unmetabolized B parent compound and via urine for B, T, E, X metabolites (summarized from ATSDR 2004, pp. 82-83, 95-96, 111-112, 123-124; WHO 2011, pp. 368, 422-423, 433).

⇒ Therefore simultaneous exposure to a BTEX mixture can cause two or more components to compete for enzyme-mediated biotransformation, resulting in an inhibition of the metabolism of at least one of the parent chemicals or its metabolites.

⇒ The threshold for competitive metabolic interaction was estimated to be 20 ppm of each component in humans (ATSDR, page 48, last paragraph). As shown in table 3, competitive metabolic interaction could be measured as increased blood levels of the inhibited parent compound.

As the metabolism of B, T, E and X can comprise several toxification and detoxification (via conjugation) pathways, inhibition of the metabolism can either increase or decrease toxicological effects. Individual metabolic pathways might be changed if oxidation or conjugation enzymes are induced or inhibited in the presence of additional B, T, E, X components and their metabolites. There also may be synergism between metabolites or between glutathione-depleting metabolites and oxygen radicals generated.

- **Additive effects of BTEX mixtures** are expected for neurotoxicity.

  ⇒ The joint neurotoxic action of B, T E and X is expected to be additive at BTEX concentrations below the threshold of ca. 20 ppm of each component for competitive metabolic interaction. BTEX-induced neurotoxicity is not dependent on metabolic activation but is a direct effect of the parent compounds. Because of their lipophilic characteristics the individual B, T, E and X compounds can directly effect the composition/structure, integrity and functionality of the CNS-cell membrane (see also table 2).

- **No additive effects of BTEX mixtures** are expected for toxicological effects that are specific for a single component.

  ⇒ Hematotoxicity and secondary carcinogenic effects on bone marrow and immunotoxicity of the quaternary BTEX mixture are benzene-specific. These effects are not changed in the presence of toluene, ethylbenzene and xylene.

  ⇒ Likewise carcinogenic effects other than leukemia are ethylbenzene-specific. Benzene, toluene, and xylene are unlikely to influence the carcinogenicity of ethylbenzene, at exposure concentrations below approximately 20 ppm of each component, i.e. environmental relevant exposure.

- **Inhibitory effects of BTEX mixtures** have been observed at exposure levels above the threshold for competitive metabolic interaction (metabolic saturation). At higher concentrations of BTEX, the individual compounds compete for the same metabolic enzymes. The available number of CYP450 binding sites is insufficient to bind and metabolize all four BTEX components. This results in increased blood levels for the parent compound (as indicated in table 3) and decreased blood levels of metabolically activated metabolites.

  ⇒ As a consequence of metabolic saturation the hematotoxicity and carcinogenicity potential of B is decreasing in the presence of E, T, and X (ATSDR 2004).

  ⇒ Toluene was found to inhibit the hematological effects of B. Although E and X are also expected to reduce the hematotoxic/carcinogenic potential of benzene due to competitive metabolic interactions, available toxicity data for these pairs of chemicals are inconclusive.

  ⇒ Similarly, there are no binary toxicity data supporting the possible reduction in E carcinogenicity due to competitive metabolic interactions with B, T, and X.

12.4 Gesundheitsbasierter Referenzwert

There is no health-based reference value that has been established for the quaternary BTEX mixture neither for any binary or ternary mixtures of BTEX.

- For the individual BTEX components health-based reference values have been established as indicated in the summary **Table 12-4**. More detailed background information is provided in the subsequent paragraphs.

Table 12-4: Selected reference points for BTEX compounds

	Toxicological endpoint	Population or animal, reference study	Reference point (mg/kg/day)	Drinking water guideline (µg/L)[a]	Tolerable intake (µg/kg bw/day)	Reference
B	Carcinogenicity	Leukemia in humans after inhalation exposure	N.A.	10[b]	ILCR = 1 x 10^{-5}	WHO 1993a, 1993b WHO 2011
	Decreased lymphocyte count	Occupational, inhalation study (Rothman et al. 1996)	$BMDL_{ADJ}$: 1.2[c]	N.A.	RfD = 4	USEPA 2003a
T	Hepatotoxicity	Rats oral subchronic (NTP 1990)	LOAEL: 312	700	TDI = 223	WHO 1993a
	Nephrotoxicity Increased kidney weight	Rats oral subchronic (NTP 1990)	$BMDL_{10}$: 238	N.A.	RfD = 80	USEPA 2005
E	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	300	TDI = 97.1	WHO 1993a
	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	N.A.	RfD = 100	USEPA 1991
X	Weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	500	TDI = 179	WHO 1993a
	Weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	N.A.	RfD = 200	USEPA 2003b

[a] Allocating 10% of TDI to drinking water.

[b] The guideline value for benzene in drinking-water was initially recommended in 1984 by WHO based on data for the production of leukemia after inhalation exposure in humans and using a linear multistage extrapolation model and a life-time risk level of 1 in 100 000 (source: WHO 1993b citing WHO 1984).

[c] The Benchmark Dosel Level (BMDL) was derived by route-to-route extrapolation with the assumptions that inhalation absorption was 50% and oral absorption was 100% in the dose range near the benchmark concentration (BMC). $BMDL_{ADJ}$ = 8.2 mg/m^3 x 20 m^3/day x 0.5 ÷ 70 kg = 1.2 mg/kg/day. (N.B: the original BMC was based on a benchmark response of one standard deviation change from the control mean) (USEPA 2003a).

Benzene

- For carcinogenicity assessment, the World Health Organization (WHO) and the EU former Scientific Committee on Food (SCF) have not established TDIs or restriction levels because B is a human carcinogen (IARC 1987, Group 1), therefore no safe level of exposure can be recommended.

  However WHO (1993a) derived concentrations in drinking water of 100, 10 and 1 µg/L, corresponding to excess lifetime cancer risk of 1 x 10^{-4}, 1 x 10^{-5}, and 1 x 10^{-6}, respectively and

recommended a guideline value for drinking water of 10 µg/L (WHO 1984, 2011). Based on leukemia data in humans, the inhalation unit risk range was extrapolated to an oral (drinking water) unit risk range of 4.4×10^{-4}-1.6×10^{-3} per mg/L (USEPA 2003a).

- For the non-carcinogenic enpoints assessment, USEPA (2003a) derived a Reference dose (RfD) of 4 µg/kg bw/day based on a Benchmark Dosel Level (BMDL) of 1.2 mg/kg/day to account for decreased lymphocyte count in a human occupational epidemiological inhalation study (Rothman et al. 1996). The BMDL was derived by route-to-route extrapolation with the assumptions that inhalation absorption was 50% and oral absorption was 100% in the dose range near the benchmark dose concentration. A comparison analysis based on BMD modeling of data from the National Toxicology Program's experimental animal gavage study (NTP 1986) was also conducted. In addition, comparison analyses using the lowest-observed-adverse-effect levels (LOAELs) from the Rothman et al. (1996) and NTP (1986) studies were performed. Additionally, oral studies in rodents gave medium supporting evidence for the chosen BMD range (Hsieh et al. 1988; Sabourin et al. 1987, 1989, cited in USEPA 2003a).

Toluene

- WHO (1993) derived a TDI of 223 µg/kg bw/day using a LOAEL for marginal hepatotoxic effects of 312 mg/kg bw/day (5 days/week) in a 13-week corn-oil gavage study (NTP 1990) in mice and applying an UF of 1000 (applied 100x default uncertainty factor to account for inter- and intraspecies extrapolations, and an extra 10x for the short duration of the study and use of a LOAEL instead of a no-observed-adverse-effect level (NOAEL) which could not been identified for chronic effects) (WHO 2011, p. 422; WHO 2000, p. 113). On this basis, a guideline value for drinking water of 700 µg/L (rounded figure) was derived, allocating 10% of the TDI to drinking water and assuming a daily consumption of 2 L and 60 kg (WHO 2011, p.422).
- The USEPA (2005) derived an RfD of 80 µg/kg bw/day for increased kidney weight (higher dose range resulting in overt signs of toxicity) in the same 13-week gavage study in rats (NTP 1990), based on a $BMDL_{10}$ of 238 mg/kg bw/day (corresponding to the NOAEL) and applying a UF of 3000 (100x default uncertainty factor, an extra 10x to account for extrapolating from a subchronic study to estimate chronic exposure conditions, and an extra 3x to account for deficiencies in the toluene database). No studies examining the chronic or subchronic effects of oral exposure to T in humans are available.

Ethylbenzene

- A TDI of 97.1 µg/kg bw/day was derived by WHO (1993), from a NOAEL of 136 mg/kg bw/day (5 days/week, conversion factor is x 5/7 days), based on a LOAEL for hepatoxicity and nephrotoxicity at 400 mg/kg bw/day in a limited 6 months study in rats (Wolf et al. 1956), and applying an uncertainty factor of 1000 (this is in line with the USEPA/IRIS 2001 RfD of 100 µg/kg bw/day); on this basis, a guideline value for drinking water of 300 µg/L (rounded figure) was derived, allocating 10 % of the TDI (60kg/2L/day) (WHO 2011, p. 368).

Xylenes

- A TDI of 179 µg/kg bw/day was derived by WHO (1993), from a NOAEL of 250 mg/kg bw/day (5 days/week) based on a decreased body weight and increased mortality at LOAEL of 500 mg/kg bw/day in a 103-week mixed xylenes gavage study in rats (NTP 1986) and applying an uncertainty factor of 1000 (this is line with the RfD of 200 µg/kg bw/day based on the same key study and UF by USEPA 2003b); on this basis, a guideline value for drinking water of 500 µg/L (rounded figure) was derived, allocating 10 % of the TDI to drinking water (WHO 2011, p.462).

12.5 Exposition

12.5.1 Äussere Exposition

BTEX are widely distributed in the environment; air, water and soil can be contaminated with BTEX through natural or anthropogenic processes. Since BTEX are naturally-occurring compounds in crude oil, BTEX can contaminate surface water, lake water and groundwater in the vicinity of natural (crude) petroleum, coal and gas deposits. Relevant natural sources of BTEX compounds for Switzerland include gas emissions from forest fires. Contamination of soil and groundwater with BTEX from anthropogenic sources typically occurs through atmospheric pollution and industrial effluents, near petroleum and natural gas production sites, petrol stations, and other areas with underground/above-ground petroleum product-containing storage tanks. The primary man-made releases of BTEX compounds are through atmospheric pollution emissions from motor vehicles and aircraft exhaust, spills (i.e. leaking underground storage tanks) and cigarette smoke.

Once released in the environment, BTEX compounds usually evaporate quickly into the air or can dissolve in aqueous media. Wet and dry deposition may introduced BTEX into the water and soil compartments. BTEX can contaminate the food chain and drinking water supplies. Low concentrations of BTEX can be found in foodstuffs (Medeiros Vinci et al. 2015) but also in many consumer products (Lim et al. 2014) (see **Table 12-5**).

Environmental exposure to BTEX for humans occurs mostly via inhalation. For example, it is considered that ca. 99.9% of human exposure to B occurs via inhalation (SCF 1999) and that more than 96% of E in the environment can be expected to be present in air (WHO 2011, p.368).

- Smoking is a large source of personal chronic exposure to benzene, and can increase daily exposure dramatically (see **Table 12-6**). According to a NICNAS (2001) evaluation, based on a value of 50 µg/cigarette, the daily intake of B for an average smoker (17.8 cigarettes per day) is increased by 0.89 mg/day (2001, p.157).
- For BTEX, high short-term exposures can occur during refuelling of motor vehicles. Extended travel in motor vehicles with elevated air benzene levels (from combustion and evaporative emissions) can contribute up to 30% to cumulative ambient benzene exposure and associated cancer risk when the travel time is one hour (WHO 2000, p.62).

Table 12-5 and **Table 12-6** below summarize the dietary and non-dietary exposure sources for BTEX compounds.

Table 12-5: Qualitative overview of main exposure sources for the four individual components

(Source: WHO 2000, 2011)

	Smoking	Combustion, evaporation gasoline	Petroleum Industry	Refuelling tanks of motor vehicles	Traffic, traveling in motor vehicles	Solvent in consumer product	Dietary sources	Reference
B	+++	+++	++	++(+)	++	+	+	WHO 2000, p.62
T	+++	+++	++	++(+)	++	+	+	WHO 2000, p. 112
E	++	+++	+++	++(+)	++	+	+	WHO 2011, p.368
X	+++	+++	++	++(+)	++	+	+	WHO 2011, p.432

SCAHT classification scheme: +++ = large source; ++ = intermediate source; + = low source.

Table 12-6: Relative importance of BTEX exposure from dietary and non dietary sources

BTEX	Exposure	Source	Pathway	Range of calculated or reported exposures for adults	References
Benzene	Dietary exposure	Food, average	Oral	0.5-2.4 µg/person/day	SCF 1999
		Food, average Food, max	Oral	0.056 µg/kg bw/day 1.149 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,c]	Inhalation	0.29-7.7 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking[d]	Inhalation	1.74-2.10 µg/kg bw/day	ATSDR 2004
		Skin contact	Dermal	*not identified*	
	Total exposure	All [all + smokers][e]		1.15-1.5 µg/kg bw/day [7.46-9.00 µg/kg bw/day]	ATSDR p.276
Toluene	Dietary exposure	Food, average	Oral	7.7 µg/person/day (UK) 0.119 µg/kg bw/day	SCF 1999 Medeiros Vinci et al. 2015[a]
		Food, max	Oral	3.290 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,f]	Inhalation	0.29-74.9 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact		*not identified*	
	Total exposure	All		*not identified*	
Ethylbenzene	Dietary exposure	Food, average	Oral	0.027 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
		Food, max	Oral	0.502 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,g]	Inhalation	0.06-7.4 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact	Dermal	*not identified*	
	Total exposure	All		*not identified*	
Xylenes	Dietary exposure	Food, average	Oral	< 5 µg/person/day (UK) 0.032 µg/kg bw/day[h]	SCF 1999 Medeiros Vinci et al. 2015[a]
		Food, max	Oral	0.945 µg/kg bw/day[h]	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b]	Inhalation	0.23-16.7 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact	Dermal	*not identified*	
	Total exposure	All		*not identified*	

[a] results from the deterministic analysis are shown, which may possibly overestimate the exposure compared to probabilistic anaylsis.

[b] Calculated for adults, based on indoor/outdoor air levels in µg/m^3 from table 3 in the literature review of Demirel et al. 2014 and USEPA/IRIS database, a body weight (bw) of 70 kg and an inhalation rate of 20 m^3/day; ranges are for **benzene**: 1-27 µg/m^3 = 20-400 µg/day /70kg => 0.29-7.7 µg/kg bw/day; for **toluene**: 1-262 µg/m3 = 20-5240 µg/day /70kg => 0.29-74.9 µg/kg bw/day; for **ethylbenzene**: 0.2-26 µg/m^3 = 4-520 µg/day /70kg => 0.06-7.4 µg/kg bw/day; for the sum of **xylenes**: 0.8-58.5 µg/m^3 = 16-1170 µg/day /70kg => 0.23-16.7 µg/kg bw/day.

[c] Mean ambient air levels of benzene in rural + urban areas are ca. 1 µg/m^3 and 5-20 µg/m^3, respectively (WHO 2000, p.62).

[d] Based on a value of 50 µg/cigarette, the daily benzene intake of an average smoker is increased by 0.89 mg per day, the average smoker (32 cigarettes per day) takes in about 1.8 mg benzene per day from smoking (ATSDR p.276). Passive smokers' estimated daily intake averages are 2.10 and 1.74 µg/kg bw/day for women and men, respectively.

[e] Urban women and men smokers intake estimates of 9.00 and 7.46 µg/kg bw/day, respectively (ATSDR p.276).

[f] Mean ambient air concentrations of toluene in rural areas are generally less than 5 µg/m^3, while urban air concentrations are in the range 5-150 µg/m^3 (WHO 2000, p.112).

[g] Values of up to 26 µg/m^3 in air have been reported (WHO 2011, p.368).

[h] estimated for o-xylene.

12.5.2 Innere Exposition

For BTEX, SCAHT applies the TIER 2-strategy as outlined in the methodology section

There are basically no information on oral bioavailability from dietary or other sources for the quaternary BTEX mixture, and many data gaps exist in humans for the four individual components as well. Nonetheless, collectively, available data suggest that oral absorption is relatively high and may be even complete depending on the B, T, E, X compound. This is also supported by evidence in laboratory animals (section 12.5.2.1).

There are no studies in humans that have investigated the impact of soil on the oral bioavailability of the quaternary mixture or any of the four individual B, T, E, X compounds (section 12.5.2.2), and similar studies in experimental animals are scarce (section 12.5.2.3). Despite the very limited evidence, these studies suggest that ingestion of soil-bound BTEX compounds may be similar or even greater that BTEX alone. It could be inferred that ingestion of BTEX adsorbed to soil matrices may be comparable as well to BTEX from dietary sources. This would support a more conservative approach to the RAF and the use of a 100% RAF value (section 12.5.2.4), which is further justified by the limited evidence from these studies.

In conclusion, considering a conservative dietary oral bioavailability of 100% in humans and a RAF of 100% to account for the higher uncertainty of the database, SCAHT uses an absolute oral bioavailability from soil of 100% for its risk assessment.

12.5.2.1 Oral bioavailability from food and/or water from dietary studies and other sources

Specific ADME/toxicokinetics information in humans is lacking for the quaternary BTEX mixture, and available oral absorption data for each of the individual B, T, E, X components are limited. Collectively, human data suggest that oral absorption for B, T, E, and X is high or nearly complete. There is also reasonable evidence from animal studies (rodents, rabbits) suggesting that absorption for B, T, E, and X is high and may be complete via ingestion (72%-100%). BTEX chemicals are generally well absorbed via inhalation (between 50-60%, see **Table 12-8**). Volatilization occurs on a time scale of minutes to hours. Therefore, inhalation of released vapors may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil. Dermal absorption occurs to a much lesser extent.

- *Benzene (ATSDR 2004; MASS DEP 1992; NICNAS, 2001; USEPA, 2002)*

  In humans, although only limited data are available on absorption of benzene by the oral route, accidental or intentional poisoning case studies indicate that benzene is readily absorbed (not quantified) (ATSDR 2004; USEPA 2002, citing Thienes and Haley, 1972). USEPA (2003a) has used an oral absorption of 100% for benzene for use in health risk assessment. Only a few experimental animal studies could be identified. Data suggest that oral doses of benzene are extensively absorbed (ca. 80-90% in rabbits, Parke and Wiliams 1953; not quantified in rats, Turkall et al., 1988), nearly competely absorbed (>97% in rats and mice, Sabourin et al 1987) or completely absorbed (100% in rabbits, Sabourin et al 1986 cited by MASS DEP 1992).

- *Toluene (ATSDR 2015; Health Canada, 2014; MASS DEP, 1992; USEPA, 2005)*

  In humans, only one study by Baelum et al. (1993) was identified which found that gastrointestinal absorption was complete in human volunteers after oral administration of toluene at 2 mg/min via a 3-hour gastric tube. Experimental animal studies suggest high oral absorption, yet slow in rats (not quantified, Pyykko et al 1977; Sullivan and Conolly 1988), nearly complete (99%, Turkall et al 1991) or virtually complete in rabbits following a single oral exposure (ca. 88%-98%, Smith et al 1954).

- *Ethylbenzene (ATSDR 2010; Health Canada, 2014; MASS DEP, 1992)*

  No studies were located regarding the absorption of ethylbenzene in humans following oral exposure (ATSDR 2010). Animal studies indicate that ethylbenzene is quickly and efficiently absorbed by the oral route. Recovery estimates range from ca. 72%-92% in rabbits (El Masry et al., 1956) to 84% in a second study (Climie et al., 1983) following a single oral dose. In the Faber et al. (2006) study, ethylbenzene was detected at 0.49, 3.51 and 18.28 mg/L in maternal blood of rats 1 hour after the last of four daily administrations of ethylbenzene by gavage, corresponding to a total dose of 26, 90 and 342 mg/kg bw/day, respectively. Since important kinetic information is missing in that study, gastrointestinal absorption cannot be estimated.

- *Xylenes (ATSDR, 2007; Health Canada, 2014; MASS DEP 1992; USEPA, 2003)*

  For humans, ATSDR (2007) and Health Canada (2014) reported up to 90% oral absorption for xylenes (studies not further specified). Several experimental animal studies were identifed. Ogata et al. (1980) reported that the absorption of xylene in human volunteers (oral ingestion of 40 mg/kg bw) was at least 34% for o-xylene and 53% for m-xylene, based on the recovery of urinary metabolites. Bray et al. (1949) found ca. 80-90% oral absorption of xylenes in rabbits following oral gavage. Rat studies (Turkall et al., 1992; Kaneko et al., 1995) showed rapid and extensive uptake via the oral route through the detection of parent material in blood or metabolites in the urine.

⇒ **Based on these data, SCAHT uses a conservative estimate of 100% for the oral bioavailability of BTEX in children.**

12.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

No studies have been located in the literature either for the quaternary BTEX mixture or its individual components.

12.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

No studies have been located in the literature either for the quaternary BTEX mixture. Three studies were identified for benzene, toluene and xylenes (Turkall et al., 1988, 1991, 1992) (Health Canada, 2014; USEPA, 2002; MASS DEP 1992) (see **Table 12-7**).

- Turkall et al. (1988) evaluated the oral bioavailability of soil-adsorbed radiolabelled-benzene in male and female rats via oral gavage (5% in aqueous suspension of gum acacia) of radiolabelled-benzene alone or adsorbed to sandy or clay soil. They found that the oral bioavailability of radiolabelled-benzene was slightly but not significantly increased by adsorption to clay soil. Adsorption of benzene to soil apparently increased the rate of gastrointestinal absorption, as the peak plasma benzene concentrations were higher in both soil treatments, and the time to peak was reduced in the sandy soil. Further metabolism and excretion data support the fact gastrointestinal absorption was apparently rapid and efficient, even in the presence of soil.

- Turkall et al. (1991) evaluated the impact on gastrointestinal absorption of radiolabelled-toluene alone or adsorbed on two types of soil (sandy soil and clay soil) in male rats, following oral gavage (aqueous suspension in gum acacia). They found that >99% of a single dose was eliminated in the urine or expired air, indicating near-total absorption of the exposure dose. Both soils reduced the peak plasma concentration of radioactivity, while sandy soil also reduced the time to reach peak vs toluene alone. However, neither soil

altered the area under the plasma radioactivity-time curve (AUC) vs toluene alone. Thus oral absorption efficiency of soil-bound toluene was not changed compared to toluene alone even though sandy soil delayed the absorption of toluene.

- Turkall et al (1992) evaluated the oral bioavailability of soil-adsorbed *m*-xylene in male and female rats via oral gavage (5% in aqueous suspension of gum acacia) of radiolabelled-m-xylene alone or adsorbed to sandy or clay soil. Adsorption to clay soil did not produce a biologically significant difference from m-xylene administered alone. Sandy and clay soil-adsorbed xylenes demonstrated significantly longer absorption half-lives, while sandy soil produced a shorter elimination half-life vs *m*-xylene alone in female rats. Increased bioavailability of sandy soil-adsorbed *m*-xylene in females was evidenced by a significantly increased (+75%) area under the plasma concentration time curve (AUC). Neither of the soils altered the maximum plasma concentration, the rate at which xylene-derived radioactivity was absorbed or eliminated, or the AUC in male rats.

Table 12-7: Impact of clay soil and sandy soil on B, T and X oral bioavailability compared to the individual compounds adminisitered alone in the Turkall experiments

Compound	Effect of sandy soil on oral absorption	Effect of clay soil on oral absorption	References
B	+, male rat	++, male rat	Turkall et al. 1988
T	∅, male rat	∅, male rat	Turkall et al. 1991
X	++, female rat ∅, male rat	∅, female rat ∅, male rat	Turkall et al. 1992

+: increased; -: decreased; ∅: unchanged (no effect)

The bioaccessibility from ingested soil and further absorption of volatile organic chemicals (VOC) such as B, T, E, X compounds depends largely on the desorption and solubilization processes from the soil matrix through the action of gastric and/or intestinal fluids.

- Significant differences in oral bioavailability are expected between freshly applied compounds at high concentrations, and aged residues present at low concentrations. These differences have been attributed to differences in partitioning between the soil and fluids within the gastrointestinal tract. These aspects however were not considered by Turkall et al.
- The BTEX bioavailability from dermal exposure is expected to be minimal, due to volatilization that occurs at the surface of the skin (NEPI 2000, p. vi). Absolute dermal absorption from soil have been estimated to be between < 0,1-8% for B, 3-12% for T and X, and 3-20% for E (NRC 2003, pp. 69-70) (see **Table 12-8**).

⇒ **While the Turkall experiments provide only very limited evidence, they suggest that soil did not reduce B, T, X oral absorption but rather increase or had no significant effect on their oral bioavailability compared to B, T, X alone. Therefore, it could be inferred that ingestion of soil-bound B, T, E, X compounds may be similar to BTEX from dietary sources. This would support a more conservative approach to the RAF (see section 12.5.2.4 below).**

12.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of BTEX in soil compared to food or water, is to use the RAF approach proposed by the USEPA, as outlined in the Methodology section. A conservative default medium-specific RAF value of 1.0 (100%) has been proposed for each of the four B, T, E and X componens by the US Massachusetts Department of Environmental Protection (MASS DEP 1992; NRC 2003, Table 2.1 pp. 69-70) (see **Table 12-8**).

⇒ **These RAF values were based on laboratory dietary animal studies in rats and rabbits which showed nearly or virtually complete oral absorption rates for each individual B, T, E, X compound alone. For B, T and X there was further indication that adsorption to a soil matrix was comparable or even greater than the compound given alone[3].**

⇒ **SCAHT takes a conservative approach and assumes a 100% oral bioavailability in humans. Taking into account a proposed relative oral absorption factor of 1.0 (100%) (NRC 2003), the absolute oral bioavailability from soil for BTEX is 100%. This means that in the present case, internal exposure equals external exposure.**

Table 12-7: Absolute and relative oral bioavailabilities for B, T, E, X compounds

(Source: NEPI 2000, p.8; NRC 2003, pp.69-70, Table 2-1; MASS DEP 1992)

BTEX	Absolute inhalation[a] bioavailability	Absolute oral bioavailability[b]	Absolute dermal Bioavailability from soil[c]	Relative Oral Bioavailability from soil[d]	Absolute oral bioavailability from soil[e]
B	50%	suggested default 100%	0.05-8%	suggested default 100%[f]	100%
T	50%		3-12%		
E	60%		3-20%		
X	60%		3-12%		

[a] As established in experimental animal studies (source: ATSDR 2004; NEPI 2000; USEPA 2003a, see note c in Table 12-4.

[b] Gastrointestinal absorption in experimental animal studies (rodents, rabbits) following oral gavage ranges between 72%-100%, depending on the individual B, T, E, X compound (see section 12.5.2.1).

[c] Absolute bioavailability of the compound in soil via the dermal route (NRC 2003, pp. 69-70, table 2-1).

[d] Relative absorption factor, equals the relative bioavailability of the compound (i.e. in soil vs in the medium used in the toxicity study) (NRC 2003, pp.69-70, table 2-1)

[e] The absolute oral bioavailability from soil is calculated using the absolute oral bioavailability found from animal studies (72-100%, suggested default 100%), adjusted by a relative oral absorption factor of 1 (100%) to account for reduced oral bioavailabilty from soil.

[f] Proposed default values by the Massachusetts Department of Environmental Protection (MASS DEP 1992, Appendix C-13 to C-15, C-55 to C56, C97 to C98, C105 to C106). Justification has been provided, and is summarized in footenote 3, page 261 of the present report.

[3] **RAF for benzene**: set based on experimental data showing virtually complete (100%) oral absorption (Sabourin et al. 1986; Parke and Wiliams, 1953) and the indication that absorption of benzene from soil is slightly increased compared to benzene alone (Turkall et al. 1988). **RAF for toluene:** set based on the indication that (i) oral absorption efficiency of soil adsorbed toluene was not changed from that of the pure compound, even though absorption was delayed in time by the presence of sandy soil (Turkall et al. 1991); and (ii) rabbit studies indicated 100% absorption efficiency by the oral route (Smith et al., 1954; El Masry et al., 1956). **RAF for ethylbenzene:** extrapolated from in vivo experimental studies (El Masry et al. 1956; Climie et al. 1983) but set at 100% since it was considered that oral absorption was underestimated by not controlling for respiratory volatilization following oral absorption. **RAF for xylenes**: extrapolated based on limited excretion data specifying that more than 98% of an oral dose of p-xylene was absorbed and excreted as metabolites in urine and expired air of the rabbit (Bray et al., 1949). The Turkall et al. (1992) study, not available yet at that time, would support a conservative RAF of 100%.

12.5.2.5 Summary of the in vitro bioaccessibility information

BTEX are widespread contaminants of the soil subsurface. The bioaccessibility of BTEX from the soil matrix will be highly dependent on the soil exposure to the atmosphere, the contact time between the BTEX and the soil, the soil organic matter content and BTEX concentrations. Since BTEX are highly volatile, reasonably water soluble and tend to biodegrade rapidly, they are not persistent in soils (NRC 2003, p. 134).

- For example, B will not usually be found in high concentrations in surface soils due to rapid loss through volatilization; since B is fairly mobile in soil, it will migrate downwards following water movement, typically remaining in subsurface soils or may migrate to the groundwater compartment (NEPI 2000, p. vi, third paragraph; NICNAS 2001, chapter 8.2.3, p.28).
- BTEX that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (= desorption resistant fraction) (NEPI 2000, p. 50). The degree of volatilization of VOCs from soils also varies greatly between freshly added compounds and aged residues. At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures (Farrell and Reinhard, 1994).
- Huesemann et al. (2005) found that leaching of BTEX in aged soils contaminated with crude oil (> 20,000 mg/kg) was not affected by soil properties or aging but rather was governed by the equilibrium dissolution of these hydrocarbons from the crude oil coating the soil particles.

No data on bioaccessibility were identified in the scientific literature for the quaternary BTEX mixture in soils, and very limited data are available for the four individual B, T, E, X components. This paucity of data may be explained by the high volatility of these compounds and the fact that there has been little or no testing of the oral bioavailability of aged VOC residues due to the difficulty in determining the amount of contaminant contained in an aged soil sample (NEPI 2000, p. 50).

⇒ Salanitro et al. (1997) reported that 40-95% BTEX spiked into a soil sample were volatilised during the preparation of the soil matrix. Other authors report that 50%-85% of BTEX may be lost within the first 30 minutes of analysis in open test system experiments (http://contamsites.landcareresearch.co.nz/btex_details.htm). Similarly, Wang et al. (2014) did not detect benzene in BTEX contaminated soil samples.

12.6 Risikoabschätzung

12.6.1 Benzene

For genotoxic carcinogens such as B, we would typically apply the ALARA ("as low as reasonably achievable") principle. However, in the present case, SCAHT assumes that the oral route of exposure is not the major exposure pathway. Therefore, SCAHT concludes that an additional health risk from direct ingestion of B-contaminated soil is low.

The Swiss Contaminated Sites Ordinance (AltIv 1998) sets a clean up value for B at 1 mg/kg soil, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

At the current clean up level, an accidental (daily) ingestion of 250 mg B-contaminated soil by a 12.5 kg child would contribute to an additional exposure of 20 ng/kg bw/day for B (assuming a conservative 100% absolute oral bioavailability from soil).

There are only a few data on background exposure estimates for the general population, against which the additional B uptake from direct soil ingestion can be compared to (see **Table 12-6**). The data vary widely and the SCAHT cannot assess the robustness and reliability of these data. Dietary exposure estimates for B range from 0.056 - 2.4 µg/kg bw/day reflecting the uncertainty associated with dietary exposure assessments. The data from different studies would suggest that dietary exposure to B has been reduced over the years.

- Despite all the uncertainties, the additional exposure from direct soil ingestion to B (20 ng/kg bw/day) is well below any estimate for dietary exposure (0.056 -2.4 µg/kg bw/day)

Dietary exposure and exposure from direct soil ingestion seems to be small in comparison to inhalation exposure.

- For B in particular, it is considered that ca. 99.9% of human exposure occurs via inhalation (SCF 1999). **Table 12-6**, which lists exposure estimates from different sources, does not support this claim. This might partly be due to the fact that data listed in **Table 12-6** have been consolidated from different international and often historical sources, which have used different methods to estimate exposure. However, the SCAHT considers it reasonable to assume that inhalation is the major route of exposure for high volatility compounds like benzene.

⇒ **There are currently no sound scientific data which would support a change in the current clean up value for benzene.**

12.6.2 Quaternary BTEX-mixtures

The Swiss Contaminated Sites Ordinance (AltlV 1998) set a clean up value for the sum of BTEX at 500 mg/kg, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

At the clean up level, an accidental (daily) ingestion of 250 mg BTEX-contaminated soil by a 12.5 kg child would contribute to an internal additional exposure of 10 µg/kg bw/day for the whole BTEX mixture (assuming a conservative 100% absolute oral bioavailability from soil).

⇒ The SCAHT concludes that a quantitative risk assessment cannot be conducted for the quaternary BTEX-mixture because there are an almost infinite number of possible combinations of different concentrations of the four chemicals to which humans can be exposed.

A focus on mixtures of potential concern would be necessary for more quantitative evaluations. Unless those mixtures of concern are defined there is no way to compare the BTEX clean up value to given background exposures to assess a potential additional risk.

In the absence of well-defined mixtures of concern the SCAHT does not see an additional value in keeping a clean up value for the quaternary BTEX mixture but recommends to establish individual clean up values for B, T, E and X.

- This would be in line with the most common practice. Our review of the scientific and regulatory literature of national soil remediation regulations reveals that besides Switzerland, Austria is the only country that has set up a remediation value for BTEX. However, Austria has not set a clean up value for benzene alone. Most countries reviewed have established individual remediation values for benzene, toluene, ethylbenzene and xylenes. Germany appears to be the only country that does not specify any clean up values for B, T, E or X in the Federal Soil Protection act and Contaminated Sites Ordinance (BBodSchV 1999).

Neurotoxicity, hematotoxicity, immunotoxicity, and carcinogenicity are the critical effects of concern for human exposure to BTEX with acute neurotoxicity being the most sensitive toxicological endpoint. Dizziness, vertigo and tremors are expected to be transient but would most likely prevent prolonged exposure to BTEX from soil.

- BTEX are VOCs and volatilization occurs on a time scale of minutes to hours. Therefore, inhalation of released vapors may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil.
- BTEX that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (i.e. desorption resistant fraction). However, since B is fairly mobile in soil, it is expected to follow the water movement downwards and remains in the soil subsurface or migrate further down to the groundwater compartment (NEPI 2000, NICNAS 2001).
- The degree of volatilization of VOCs from soils is assumed to vary between freshly added compounds and aged residues. The SCAHT scenario focuses on potential human health effects from aged residues. Freshly applied residues e.g. from leaking underground storage tanks are not considered.
- At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures. Furthermore, significant differences in oral bioavailability are expected between freshly applied compounds present at high concentrations, and aged residues present at low concentrations (NEPI 2000).

⇒ **Despite the fact that no quantitative risk assessment can be conducted for the quaternary BTEX-mixture, the SCAHT assumes that an additional health risk from direct soil ingestion is low, because a sufficiently high oral exposure to BTEX from direct soil ingestion to cause intransient toxic effects is unlikely.**

12.7 Grenzwerte im internationalen Vergleich

Based on a review in the scientific and regulatory literature of national soil remediation regulations in Europe, USA and Canada (e.g. Carlon 2007; CCME 2010; City of Copenhagen 2011), it appears that the clean up value as defined by the Swiss Ordinance on Polluted Soils is in international comparison (refer to **Annex 1**):

- The highest for the BTEX mixture, however only Austria besides Switzerland has set a remediation value (**CH: 500;** A: 6 mg/kg dm)
- In the higher range for benzene (USA: 2; USA: 1.2; **CH**, E, NL: **1**; CZ: 0.8; B, CAN: 0.5; UK: 0.33; I: 0.1; S: 0.06 (mg/kg dm)

It should be noted that, based on this 13 countries reviewed, Switzerland was found to be the only country to set a clean up value both for the sum of BTEX and benzene alone.

In the other hand, all the other countries reviewed except A, D and CH have established remediation values for T, E and X.

Germany appears to be the only country that does not specifiy any clean up values for B, T, E or X in the Federal Soil Protection act and Contaminated Sites Ordinance (BBodSchV 1999).

The range of clean up values are the following, excluding USA (refer to **Annex 1**):

- Toluene: 0.5 (I) – 610 (UK) (mg/kg dm)
- Ethylbenzene: 0.5 (I) – 350 (UK) (mg/kg dm)
- Xylenes: 0.5 (I) – 720 (UK) (mg/kg dm)

Further information on BTEX regulatory guidance values in the US can be found in Jennings (2009).

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14 Aliphatics, inklusive C_5-C_{10} and C_{11}-C_{40}

14.1 Datenblatt

Handlungsbedarf	Nein	Die aktuellen Sanierungswerte von 5 mg C_5-C_{10}/kg Boden und 500 mg C_{11}-C_{40}/kg Boden können beibehalten werden. Das Gefährungspotential ist vergleichsweise gering und die zusätzliche Exposition durch das Verschlucken von kontaminiertem Boden ist klein, sowohl gegenüber der diätischen Exposition als auch den TDIs.
Gefährdungspotential	Gering	Vor allem akute Neurotoxizität (reversibel) nach Inhalation kurzkettiger Aliphaten. Tierversuche mit sog. Indikatorsubstanzen, die stellvertretend für verschiedene Gruppen von Kohlenwasserstoffen stehen, zeigten weitere Befunde (siehe unten). Die Relevanz dieser Befunde für die menschliche Gesundheit wird jedoch in Frage gestellt. Ausserdem bleibt unklar inwieweit die Resultate durch Kontamination der untersuchten Aliphaten mit aromatischen Verbindungen beeinflusst worden sind.
Kanzerogen	Nein	Keine der aliphatischen Verbindungen wurde von der IARC als krebserregend eingestuft.
Mutagen	Nein	
Reprotoxisch	Nein	Vereinzelt positive in vivo Befunde bei hohen Dosen mit n-Hexan, die in den Muttertieren toxisch waren. Im Menschen gibt es keine Hinweise auf Reproduktionstoxizität.
Neurotoxisch	Ja	Vor allem akute Neurotoxizität (reversibel) nach Inhalation kurzkettiger Aliphaten (VOC). • Periphere Neurotoxizität nach Inhalation von n-Hexan z.B. Taubheit in Armen und Beinen. • Zentralnervöse Störungen nach Inhalation von Kerosin (enthält auch Aromaten z.B. BTEX): Bewusstseinstörungen (Benommenheit), kognitive Störungen (Orientierung, Aufmerksamkeit), Störungen von Affektivität und Antrieb.

Andere	Ja	Hepatotoxizität ist der kritischste toxikologische Endpunkt, vor allem die Bildung von Mikrogranulomen in der Leber (entzündungsbedingte, knotenartige Gewebeneubildung als Reaktion auf chronische, allergische oder infektiöse Prozesse). Diese Befunde werden im Allgemeinen als wenig relevant für den Menschen betrachtet. Zur endgültigen Klärung bräuchte es mehr toxikologishe Daten.
Gesundheitsbasierter Referenzwert		Die TPHCWG hat TDIs zur humantoxikologischen Risikoabschätzung von kontaminierten Böden wie folgt abgeleitet: C_6 – C_8: 5 mg/kg KG/Tag C_9 – C_{16}: 0.1 mg/kg KG/Tag C_{17} – C_{34}: 2 mg/kg KG/Tag $C_{>34}$: 20 mg/kg KG/Tag Die EFSA ist der Meinung, dass für Mineralöl in Lebensmittelqualität (C_{12}-C_{40}) aufgrund mangelnder toxikologischer Daten, zu für den Menschen relevanten Mischungen, keine ADIs abgeleitet werden können. Sie wendet bei der Risikobeurteilung einen MOE-Ansatz an.
Exposition		
Äussere Exposition Boden (250 mg)		5 mg C_5-C_{10}/kg Boden = 1.25 µg /250 mg Boden = 0.1 µg/kg KG/Tag (bei KG: 12.5kg) und 500 mg C_{11}-C_{40}/kg Boden = 125 µg /250 mg Boden = 10 µg/kg KG/Tag (bei KG: 12.5kg)
Innere Exposition Boden „Bioavailability“		Bei 100% Bioavailability: **5 mg C_5-C_{10}/kg Boden** = 0.1 µg C_5-C_{10}/kg KG/Tag = 0.002% des TDI $_{C6-C8}$ und 0.1% des TDI $_{C9-C16}$ **500 mg C_{11}-C_{40}/kg Boden** = 10 µg C_{11}-C_{40}/kg KG/Tag = 10% des TDI $_{C9-C16}$ und 0.5% des TDI $_{C17-C34}$ und 0.05% des TDI $_{>C34}$ (Tabelle unten).

<table>
<tr><td></td><td></td><td>
<table>
<tr><th>Fraktion
AltV</th><th>Fraktion
TPHCWG</th><th>Exposition via Boden AltV[a]
µg /kg KG/Tag</th><th>TDI (TPHCWG) [b]
µg /kg KG/Tag</th><th>Diätische Exposition[c]
µg /kg KG/Tag</th><th>Exposition via Boden AltV
in % TDI</th><th>Exposition via Boden
in % Diät. Exp.</th></tr>
<tr><td>$C_5 – C_{10}$</td><td>$C_6 – C_8$</td><td>0.1 für C5-C10</td><td>5000</td><td>Keine Angaben[d]</td><td>0.002 des TDI C6 – C8</td><td></td></tr>
<tr><td>$C_{11} – C_{40}$</td><td>$C_9 – C_{16}$</td><td>0.1 für C5-C10
10 für C11-C40</td><td>100</td><td>1187– 3880[c] für C11-C40</td><td>0.1 des TDI C9 – C16
10 des TDI C9 – C16</td><td>0.003 – 0.008
0.258 – 0.842</td></tr>
<tr><td></td><td>$C_{17} – C_{34}$</td><td>10 für C11-C40</td><td>2000</td><td>1187– 3880[c] für C11-C40</td><td>0.5 des TDI C17 – C34</td><td>0.258 – 0.842</td></tr>
<tr><td></td><td>$C_{>34}$</td><td>10 für C11-C40</td><td>20000</td><td>1187– 3880[c] für C11-C40</td><td>0.05 des TDI >C34.</td><td>0.258 – 0.842</td></tr>
</table>
[a] Assuming daily ingestion of 250 mg soil, an time weighted average body weight of 12.5 kg and a bioaccessibility of soil derived hydrocarbons of 100%.
[b] data represent TPHCWG TDIs from table 14-6 which are sufficiently similar to the CSO-grouping and are therefore considered relevant for risk assessment. EFSA did not derive ADIs for food grade hydrocarbons because there is a lack of toxicological data on relevant mixtures (of food grade hydrocarbons).
[c] data represent the sums of scenario 1 and 2 in table 14-6.
[d] EFSA considers only C_{10}–C_{50} as food grade hydrocarbons relevant for dietary risk assessment. Most relevant are C_{12}-C_{40}.
</td></tr>
<tr><td>Hintergrundexposition
Nahrung, Wasser, Luft</td><td></td><td>Diätische Exposition (C_{11}-C_{40}): 1187– 3880 µg /kg KG/Tag (Kinder 1 - 3 Jahre) (Tabelle oben).</td></tr>
<tr><td>Zusätzliches Gesundheitsrisiko

durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.</td><td>Unwahrscheinlich</td><td>Für die C_{11}-C_{40}-Fraktion ist, unter der Annahme einer 100% Bioverfügbarkeit der Kontaminanten aus dem Boden, die zusätzliche Exposition durch das Verschlucken von kontaminiertem Boden (10 µg C_{11}-C_{40}/kg KG/Tag) klein im Vergleich zur diätischen Exposition (1187-3880 µg C_{11}-C_{40}/kg KG/Tag). Dieses Szenario geht davon aus, dass Brot und Brötchen-Szenario ein wesentlicher Bestandteil der Ernährung sind und wesentlich zur diätischen Exposition gegenüber C_{11}-C_{40} beitragen.
Selbst wenn Brot und Brötchen kein wesentlicher Bestandteil der Ernährung sind, wird die diätische Exposition auf > 100 µg C_{11}-C_{40}/kg KG/Tag geschätzt. Die zusätzliche Belastung mit C_{11}-C_{40} läge dann immer noch unter 10% der diätischen Belastung und ein zusätzliches Gesundheitsrisiko wäre gering.
Für C_5-C_{10}-Fraktion gibt es keine Vergleichsdaten zur diätischen Exposition. Allerdings liegt die Exposition durch Verschlucken von Boden bei dieser Fraktion deutlich unter den abgeleiteten TDIs</td></tr>
</table>

<table>
<tr><td></td><td></td><td>für die einzelnen relevanten TPH-Fraktionen (Exposition max. 0.1% des niedrigsten TDI).</td></tr>
<tr><td>Grenzwert im Vergleich</td><td></td><td>
<table>
<tr><th>Country</th><th>TPH-Fraktion $C_{<12}$</th><th>Grenzwert (mg/kg dm)</th></tr>
<tr><td>CAN</td><td>C_6-C_{10}</td><td>15000</td></tr>
<tr><td>A</td><td>ca. C_5-C_{10}</td><td>500</td></tr>
<tr><td>I</td><td>$<C_{12}$</td><td>10</td></tr>
<tr><td>CH</td><td>C_5-C_{10}</td><td>5</td></tr>
</table>
<table>
<tr><th>Country</th><th>TPH-Fraktion $C_{>10}$</th><th>Grenzwert (mg/kg dm)</th></tr>
<tr><td>CAN</td><td>$>C_{10}$-C_{16}
$>C_{16}$-C_{34}
$>C_{34}$</td><td>8000
18000
25000</td></tr>
<tr><td>A</td><td>ca. $>C_{17}$
ca. C_9-C_{17}</td><td>1000
500</td></tr>
<tr><td>CH</td><td>C_{11}-C_{40}</td><td>500</td></tr>
<tr><td>D</td><td>C_{10} - C_{40}</td><td>500</td></tr>
<tr><td>CZ</td><td>unspecified total nonpolar extractable substances</td><td>500</td></tr>
<tr><td>I</td><td>$>C_{12}$</td><td>50</td></tr>
</table>
Keine Bodensanierungswerte für Aliphaten in 7 Ländern: B, E, F, NL, S, UK, USA
Bodensanierungswerte für Mineralöle in 3 der 7 Länder: B, F, NL
</td></tr>
<tr><td>Datenlage</td><td>Unzureichend</td><td>Es gint keine Studien zur Bioverfügbarkeit von Aliphatics aus dem Boden im Mensch oder Tier. Nur für Mineralöle in Lebensmitteln (MOSH) gibt es Daten zur oralen chronischen Toxizität.
Der Mensch ist gegenüber Mischungen verschiedener Aliphaten exponiert, aber toxikologische Daten zur Mischungstöxizität beschränken sich auf Versuche mit Mineralölprodukten wie Kerosin, das als Indikatorsubstanz bereits eine Mischung darstellt.
Aber da die Absoprtion von längkettigen Aliphaten gering ist, besteht keine Unsicherheit bezüglich der Risikobeurteilung.</td></tr>
</table>

14.2 Zusammenfassung

For the sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly, the Swiss Contaminated Sites Ordinance (CSO) sets a concentration value for remediation of 5 mg/kg soil for C_5 to C_{10} aliphatic hydrocarbons and a concentration value of 500 mg/kg soil for the C_{11} to C_{40} aliphatic hydrocarbons. This translates into a daily exposure from incidental ingestion of 250 mg soil of 0.1 µg/kg/day for C_5 to C_{10} and 10 µg/kg/day for C_{11} to C_{40} for a 12.5 kg child, assuming 100% absolute oral bioavailability from soil.

The SCAHT risk assessment reveals that at these threshold values incidental soil ingestion does not present a major additional health risk and therefore the current threshold values can be kept.

Toxicity of aliphatics is generally expected to be low. Acute neurotoxicity after inhalation exposure is most relevant in humans but these effects are to a large extent reversible. Hepatotoxic effects observed in animal studies are considered to be of low relevance for human health.

Additional exposure from incidental soil ingestion would be negligible compared to dietary exposure. Under the assumption that Swiss are high bread consumers additional exposure to the C_{11}-C_{40}-fraction from incidental soil ingestion accounts for less than 1% of dietary exposure and is therefore of low relevance. The aliphatic C_5-C_{10}-components are not considered relevant for dietary exposure because of their high volatility and therefore no dietary exposure data are available for this fraction. However, the exposure from incidental soil ingestion would only contribute to 0.002% of the most relevant TDI that has been derived by an expert consortium (Total Petroleum Hydrocarbon TPH Criteria Working Group, TPHCWG) for the lighter chain aliphatic fraction in order to protect human health from chronic exposures to environmental media contaminated with different TPH subfractions.

Anyway oral exposure to the lighter aliphatic fractions is expected to be negligible because they will easily volatilize into the air. The remainder will readily migrate through the soil and biodegrade. As volatilization occurs within minutes to hours, it only represents a potential significant exposure pathway to persons in the immediate vicinity of highly contaminated freshly excavated soil. For our soil ingestion scenario of a child playing in the private garden this is not a relevant exposure scenario. Aliphatics in the intermediate carbon number range (C_{11}-C_{18}) typically migrate through soil and only a small amount of the product is retained in the top surface layer, which is relevant for the SCAHT risk assessment scenario. The longer chain / branched aliphatics tend to sorb to soil or sediment, and remain relatively immobile at the site of release but human exposure is expected to be low because oral absorption is expected to decrease with molecular weight and branching of the aliphatics.

EFSA is concerned about the low biotransformation rates, in particular for some branched- and cyclo-alkanes. Aliphatic hydrocarbons from C_{16}-C_{35} may accumulate in several tissues but the SCAHT assumes that the additional burden from soil ingestion during childhood is negligible, particularly because exposure from soil is extremely low compared to dietary exposure (<1%).

14.3 Gefährdungspotential

14.3.1 Aliphatic compounds as a fraction of total petroleum hydrocarbons

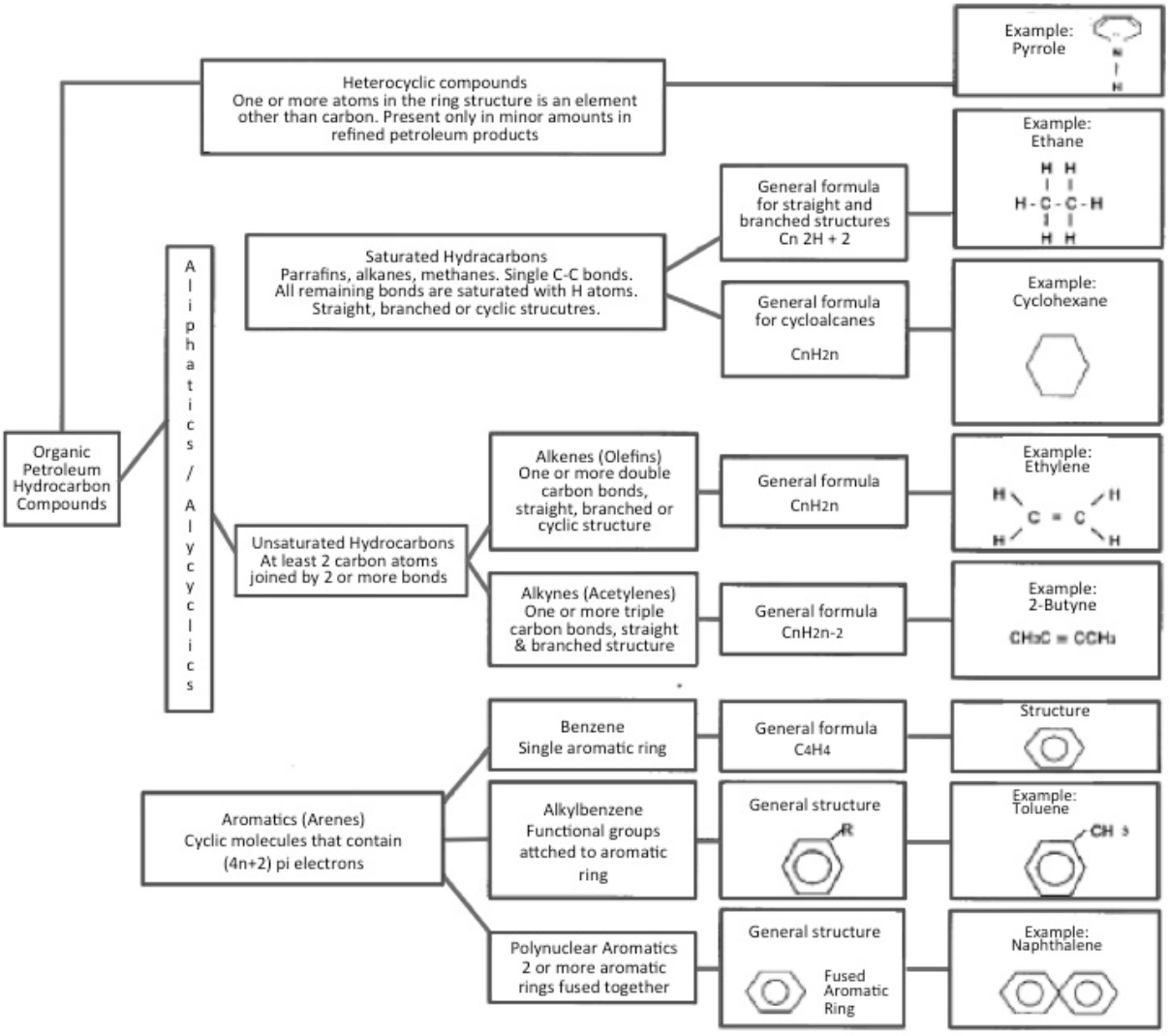
Aliphatics are a fraction of "total petroleum hydrocarbons" (TPH) derived from crude oil. Aliphatics are carbon- and hydrogen- based compounds that can be either saturated or unsaturated linear (e.g. *n*-alcanes, alkenes, alkynes), branched (e.g. *iso*-alcanes, alkenes, alkynes) or cyclic (e.g. cycloalcanes) structures.

Aliphatic compounds are obtained from the processing of crude petroleum oil, and constitute but one of the several fractions of what is commonly referred to as "total petroleum hydrocarbons" (TPH) (see **Figure 14-1**).

Besides aliphatic compounds *per se*, other fractions are included in the TPH mixture, such as monoaromatics (e.g. BTEX), simple polyaromatics (e.g. naphthalene, fluorene) or more complex poly-aromatics (e.g. PAHs such as benzoapyrene) (Heath et al 1993, p.267; USEPA 2015).

Figure 14-1: Illustration of the different TPH-fractions

(Source: TPHCWG 1997, Vol 3, p.54)



14.3.2 Characterization of the total petroleum fraction

There is no sharp differentiation between individual refined petroleum products. Refined petroleum products are primarily manufactured through distillation processes that separate fractions from crude oil by their boiling points but distillations are not capable of producing sharp distinctions in boiling point cut-offs because boiling points increase with increasing number of carbons (more atoms, more electrons, more opportunities for induced dipole-induced dipole forces) but decrease with chain branching (more compact, smaller surface, fewer points of contact with other molecules). Therefore the boiling point is not an explicit differentiator and boiling point ranges and carbon number ranges of refined petroleum products often overlap and the same product can appear in neighboring distillation fractions.

Fractions obtained after initial destilation are modified by cracking, condensation, polymerization, and alkylation processes, and are formulated into petroleum-derived final products such as gasoline, diesel, jet fuel and fuel oils (see **Table 14-1**). The chemical composition of any one of these final products can vary based on the refinery involved, the time of year, variation in additives or modifiers, and other factors. The composition of the product can be further affected by weathering and/or biological modification upon release to the environment (ATSDR 1999, page 20, first paragraph).

Table 14-1: Classification of total petroleum hydrocarbon (TPH) fractions in petroleum derived products

TPH fractions can be distinguished, based on their Equivalent Carbon Number Index (EC). EC is an artificial grouping system for hydrocarbons based on analytical separation methods largely based on equivalent boiling points and retention times in gas chromatography normalized to the n-alkanes. Different parameters such as solubility, vapor pressure, molecular weight, Henry's law constant or the organic carbon partition coefficient (Koc) can be defined for each fraction using correlations with the EC number.

(Source: HLUG 2002, page 48 sq; BLFW 2001, page 38 sq; CCME 2008, Table 3-4, page 3-47)

Aliphatic fraction			Equivalent carbon number	Vapor pressure (atm)[a]	Solubility (mg/L)[a]	Henry's law (cm^3/cm^3)[a]	Log K_{oc}[a]	Toxicological endpoints[b]
Benzine (C_5-C_{10})	Petrolether		EC_5 - EC_6	0.35	36	47	2.9	Neurotoxicity
	Ligroin		$EC_{>6}$ - EC_8	0.063	5.4	50	3.6	Neurotoxicity
	Kerosene (ca. C_8-C_{17})		$EC_{>8}$ - EC_{10}	0.0063	0.43	55	4.5	Hepatic and hematological changes
Heizöl EL (ca. C_9-C_{24})		Diesel (ca. C_{10}-C_{21})	$EC_{>10}$ - EC_{12}	0.00063	0.034	60	5.4	Hepatic and hematological changes
			$EC_{>12}$ - EC_{16}	0.000076	0.00076	69	6.7	Hepatic and hematological changes
	Schmieröle, Heizöl S (ca. C_{17}-C_{39})		$EC_{>16}$ - EC_{21}	0.0000011	0.0000025	85	8.8	Hepatic granuloma
		Mineral oils (ca. C_{17}-C_{39})	$EC_{>21}$ - EC_{34}	0.0000011	0.0000025	85	8.8	Hepatic granuloma
			$EC_{>34}$					Hepatic granuloma

[a] Representative physical parameters for TPH fractions, based on correlation to relative boiling point index (ATSDR 1999, page 82, table 5-7).

[b] Toxicological endpoints reported for the corresponding TPH subfraction developed by the TPHCWG (1997) (CCME 2008, Table 3-4, p. 3-47 citing Edwards et al. 1997).

14.3.3 Use of the total TPH-value in environmental monitoring

For environmental monitoring the total TPH-value is used. Since there are several hundred individual hydrocarbon chemicals defined as petroleum-derived compounds, it is not practical to measure each one separately. TPH is traditionally used as a sum parameter to estimate environmental site contamination with crude oil and petroleum products. TPH is a measured, gross quantity without identification of the individual constituents and their quantitative representation within the mixture. In parallel to TPH some targeted mixtures of concern such as BTEX and BTEX-napthalene (Brewer et al 2013; USEPA 2015) are evaluated.

14.3.4 Use of TPH-subfractions in human health risk assesment

Human health risk assesment is not based on the total TPH-value but on TPH-subfractions. The total TPH value is not adequate for human health risk assessment because TPH represents a mixture of petroleum hydrocarbons fractions. As the composition of crude oil itself varies, this variation is reflected in the finished petroleum product and each petroleum product has its own mix of individual constituents with very different physico-chemical and toxicological properties (see **Table 14-1**).

In a realistic exposure scenario, individuals will not be exposed to heterogenous mixtures of TPH but to specific fractions as a result of fractionation and various transport processes occurring in the environment.

The TPH fractions can be defined by the physico-chemical properties of constituents in order to address this question of predicting risks associated with TPH contamination. It is generally assumed that fractions with similar physico-chemical properties have similar toxicological properties, though this is not always the case (ATSDR 1999, page 13, first paragraph) (see below). Therefore, for the purpose of human health risk assessment, ATSDR follows the TPH Criteria Working Group[1] (TPHCWG) guidance and divides TPH into aliphatic and aromatic fractions, which are further divided into subfractions. In particular the aliphatic fraction is subdivided into three subfractions as follows: C_5-C_8; >C_8-C_{16} and >C_{16}-C_{35} (ATSDR 1999, page 13, last paragraph and page 15, table 2.2) (see **Table 14-2** below). The TPHCWG approach was also recommended by other regulatory authorities, sometimes with minor modifications proposed (e.g. RIVM 2001, CCME 2008), and represent to date the most reasonable published approach for addressing risk from petroleum hydrocarbons. (For a regualtory comparative analysis, see UKEA 2003).

14.3.4.1 Use of a representative TPH compound as a proxy for risk assessment

A representative compound within the TPH-subfractions is used as a proxy for risk assessment. It is frequently recommended for the purpose of health risk assessment to use the physical and toxicological properties of a given aliphatic fraction, based on their components or representative compounds. In general, the most toxic representative compound or mixture for each fraction is used to indicate the potential toxicity of the entire fraction.

This approach has been termed "*Combination indicator compound and fraction approach for TPH*"; n-hexane, jet fuels and mineral oils are proxys commonly used for the the C_5-C_8, >C_8-C_{16} and >C_{16}-C_{35} fractions (see **Table 14-2** below).

[1] Established in 1993, the TPHCWG is a consortium of scientists from the oil and gas industry, the consulting community, the U.S. military, state regulatory agencies, and the University of Massachusetts, which sought to address the great disparity between state regulatory directives in relation to the cleaning up of petroleum hydrocarbons-contaminated sites (inter-State variability in cleanup standards from 10 to 10'000 ppm). To date, the TPHCWG has put together the most comprehensive data set on TPH (Sawyer 2015).

Table 14-2: "Combination indicator compound and fraction approach for TPH" used for health risk assessment of hydrocarbon-contaminated sites.

(Source: ATSDR 1999, page 15, table 2.2)

Chemical fraction, in EC[a]	Representative compounds
Aromatics	
EC_6 - EC_9	Benzene, toluene, ethylbenzene, xylenes
$EC_{>9}$ - EC_{16}	Isopropyl benzene, naphthalene
$EC_{>16}$ - EC_{35}	Fluorene, fluoranthene, benzo(a)pyrene
Aliphatics	
EC_5 - EC_8	*n*-Hexane
$EC_{>8}$ - EC_{16}	JP-5, JP-7, JP-8, kerosene, dearomatized petroleum stream
$EC_{>16}$ - EC_{35}	Mineral oils

[a] EC = equivalent carbon number index. EC is based on equivalent retention times on a boiling point GC column, normalized to n-alkanes

14.3.5 Toxicological endpoints

⇒ **Neurotoxicity and hepatotoxicity are the two major toxicological endpoints observed in experimentals studies.**

⇒ **Acute neurotoxicity after inhalation of lighter chain fractions is most relevant for humans.**

While the health effects of the lighter aliphatic subfractions have been relatively well characterized, based on the toxicity profile of their individual components, the toxicity of the heavier aliphatic subfractions is generally less well characterized (ATSDR 1999; EFSA 2012).

- For the C5-C8 and >C8-C16-fractions, due to their physicochemical properties, there are more inhalation toxicity data available than oral data.
- For the >C16-C35 fraction, there are only oral toxicity data available (ATSDR 1999, page 134, chapter 6.2.6.1).
- Little information is available to suggest systemic toxicity from dermal exposure for all three aliphatic fractions (ATSDR 1999, page 127, chapter 6.2.4.3; page 132, chapter 6.2.5.3; page 135, chapter 6.2.6.3)

Table 14-3 below presents a summary of toxicological findings as described by ATSDR (1999).

Table 14-3: **Toxicological endpoints for three selected aliphatic subfractions derived from studies on representative compounds which are used as a proxy for human health risk assessment**

(Source: ATSDR 1999, chapters 6.2.4 - 6.2.6, pages 122 - 135).

Toxicological endpoints	Fraction/ Proxy	Comments
Neurotoxicity	C_5-C_8 *n*-Hexane[a]	Peripheral neuropathy from n-hexane metabolites requiring metabolic bioactivation of parent n-hexane by CYP-450s. In humans after inhalation and in animals after oral exposure to n-hexane: Peripheral neuropathy, i.e. numbness in the feet and legs and in severe cases paralysis. Apart from n-hexane the other compounds in the C_5-C_8 fraction do not appear to cause peripheral neuropathy (ATSDR 1999, page 124, chapter 6.2.4.1, first paragraph and chapter 6.2.4.2, page 127, first paragraph). Depression of the central nervous system from parent n-hexane Observed at high doses after inhalation exposure (ATSDR 1999, page 125, third paragraph). MoA: Lipophilic parent hydrocarbon dissolves in nerve cell membranes, and disrupts the function of membrane proteins by disrupting their lipid environment or by directly altering protein conformation. Other compounds than n-hexane Reduced nerve conduction velocity has been observed for 2-Methylpentane and methylcyclopentane in an oral subchronic study in rats and chicken, but these compounds were not as effective as n-hexane in that same study (ATSDR 1999, page 127, chapter 6.2.4.2, first paragraph). Some data suggest that some metabolites e.g. of heptane or nonane may be neurotoxic, but very little information is available. Following acute inhalation exposure, n-heptane, methylcyclohexane and cyclohexane have also been shown to be neurotoxic to some extent in rodents only (ATSDR 1999, page 125).
	>C_8-C_{16} Jet fuels[b]	Depression of the central nervous system after inhalation exposure Neurological effects, particularly central nervous depression, have been seen in humans exposed to JP-5 vapors, but exposure-effect relationships have not been established (ATSDR 1999, p. 130, chapter 6.2.5.1, first paragraph). Neurotoxic effects after oral exposure only at lethal doses

		After acute oral exposure in animals neurotoxic effects have been seen at fatal doses. At lower doses neurotoxic effects were observed, but no dose-effect could be defined (ATSDR 1999, page 130, chapter 6.2.5.2).
	>C_{16}-C_{35} Mineral oils[c]	No neurotoxic effects identified for this sub-fraction.
Hepatotoxicity	C_5-C_8	Inconsistent liver tumor findings in some rat species but no aliphatic compounds have been classified for carcinogenicity. Some evidence of carcinogenic potential (liver) has been reported in chronic inhalation (ATSDR 1999, page 125, first paragraph) and oral studies (ATSDR 1999, page 127, second paragraph) with commercial n-hexane mixtures in female mice. However, none of the aliphatic compounds have been classified for carcinogenicity by IARC. Contamination of commercial n-hexane mixtures with aromatic impurities might have impacted teh study results.
	>C_8-C_{16} Jet fuels[b]	Increased liver weights in animals are considered of low toxicological relevance for humans. Hepatic effects are the most sensitive endpoints for inhalation exposure to JP-5, JP-7, JP-8, and kerosene (ATSDR 1999, page 130, chapter 6.2.5.1, first paragraph). Increased liver weights were not considered significant (ATSDR 1999, page 130, second paragraph) but adaptive rather than adverse effects (ATSDR 1999, page 176, footnotes b and c to table 6.9) After acute oral exposure hepatic effects have been seen at fatal doses. At lower doses hepatic effects were observed, but no dose-effect could be defined (ATSDR 1999, page 130, chapter 6.2.5.2). Hepatocellular hypertrophy and increased liver weight has also been observed.
	>C_{16}-C_{35} Mineral oils[c]	Hepatic lipid granulomas have been observed in humans and rats. In humans they are considered of low toxicological relevance. Hepatic lipid granulomas (benign structures in human liver and spleen tissue composed of lipoid droplets surrounded by lymphocytes and macrophages) have been described in humans exposed to mineral oils through the diet and by ingestion of medicinal (purified) mineral oils, but dose-effects relationships are poorly characterized. According to TPHCWG (1997c), the granulomas in humans were circumscribed lesions with no inflammation, fibrosis, or significant liver dysfunction (which is consistent with their slow metabolism), whereas the granulomas in F344 rats were reactive with associated inflammation and occasional parenchymal cell necrosis (ATSDR 1999, p.134-135, 149). Excessive number of histiocytes (tissue macrophages) in rats is considered of low toxicological relevance The effects on mesenteric lymph nodes (histiocytosis) in F344 rats, which occurred at lower exposure levels than did the

		hepatic effects, was judged a nonadverse, adaptive response to the ingestion of foreign material (ATSDR 1999, p.134, chapter 6.2.6.2).
Nephrotoxicity	C_5-C_8	Not identified.
	>C_8-C_{16} Jet fuels[b]	Male rat specific α2μ-globulin nephropathy has no human relevance[d] Male rat specific α2μ-globulin nephropathy was observed after inhalative exposure to jet fuels (ATSDR 1999, page 130, chapter 6.2.5.1, second paragraph), dearomatized petroleum streams (ATSDR 1999, page 130, chapter 6.2.5.1, second paragraph) and after oral exposure to jet fuels (ATSDR 1999, page 130, last paragraph) and dearomatized petroleum streams (ATSDR 1999, page 132, second paragraph).
	>C_{16}-C_{35}	Not identified.
Pulmonary irritation	C_5-C_8	Pulmonary irritation and pneumonia from inhalation and oral exposure has been observed (ATSDR 1999, page 161, ATSDR 1999, page 124, last paragraph). Because of their low viscosity, aliphatic hydrocarbons in the C5-C8 and >C8-C16 fractions are aspirated to the lungs following oral exposure (the lower the viscosity, the more extreme the aspiration risk) (ATSDR 1999, page 189, first paragraph).
	>C_8-C_{16}	See C_5-C_8
	>C_{16}-C_{35}	Not applicable, due to the high viscosity of these alipahtic hydrocarbons.
Repro- and developmental toxicity	C_5-C_8	Reproductive (testicular) and developmental effects have been seen in animals following exposure to higher doses of n-hexane.
	>C_8-C_{16}	Developmental toxicity studies of dearomatized petroleum streams following inhalative exposure in rats revealed no developmental or maternal toxicity at exposure levels, which produced male rate nephropathy and hepatotoxicity (ATSDR 1999, page 130, chapter 6.2.5.1, second paragraph). Oral exposure studies were also negative (ATSDR 1999, page 132, second paragraph).
	>C_{16}-C_{35}[e]	There is little evidence to suggest adverse reproductive or foetal effects following exposure to aliphatic petroleum hydrocarbons and mineral oils in the C_{15}-C_{50} range, occuring at doses not also having maternal toxicity.
Carcinogenicity, genotoxicity	-	None of the aliphatic compounds have been classified for carcinogenicity by the International Agency for Research on Cancer (IARC). Long chain MOSH can act as tumour promoters at high doses (EFSA 2012, Summary, pp.5-6). It cannot be excluded that this is because

		of the aromatic fraction within the MOSH.

[a] Studies use either pure n-hexane or commercially available hexane typically containing 40% n-hexane, 24% 3-methylpentane, 24% dimethylbutane, 9% cyclopentane, 2.5% cyclohexane, and 12% 2-methylpentane.

[b] Jet fuels are primarily mixtures of aliphatics in the C_9-C_{16} fraction range but may also contain 5-24% aromatics, incl. BTEX that might affect the toxicity profile. Jet fuels also contain additives (e.g. antioxidants, metal deactivators, fuel system incl. (corrosion) inhibitors, static dissipaters). TPHCWG (1997) identified a number of (un)published studies on dearomatized petroleum streams matching to portions of this range, containing generally < 0.1% aromatics (at most 1.5%) and no additives. Therefore dearomatized petroleum streams may serve as a better proxy for the health effects assessment of this fraction, however their exact compositions is often not known (ATSDR 1999, pp.129-130).

[c] The TPHCWG (1997) concluded that food and medicinal grade mineral oils, which are relatively pure, represent a good proxy for the $>C_{16}$-C_{35} fraction, rather than mineral-based crankcase oil and hydraulic fluids which contain many additives and contaminants.

[d] α2μ-Globulin nephropathy following exposure to certain type of chemicals agents is a well-characterized sex- and species-specific disease that only occurs in male rats and not in female rats and either sex of mice, guinea pigs, hamsters, dogs, and monkeys. There are no data suggesting protein droplet accumulation in the kidneys of humans. USEPA concluded that renal tumors mediated through α2μ should not be used in human risk assessment (Swenberg, 1994).

[e] Absorption of alkanes with carbon number above C_{35} is negligible (EFSA 2012, abstract).

14.4 Gesundheitsbasierter Referenzwert

Two groups of health-based guidance values have been established for human risk assessment

- Tolerable Daily Intakes (TDIs[1])

  The recommendations of the TPHCWG are based on the Tolerable Daily Intakes (TDIs) established by Edwards et al. (1997). These TDIs are meant to protect human health from chronic exposures to environmental media contaminated with different TPH-subfractions (C_6-$C_{8;}$ >C_8-$C_{16;}$ >C_{16}-$C_{35;\ and}$ >C_{35}) (see **Table 14-4** below).

- Admissible Daily Intakes (ADIs[1,2])

  The former EU Scientific Committee on Food (SCF), the European Food Safety Authority (EFSA), and the Agriculture Organization of the United Nations/World Helath Organization (FAO/WHO) have established Admissible Daily Intakes (ADIs) to protect human health from chronic exposures to food-grade mineral hydrocarbons (see **Table 14-5** below). TDIs have also been established for food contamination with MOH originating from e.g. harvesting processes and pesticide applications.

  Nota bene: the TPHCWG and SCF/EFSA and FAO/WHO-specification schemes are not harmonized and the protection goals are different. Therefore a one-to-one comparison of the TDIs and ADIs is not straightforward.

14.4.1 Derivation of TDIs for environmental exposure to TPH-subfractions

Several analytical fractions of assumed similar toxicological profiles were combined for the toxicology-based grouping. The grouping is solely based on physico-chemical properties (viscosity). TDIs for aromatic sub-fractions have also been developed but are not listed here.

[1] ADI and TDI are health-based references values which both refer to the amount of a specific substance that can be ingested (orally) on a daily basis over a lifetime without an appreciable health risk and are therefore similar from a toxicological point of view. The only difference is that ADI refers to substances intentionally added to food (e.g. food additives) whereas TDI refers to unwanted substances not deliberately added to food (e.g. impurities, contaminants).

[2] See[3]

Table 14-4: TDIs for TPH aliphatic sub-fractions in environmental media as developed by TPHCWG.

(Source: CCME 2008, page 3-47, Table 3-4, citing Edwards et al., 1997).

	Toxicological[b] TPH sub-fraction (THPCWG)	Analytical[c] TPH sub-fraction (THPCWG)	TDI (mg/kg bw/day)	RfC[d] (mg/m³)	Critical human health effect
Low Viscosity[a] Liquids	C_6-C_8	C_6-C_8	5.0	18.4	Neurotoxicity
Medium Viscosity Liquids	$C_{>8}$-C_{16}	$C_{>8}$-C_{10} $C_{>10}$-C_{12} $C_{>12}$-C_{16}	0.1	1.0	Hepatic and haematological effects
High Viscosity Liquids	$C_{>16}$-C_{34}	$C_{>16}$-C_{21} $C_{>21}$-C_{34}	2.0	n.a.[e]	Hepatic granuloma
Waxes	$C_{>34}$	$C_{>34}$	20.0	n.a.	Hepatic granuloma

[a] For a liquid to boil, it is necessary to break the intermolecular forces of attraction between its particles so that they separate and vaporize; the stronger the bond, the more energy required. Viscosity is a measure of these particle bond strengths.

[b] Separation into fractions is based on toxicological enpoints

[c] Separation into fractions is based on physicochemical considerations (e.g. boiling point, carbon number, etc).

[d] RfC is the reference dose for inhalation.

[e] n.a. = not applicable; TPH subfraction is not sufficiently volatile to present air-borne exposure.

14.4.2 Derivation of ADIs for dietary exposures and food safety

Food grade mineral hydrocarbons[3] (MOSH) are produced as by-products during the refining and distillation of crude mineral oils. There are three main types of products; liquids, semi-liquids and solids, examples of each being mineral (white) oils, petroleum jellies and mineral waxes. Since petroleum jellies are prepared by mixing oils and waxes, only mineral oils and mineral waxes need be considered when assessing the dietary safety of mineral hydrocarbons (SCF 1995, p.31, first paragraph).

Classification of food grade Mineral Oil Hydrocarbons based on viscosity (Fig. 14-1 and Table 14-5)

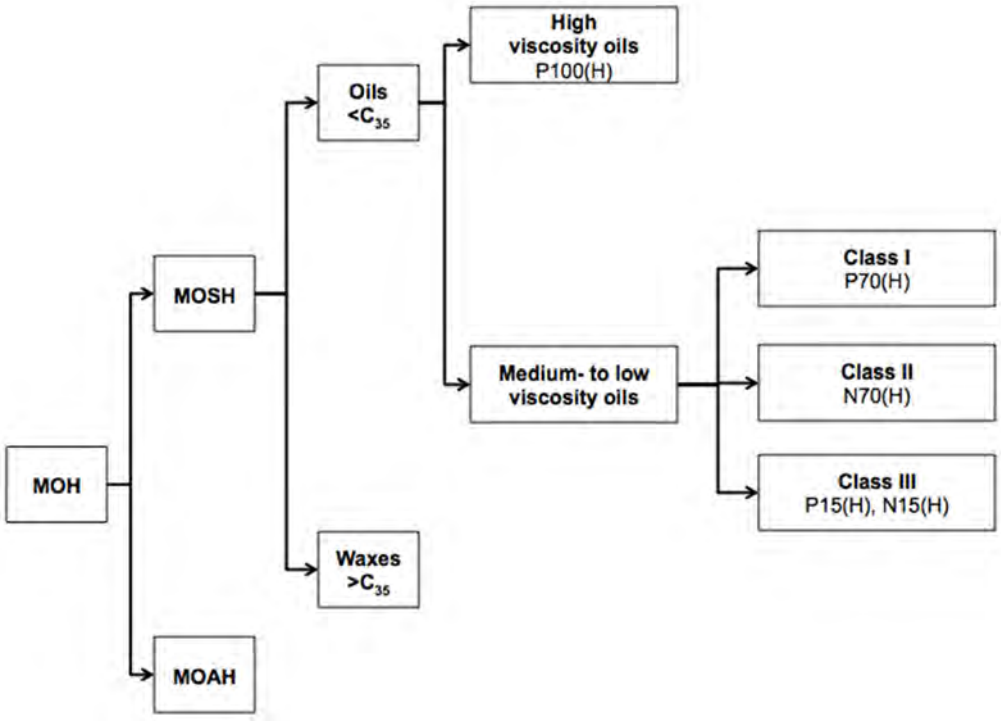
The food grade specification scheme (**Fig. 14-1**) is different from the environmental media grouping. Consumers are exposed to a range of mineral oil hydrocarbons (MOH) via food originating from food packaging and additives, processing aids, and lubricants. MOH can be divided into mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH) (EFSA 2012). The later are outside the focus of this report.

MOSH consist of linear and branched alkanes, and alkyl-substituted cyclo-alkanes and mineral oil aromatic hydrocarbons (MOAH) are mainly alkyl-substituted polyaromatic hydrocarbons. Technical grade MOH contain 15 - 35 % MOAH, food grade MOSH (white oils) contain less „MOAH-impurities“ (EFSA 2012).

[3] Different terms are used for food grade hydrocarbons: White oils (and waxes) and MOSH (mineral oil saturated hydrocarbons).

Based on their viscosity, MOSH are divided into mineral oils (<C_{35}) and waxes (>C_{35}). Based on their composition oils are subdivided into high viscosity oils and medium- to low-viscosity oils. High viscosity oils consist of parafinic hydrocarbons only (see P100(H) in **Table 14-5**) but medium- to low-viscosity oils are further subdivided into three classes, depending on their composition of paraffinic and naphthenic liquid hydrocarbons (see class I: P70(H), class II: N70(H) and class III: P15(H), N15(H) in **Table 14-5**. Waxes are divided into two groups of high and low melting points.

Fig. 14-1: **Food grade Mineral Oil Hydrocarbons**



EFSA challenged this grouping solely based on viscosity and recommends that mineral oil hydrocarbon mixtures should be assessed by considering the molecular mass range and subclass composition (e.g. n-, branched- or cyclo-alkanes) (EFSA 2012, summary) because absorption and biotransformation are different:

Absorption:

- Absorption of alkanes may occur through the portal and/or the lymphatic system. For n- and cyclo-alkanes the absorption varies from 90% for C_{14}-C_{18} to 25 % for C_{26}-C_{29}. The absorption further decreases with increasing carbon number, until above C_{35} when it is negligible.
- Limited data suggest that cyclo-alkanes are absorbed at similar levels as n-alkanes of comparable molecular weight.
- Absorption of branched alkanes is slightly less compared to n-alkanes.

Biotransformation:

Alkanes are initially oxidised to the corresponding fatty alcohols by the cytochrome P450 system, subsequently biotransformed to fatty acids and in some cases subjected to the normal β-oxidation pathway.

- This reaction is more rapid for n-alkanes than for branched- and cyclo-alkanes.

- Due to low biotransformation rates, in particular for some branched- and cyclo-alkanes, MOSH having carbon number in the range C_{16}-C_{35} may accumulate in different tissues including adipose tissue, lymph nodes, spleen and liver. This has been confirmed in experimental animals and humans.
- Although limited information exists on toxicokinetics of MOAH, the available data indicate that these compounds are well absorbed and are rapidly distributed to all organs. The data also indicate that MOAH are extensively metabolised and do not bioaccumulate.

14.4.2.1 ADIs for individual food grade mineral hydrocarbons

ADIs as defined in **Table 14-5** were derived by SCF (1995), FAO/WHO-JECFA (2002 and 2012) and EFSA (2009, 2012).

1995

The Scientific Committee on Food (SCF) evaluated the safety of mineral and synthetic hydrocarbon oils and waxes for use as food additives, in food processing and for use in food packaging materials (SCF 1995). **SCF established two group ADIs, one for oils and one for waxes:**

- **For the C_{25}-C_{34} fraction** (food grade MOSH / white paraffinic mineral oils, including P70(H) and P100(H) oils), a **temporary Group ADI of 0-4 mg/kg b.w.** was derived based on a NOAEL derived from 90-day studies using a safety factor of 500 for increased liver weight[4].
- **For waxes ca. > C_{35}** (highly refined microcrystalline and synthetic waxes largely consisting of n-alkanes) a **Group ADI of 0-20 mg/kg b.w** was derived, applying an UF of 100 to the NOAEL, based on the liver and lymph node hydrocarbons accumulation in a 90-day study in Fischer 344 rats (EFSA 2012, pp.26-27; SCF 1995, p.35, last paragraph).

2002

Individual ADIs for all the individual subfractions were established at the 44th and 59th FAO/WHO JECFA meeting the Expert Committee on Food Additives (JECFA) (FAO/WHO 2002 chapter 3.1.3, pages 11 ff and table 1, page 12) based on results from 90-days studies in Fisher rats as outlined in **Table 14-5**.

The group ADI for waxes established by SCF in 1995 was withdrawn for low and intermediate melting point waxes.

The temporary group ADIs of 0.01 for medium and low viscosity mineral oils class II and III were established and/or reconfirmed. These ADIs were withdrawn in 2012.

2009

An new ADI for **high viscosity white mineral oils (ca. C_{22}-C_{60})** (see P100(H) in **Table 14-5**) used as food additives was established by the EFSA Panel on Food Additives and Nutrient Sources added to Food

[4] "This temporary ADI is based on a 90 day study. A pending 2-year chronic study on P70(H) oil, which includes a satellite group dosed for 1 year only and then left untreated for a further year will provide information on whether or not the very limited accumulation observed with these oils in the 90-day studies would give rise to any toxicity if administration was continued for a longer period and information on the reversibility of any effects observed. Until these results are available, a safety factor of 500 (instead of the standard factor of 100) has been applied.

(ANS Panel) in 2009. The new ADI is based on the results of a 2-year chronic rat study and is in the same order of magnitude as the ADI initially established by FAO/WHO/JECFA at its 44th meeting in 1995.

It established an ADI of 12 mg/kg b.w. based on a NOAEL of 1 200 mg/ kg bw/day in a 2-year chronic study in rats (highest dose tested).

The ANS Panel concluded that the same ADI could have been potentially applicable also to **medium and low viscosity mineral oil class I**, but acknowledged that this class was not covered by the terms of reference of the European Commission (EFSA, 2009 in EFSA 2012) (EFSA 2012, p.29).

2012

A re-evaluation of white mineral oils and waxes was carried out by both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (76th FAO/WHO JECFA meeting, 2012) and the EFSA CONTAM Panel (EFSA 2012) because new information about the lack of toxicological relevance for humans of the effects in mesenteric lymph nodes (MLN) observed in the (sub)chronic studies in Fischer 344 rats and new toxicokinetics studies became available. EFSA also conducted a dietary exposure assessment of Mineral Oil Hydrocarbons (MOH) **C_{10}-C_{50}**[5] in food (in 2009 it only focused on a limited range of hydrocarbons as outlined in **Table 14-5**, footnote a).

JECFA withdraw the temporary group ADIs of 0.01 for medium and low viscosity mineral oils class II and III because it was concluded that all mineral oil products except microcrystalline **waxes accumulated in tissues** in a dose and time-dependent manner. With the exception of the ca. C_{25}-C_{34} the mineral oil accumulation in tissues caused inflammatory effects indicative of a reaction to the presence of a foreign body. Such effects included focal histiocytosis, increased liver weight, lymph nodes, spleen and kidneys, granulomas or microgranulomas in the liver, haematological changes typical of a mild chronic inflammation reaction and biochemical changes associated with mild hepatic damage.

EFSA concluded that no ADI could be established for any of the MOSH-fractions (EFSA 2012, page 7, paragraph 2) and none of the existing ADIs was considered adequate for the risk characterisation of the range of MOH present in the background exposure of humans (C_{12}-C_{40} with centres ranging from C_{18}-C_{34} in different foods).

In the absence of toxicological studies on MOSH mixtures typical of those humans are exposed to, the CONTAM Panel considered it inappropriate to establish a health based guidance value for MOSH. Given the deficiencies in the toxicity data base, **the CONTAM Panel decided to use an MOE approach**.

For the **background exposure scenario** the CONTAM Panel selected a NOAEL of 19 mg/kg bw/day for formation of microgranulomas in the liver from the low and intermediate melting point waxes (the most potent MOSH grades) as a reference point (RP). For the high exposure scenarios the MOSH contamination is due to the use as release agents for bread and rolls and for spraying of grains. Here the range of MOSH grades is different than that for the background exposure. The CONTAM Panel used 45 mg/kg b.w. per day, as an RP.

[5] Hydrocarbons with $<C_{10}$ are likely not relevant for food, because of their high volatility. Hydrocarbons with C_{16}-C_{35} may accumulate in different tissues due to low biotransformation (EFSA 2012, p.5 paragraph 7). Hydrocarbons with $>C_{35}$ are not absorbed (absorption of alkanes decreases with increasing carbon number until above $>C_{35}$ when it is negligible) (EFSA 2012, p.5 paragraph 7).

- A revision of existing ADIs for microcrystalline waxes, high-viscosity mineral oils and medium- and low-viscosity class I mineral oils was considered to be of low priority.
- Hydrocarbons with $<C_{10}$ were considered not relevant for food contamination given their high volatility, whereas hydrocarbons with $>C_{50}$ are unlikely to be systemically absorbed following ingestion (EFSA 2012, p.78).
- For the microcrystalline waxes and ca. C_{34} mineral oils, an ADI of 20 mg/kg bw was based on NOELs at the highest dose tested in a 90 day study in Fischer rats (EFSA 2012, pp.27-28). This is in agreement with SCF (1995).

Table 14-5: Comparison of ADIs established by SCF (1995), FAO/WHO (2002) and EFSA (2009 and 2012) for mineral and synthetic hydrocarbon oils and waxes used as food additives, in food processing and in food packaging materials.

(Source: EFSA 2012, p.133, table 23; EFSA 2012, p.28, table 1)

		SCF (1995)				FAO/WHO (2002)				EFSA (2009)				EFSA (2012)			
	Mineral Hydrocarbons Classification[a]	ADI[b] (mg/kg bw/day)	NOAEL (mg/kg bw/day)	UF*	Comments	ADI[b] (mg/kg bw/day)	NOAEL (mg/kg bw/day)	UF*	Comments	ADI[b] (mg/kg bw/day)	NOAEL (mg/kg bw/day)	UF*	Comments	ADI[b] (mg/kg bw/day)	NOAEL (mg/kg bw/day)	Endpoint	Comments
Oils	High viscosity P100(H)	0-4[c]	1 951	500	90-day NOAEL	0-20	1951	100	90-day NOAEL	12	1200	100	2-year NOAEL	ADIs withdrawn Mineral oil can accumulate in tissues and cause microgranulomas in the liver, which is considered as the most sensitive endpoint of toxicity for mineral ail products.			
	Medium and low viscosity, class I P70(H)					0-10[d]	1200	100	2-year NOAEL	(12)[f]	(1200)	(100)	2-year NOAEL				
	Medium and low viscosity, class II N70(H)	No ADIs established				0-0.01[c,e] withdrawn in 2012	2	200	90-day NOAEL	not investigated							
	Medium and low viscosity, class III P15(H), N15(H)	No ADIs established				0-0.01[c,e] withdrawn in 2012	2	200	90-day NOAEL								
Waxes	Microcrystalline wax, high melting point wax	0-20	1 951	n.a.	90-day NOAEL	0-20	1951	100	90-day NOAEL								
	Low and inter-mediate melting point waxes					ADI Withdrawn								–[b]	19/45[g]	Liver micro-granuloma	90 days-study

[a] Classification of mineral hydrocarbons (all hydrotreated by catalytic hydrogenation): **P100(H)** oil, crude = paraffinic fraction (alkanes), viscosity (40 °C) 100 mm^2/s; **P70(H)** oil, crude = paraffinic fraction (alkanes), viscosity (40 °C) 70 mm^2/s; **N70(H)** oil, crude = naphtenic fraction (cycloalkanes), viscosity (40 °C) 70 mm^2/s; **P15(H)** oil, crude = paraffinic fraction (alkanes), viscosity (40 °C) 15 mm^2/s; **N15(H)** oil, crude = naphtenic fraction (cycloalkanes), viscosity (40 °C) 15 mm^2/s.

[b] EFSA (2012) concluded that no ADI for MOSH could be established and that none of the existing ADIs were adequate for the risk characterisation of the mineral oil hydrocarbons humans are typically exposed to. Refer to the main text for more information.

[c] Temporary group ADI established at the 59th FAO/WHO JECFA (2002) but withdrawn at the 76th FAO/WHO JECFA (2012) because these mineral oils accumulated in tissues.

[d] ADI based on increased incidence of pigmented macrophages in male rats, not relevant for humans.

[e] ADI based on increased incidence of histiocysis in the mesenteric lymph node.

[f] EFSA (2009) concluded that the same ADI could have been potentially applicable also to medium and low viscosity mineral oil class I, but did not since this was not covered by the terms of reference.

[g] A NOAEL of 19 mg/kg bw/day was selected in the background exposure scenario for the low and intermediate melting point waxes, while a reference point of 45 mg/kg bw/day, corresponding to the highest NOAEL below the lowest LOAEL, was used in the high exposure scenarios for higher MOSH grades.

* UF: Uncertainty factor

14.5 Exposition

14.5.1 Äussere Exposition

14.5.1.1 Exposure pathways for aliphatic compounds

Aliphatic compounds are ubiquitous but the only quantitative data on human hydrocarbon exposure comes from dietary exposure assessments. As petroleum derivatives, aliphatic compounds are ubiquitous, and it is nearly impossible to avoid exposure, whether it is through accidents, as managed releases, or as unintended by-products of industrial, commercial or private actions, e.g. via environmental exposure to contaminated air (e.g. gazoline fuels at the pump); soil (spilled motor oil, asphalt or tires debris); or in a residential context via the use of solvents or application of pesticides containing petroleum products as carriers.

Aliphatic compounds can also contaminate the foodchain, e.g. crop or grain contamination by lubricating oil from harvest machines engines is possible. However, contamination of foodstuffs is more likely to occur via food processing and packaging (e.g. migration of food contact material, intended additives), which accounts for the major food-derived TPH exposure. It is assumed that TPH uptake via the environment and drinking water are minor exposure pathways, and uptake via plant roots would only occur to a very limited extent due to the envrionmental fate of TPH.

14.5.1.2 Environmental exposures to alipahtic compounds and other TPH fractions

Humans are exposed only to fractions of TPH because the environmental fate differs by fraction. Since TPH undergo significant changes in the environment over time in their concentration and composition, typical exposures to TPH will tend to be to fractions of the product (i.e. to the more volatile or more soluble compounds) rather than to the whole petroleum product. For example, bulk oil flow after a spill of gazoline or motor oil in soil is affected by numerous product-specific and site-specific factors. As a consequence, product distribution in the subsurface soil can be quite complex. Petroleum products and mineral oils >C10 typically migrate through soil along with the bulk oil flow, and a small amount of the product is retained by soil particles as “residual saturation.” Depending upon the persistence of the bulk oil, residual saturation can potentially reside in the soil for years (ATSDR 1999, p.69).

Upon release to the environment, e.g. a spill of gazoline or motor oil in soil, the most volatile components of the lighter fraction will be likely and rapidly lost through volatilization to the air, leaving longer chain / branched aliphatics at the site or migrate downwards to the groundwater. The lower density fraction will float at the soil-water interface and the higher density fraction will penetrate the aquifer. Downward migration ceases when the product is retained by soil particles as “residual saturation” or when an impermeable surface is encountered. When the amount of product released to the environment is small relative to the volume of available soil, all of the product is converted to residual saturation and downward migration of the bulk product usually ceases prior to affecting groundwater resources (ATSDR 1999, pp.69-70).

However, for most spill or release sites, there is generally a lack of detailed information about the aliphatic fraction in the environment because the composition of the various petroeum derived products may vary significantly, depending on the TPH composition, the weathering of the product over time, and differential movements of the components fraction in the environment (ATSDR 1999, pp.69-70). Hydrodynamic, abiotic, and biotic processes contribute to change the release, fractionation and chemical character of TPH, but environmental factors also contribute, such as air and soil temperature, humidity, wind speed, soil type, moisture content, oil composition, solar radiation, and thickness of the oil layer. For example, high summer temperatures enhance volatilization, particularly when soils begin to dry out (ATSDR 1999, pp. 68-69).

14.5.1.3 Dietary exposure

14.5.1.3.1 Food processing and packaging as major exposure pathways for TPH

It is assumed that uptake via plant roots would only occur to a very limited extent due to the envrionmental fate of TPH. Contamination of foodstuffs is more likely to occur via food processing and packaging (e.g. migration of food contact material, use of intented additives).

Aliphatic compounds can occur as contaminants through the foodchain and in nearly all foodstuffs, but also as intended additives, through numerous sources: food packaging materials, additives in the manufacture of plastics, wax paper and board, jute or sisal bags, lubricants for can manufacture and wax coating directly applied, food additives, processing aids, release agents for bakery ware and sugar products, and oils for surface treatment of foods, etc (EFSA 2012, p.4, Summary).

14.5.1.3.2 Human dietary exposure assessment of mineral oil hydrocarbons

The only quantitative data on human hydrocarbon exposure comes from dietary exposure assessments. In 2012, EFSA assessed the risks related to the occurrence of mineral oil saturated hydrocarbons (MOSH) in the C_{10}-C_{50} range in food, as a result of contamination and from various intentional uses in food production. Hydrocarbons with $<C_{10}$ were considered not relevant for food contamination given their high volatility, whereas hydrocarbons with $>C_{50}$ are unlikely to be systemically absorbed following ingestion (EFSA 2012, p.78).

EFSA investigated the chronic background dietary exposure to MOSH in Europe, plus three additional exposure scenarios to account for specific dietary exposure of specific sub-populations, for four different age classes, including toddlers (EFSA 2012, pp.66-67).

A chronic background dietary exposure to MOSH in Europe was established (scenario 1). Additional exposure on top of the background was calculated for specific consumers of "Bread and rolls" (scenario 2) or "Grains for human consumption" (scenario 3) with high levels of MOSH originating from release- or spraying agents.

Although it would not be appropriate to include such discrete high values in the background occurrence, for calculation of chronic exposure, it cannot be excluded that some groups of consumers (buying always from the same source or having brand loyalty) are exposed on a regular basis to food with such levels. Scenario 4 was developed for exclusively breast-fed infants (EFSA 2012, pp.66-67). Exposure data for toddlers are listed in **Table 14-6** below.

Table 14-6: Three dietary MOSH (C_{10}-C_{50}) exposure scenarios for toddlers (mg/kg bw/day) in Europe (EFSA 2012).

The table aggregates EFSA findings for the category "toddlers" as presented in EFSA 2012, Table 9, p.68 (Scenario 1); Table 12, p.73 (Scenario 2); Table 13, p.73 (Scenario 3).

Scenario no. :	1	2	3
Scenario name:	Background	Bread and rolls [b]	Grains for humans [b]
Average exposure (mg/kg b.w. per day) across national dietary surveys			
Min	0.083 - 0.087[a]	1.1	0.24
Median	0.11	2.3	0.44
Max	0.19	3.1	1.3
95th percentile exposure (mg/kg b.w. per day) across national dietary surveys			
Min	0.18	3.7	1.9
Median	0.22	4.7	2.1
Max	0.25 - 0.26[a]	5.8	3.1

[a] Values are lower-bound and upper-bound values in mg MOSH/kg bw/day. Lower-bound values = values below the LOD and values between the LOD and LOQ which were set to zero and to LOD, respectively. Upper-bound values: values below LOD and values between the LOD and LOQ, which were set to LOD or LOQ value, respectively.

[b] Scenario 1 is a background chronic exposure scenario (P50 and P95) based on mean food occurrence data; Scenario 2 represents an additional chronic exposure for specific consumers of bread with high levels of MOSH; Scenario 3 represents an additional chronic exposure for specific consumers of grains with high levels of MOSH.

14.5.1.3.3 EFSA's summary conclusions of the exposure assessment to MOSH for toddlers (1-3 yrs)

The exposure to MOSH (min LB and max UB across national dietary surveys) for the category "toddlers" ranged from 0.083 to 0.19 mg/kg bw/day and from 0.18 to 0.26 mg/kg bw/day for mean and high consumption (P95), respectively. These values are the highest among the different age classes, due to the ratio between body weight and amount of food consumed (EFSA 2012, p.68).

In comparison, the dietary exposure to MOSH ranges in the general population between approximately 0.03 and 0.3 mg/kg bw/day and is higher in younger consumers (3-10 yrs of age) than in adults and older age classes. With increasing age, the exposure per kg bw considerably decreases. This is, at least partly, explained by the lower intake of food per kg b.w. per day in higher age classes (EFSA 2012, Summary, p.5).

Special cases where identified, when "bread and rolls" or "grains for human consumption" with high levels of MOSH, due to the use of food grade MOSH as release agents or spraying agents, are consumed on a regular basis. In these cases, the additional exposure to MOSH was up to 5.8 mg/kg bw/day for bread and up to 3.1 mg/kg bw/day for grains. In contrast to the background exposure, the additional exposure is related to virtually aromatic-free MOH.

14.5.1.3.4 Background exposure to MOSH via food is of potential concern

EFSA concluded that no ADI for MOSH could be established for food grad mineral hydrocarbons (EFSA 2012, p.7, paragraph 2) and none of the existing ADIs was considered adequate for the risk characterisation of the range of MOH present in the background exposure of humans (C_{12}-C_{40} with centres ranging from C_{18}-C_{34} in different foods). In the absence of toxicological studies on MOSH

mixtures typical of those humans are exposed to, the CONTAM Panel considered it inappropriate to establish a health based guidance value for MOSH. Given the deficiencies in the toxicity data base, the CONTAM Panel decided to use an MOE approach. The results are listed in table x.

EFSA used two different reference points for their MOE. For the background scenario they used a NOAEL 19 mg/kg bw/day from a 90 day rat and compared it to dietary exposure to derive the MOE. For the bread and rolls scenario EFSA used a NOAEL 45 mg/kg bw/day and compared it to dietary exposure to derive the MOE. In 2012 EFSA calculated Margins of Exposure (MOEs) for four different exposure scenarios. The different scenarios are listed in **Table 14-7**, the calculated MOEs are listed in **Table 14-8**.

Table 14-7: Four dietary MOSH (C_{10}-C_{50}) exposure scenarios according to EFSA (EFSA 2012).

Scenario no.: **Scenario name:**	**Description**
Scenario 1 **Background**	Chronic background dietary exposure to MOSH in Europe
Scenario 2 **"Bread and rolls"**	Additional exposure on top of the background for specific consumers of "Bread and rolls" with high levels of MOSH originating from release- or spraying agents.
Scenario 3 **"Grains for human consumption"**	Additional exposure on top of the background for specific consumers of "Grains for human consumption" with high levels of MOSH originating from release- or spraying agents.
Scenario 3 **Exclusively breast-fed infants**	Exclusive exposure from breast-feeding

Table 14-8: MOEs calculated for three dietary MOSH (C_{10}-C_{50}) exposure scenarios for toddlers in Europe (EFSA 2012).

Please note that this table aggregates EFSA 2012 findings for the category „Toddlers" as presented in Table 24, p.134 (Scenario 1); Table 25, p.135 (Scenario 2); Table 26, p.136 (Scenario 3).

Scenario no. : Scenario name:	1 Background	2 Bread and rolls	3 Grains for humans
Average (min LB – max UB) based on a NOAEL of 19 mg/kg bw/day[a]			
Min	230 - 100	41 - 15	190 - 35
95th percentile exposure (min LB – max UB) based on a NOAEL of 45 mg/kg bw/day[a]			
Min	110 - 73	12 - 7.8	24 -15

[a] Reason for the different reference points in the average and high exposure scenarios: As a RP for the background exposure scenario 1, the panel selected a NOAEL of 19 mg/kg bw/day for formation of microgranulomas in the liver from the most potent MOSH grades (the low and intermediate melting point waxes). The range of MOSH grades involved in the high exposure scenarios 2 and 3 (MOSH used as release agents for bread and rolls and for spraying of grains) is more restricted than that for the background exposure (white oils and not waxes are used in this case) and therefore the CONTAM Panel used the highest NOAEL below the lowest LOAEL (lowest-observed-adverse-effect level) for these grades of MOSH, 45 mg/ kg bw/day, as an RP.

The CONTAM Panel took into account that the basis for the RPs was 90-day studies and that some of these compounds might have very long elimination half lives in humans, when interpreting the obtained MOEs.

⇒ **Consequently, the CONTAM Panel considers the MOEs obtained for the chronic background exposure to MOSH via food to be low and therefore this exposure is of potential concern. Of particular concern is the use of white oils as release agents for bread and to some extent for spraying of grains (EFSA 2012, p.136).**

14.5.2 Innere Exposition

For the aliphatics, SCAHT applies the TIER 3-strategy as outlined in the methodology section

There are basically no information on oral bioavailability from dietary sources in humans; information in experimental animals is limited but shows that bioavailability decreases with increasing carbon number and branching (section 14.5.2.1), and that it can be as high as 90% or the C_{14}-C_{18} mineral hydrocarbons. Therefore, SCAHT uses a conservative 100% oral absorption value from aliphatics in food.

There are no studies in humans (section 14.5.2.2) or in experimental animals (section 14.5.2.3) that have investigated the impact of soil on the oral bioavailability of aliphatic compounds/mineral hydrocarbons. All these data gaps support a conservative approach to the RAF and the use of a 100% RAF value (section 12.5.2.4). This is also further supported by the fact that information derived from in vitro bioaccessibility studies is quasi inexistant (section 12.5.2.5).

In conclusion, considering a conservative dietary oral bioavailability of 100% in humans and a RAF of 100% to account for the large data gaps, SCAHT uses an absolute oral bioavailability from soil of 100% for its risk assessment.

14.5.2.1 Oral bioavailability from food and/or water from dietary studies

Typically, bioavailability decreases with increasing carbon number and branching. Studies in rats show that oral absorption of aliphatic hydrocarbons (such as *n*-alkanes, isoparaffins, and naphthenes) is inversely related to molecular weight (MW), ranging from complete absorption at the lower end of the molecular weight range to about 60% for C_{14} hydrocarbons, 5% for C_{28} hydrocarbons, and essentially no absorption for aliphatic hydrocarbons with >C_{32} carbons (ATSDR 1999, pp.147-149). Similarly, EFSA (2012) reported that for n-alkanes and cycloalkanes the absorption varies from 90 % for C_{14}-C_{18} to 25 % for C_{26}-C_{29}. Limited data suggest that cycloalkanes are absorbed at similar levels as n-alkanes of comparable molecular weight, whereas absorption of branched alkanes is slightly less (EFSA 2012, Summary, p.5, chapter 7.1.5, p.91).

No oral data were located for humans. Inhalation data are usually available in animals and sometimes in humans. In human volunteers about 28% of inhaled n-Hexane was taken up by the lungs. Alveolar retention is about 25% of the inhaled dose of n-hexane and the final absorption is 15%-17% in relation to the total respiratory uptake (HSDB 2015).

Due to low biotransformation rates, in particular for some branched- and cyclo-alkanes, aliphatic hydrocarbons from C_{16}-C_{35} may accumulate in several tissues including body fat, lymph nodes, spleen and liver (ATSDR 1999, pp.147-149; EFSA 2012, Summary, p.5, chapter 7.1.5, p.91). However, the SCAHT assumes that the additional burden for aliphatics from soil ingestion during childhood is negligible, particularly because exposure from soil is extremely low compared to dietary exposure.

⇒ **Based on these limited data, and considering the potential broad range in absorption values between short and long chain alkanes vs branched or cyclic compounds, SCAHT assumes a conservative 100% value for oral bioavailability from dietary sources.**

14.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

No human data could be located in relation to oral absorption of TPH- or aliphatics-contaminated soil.

14.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

No experimental *in vivo* data could be located in relation to oral absorption of TPH- or aliphatics-contaminated soil.

14.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of aliphatics in soil compared to food or water, is to use the RAF approach proposed by the USEPA, as outlined in the Methodology section. A default medium-specific RAF value of 0.91 (91%) has been proposed for n-hexane, nonane and eicosane as representative compounds of the TPH fraction by the US Massachussetts State Department of Environmental Protection (MASS DEP 1992) (as cited by NRC 2003, Table 2.1 pp.69-70) (see **Table 14-9**). However, the justification for this value is not made explicit in the MASS DEP report.

⇒ **In the absence of any human or *in vivo* animal soil ingestion studies, SCAHT uses a conservative RAF of 100%. This is further supported by the lack of in vitro bioaccessibility information (see section 12.5.2.5).**

⇒ **In conclusion, considering a conservative dietary oral bioavailability of 100% in humans and a RAF of 100% to account for the large gaps in the underlying database, SCAHT uses an absolute oral bioavailability from soil of 100% for its risk assessment.**

Table 14-9: Absolute and relative bioavailability for aliphatic compounds

(Source: NRC 2003, pp.69-70, Table 2-1)

TPH	Inhalation bioavailability	Oral bioavailability[b]	Absolute dermal Bioavailability from soil[c]	Relative Oral Bioavailability from soil[d]	Absolute oral bioavailability from soil[e]
n-Hexane (C_6)	20%[a]	suggested default 100%	50%	91%	suggested default 100%
Nonane (C_9)	n.a.		20%		
Eicosane(C_{20})	n.a.		10%		

[a] Sources: ATSDR 1999; HSDB 2015.

[b] No studies were located that specifically addressed absorption of *these three susbtances* after oral exposure in humans or animals. inference from ATSDR 1999, pp.147-149, would suggest 60% or more for n-hexane and nonane, but smaller for eicosane. Given the lack of data, SCAHT suggests a default 100% oral bioavailability.

[c] Absolute bioavailability of the compound in soil via the dermal route (NRC 2003, pp. 69-70, table 2-1).

[d] Relative absorption factor, equals the relative bioavailability of the compound (i.e. in soil vs in the medium used in the toxicity study) (NRC 2003, pp.69-70, table 2-1). MASS DEP (1992) is cited by NRC (2003) as primary source, but justification for these RAFs was not found in the report.

[e] The absolute oral bioavailability from soil is calculated based on the oral bioavailability adjusted by the relative oral absorption factor to account for reduced oral bioavailabilty from soil. SCAHT proposes to use a default value of 100% as a conservative estimate given the present uncertainties.

14.5.2.5 Summary of the in vitro bioaccessibility information

Bioaccessibility is influenced by environmental fate. The smaller molecular weight hydrocarbons (the light VOCs aliphatic fraction <C_{11}), which tend to have relatively high vapor pressures and/or water solubilities, and lower sorption potential, tend to volatilize into the air, migrate readily through soil, dissolve into infiltrating rainwater or groundwater and migrate away from the release area, and biodegrade.

- The VOC fraction will be highly dependent on the exposure of the soil to the atmosphere, the contact time between the contaminant and the soil, the soil organic matter content and aliphatic hydrocarbons concentration (ATSDR 1999, pp. 72-73; USEPA 2006). The degree of volatilization of VOCs from soils varies greatly between freshly added compounds and aged residues (NEPI 2000, p.50; Farrell and Reinhard, 1994). The fractions that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (i.e the desorption resistant fraction). Since volatilization occurs on a time scale of minutes to hours, therefore inhalation of released vapors may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil. However, given our soil ingestion scenario of a child playing in the private garden this is not a relevant exposure scenario.

Petroleum products and mineral oils in the intermediate carbon number range (*SCAHT notes*: the C_{11}-C_{18} range) typically migrate through soil along with the bulk oil flow, and a small amount of the product is retained by soil particles as “residual saturation”. Depending upon the persistence of the bulk oil, residual saturation can potentially reside in the soil for years (ATSDR 1999, p.69).

- Volatilization of the lighter fractions (<C_{18}) may happen, but to a much lower degree (ATSDR 1999, p.65). Serrano et al. (2008) have determined that after a diesel fuel spill in an agricultural soil, aliphatic hydrocarbons remained largely in the top surface layer (0-10 cm), and that volatilization, which took place shortly afterwards, was mainly responsible for their decrease in soil.

The larger molecular weight constituents (e.g. longer chain / branched aliphatics such as in motor oil, fuel, mineral oil) tend to sorb to soil or sediment, due to their relatively low water solubility and volatility, high octanol-water partition coefficients and high sorption capacity to organic matter, so that they are usually more persistent and tend to remain relatively immobile at the site of release (ATSDR 1999, pp.68, 89, 72-73; USEPA 2006). Bossert and Bartha (1986) indicated that *n*-alkanes >C_{18} exhibit no substantial volatilization at ambient temperatures (ATSDR 1999, p.65). Aliphatics can also remain sorbed on foliar surfaces (e.g. when present as carriers in plants protection products formulations to be applied in the garden).

The gastrointestinal solubility of TPH is profoundly influenced by the digestion state/fasting state, the type, and the concentration of petroleum hydrocarbons present and modified by other site-specific conditions such as the relative abundance of soil organic content.

In vitro bioaccessibility studies with aliphatic compounds or specific TPH fractions are quasi inexistant. Holman et al (2002) have evaluated the bioaccessibility of petroleum hydrocarbon residues in nine weathered soils in order to assess the human health risk from soil ingestion, based on an *in vitro* physiologically based small intestine extraction model (assuming that most solubilization of soil-bound TPH occurs in the upper small intestine because of the “detergency” characteristics of the bile salts from the gallbladder). Holman et al (2002) indicate that an average of 12% (2-31%) of the TPH residues in these soils can be solubilized in human gastrointestinal tract environments. They further found that TPH residues from diesel-contaminated soils are more soluble in the gut than those from soils contaminated by crude oil.

14.6 Risikoabschätzung

14.6.1 Comparative hazard and exposure assessment

For the sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly, the Swiss Contaminated Sites Ordinance (CSO) sets a concentration value for remediation of 5 mg/kg soil for C_5-C_{10} aliphatic hydrocarbons[6] and a concentration value of 500 mg/kg soil for the C_{11}-C_{40} aliphatic hydrocarbons. This translates into a daily exposure from incidental ingestion of 250 mg soil of 0.1 µg/kg/day for C_5-C_{10} and 10 µg/kg/day for C_{11}-C_{40} for a 12.5 kg child, assuming 100% absolute oral bioavailability from soil (column 3, **Table 14-10**).

The **additional health risk from soil ingestion** of aliphatic compounds is expected to be low because compared to background exposure the additional exposure is low and the hazard potential from oral ingestion of aliphatics is low.

- Based on the existing threshold levels in the CSO the additional external exposure from soil ingestion is low in absolute terms, i.e. 0.1 µg/kg/day for C_5-C_{10} and 10 µg/kg/day for C_{11}-C_{40} (column 3, **Table 14-10**), respectively.
- A comparison with the most appropriate TDIs derived by the TPHCWG (column 4, **Table 14-8**) reveals that soil ingestion contributes 0.002 to 10% of the respective TDIs (column 6, **Table 14-10**).
- For the C_{11}-C_{40} fraction expected exposure is also low in comparison to dietary exposure. SCAHT assumes that Swiss are high bread consumers. Therefore a combined background exposure scenario (scenario 1) and the bread and rolls scenario (scenario 2) listed in **Table 14-6** represents a realistic worst case dietary exposure scenario for Switzerland (column 4, **Table 14-10**). The additional exposure from soil ingestion accounts for max. 0.842% of the dietary exposure (column 7, **Table 14-10**) and is therefore of low relevance.
- For the C_5-C_{10} fraction, no such comparison can be made. The lighter aliphatic fractions are not considered relevant for dietary exposure assessment because of their high volatility (food grade mineral oil hydrocarbons are in the C_{10}-C_{50} range). However, a comparison with the most appropriate TDIs derived by the TPHCWG (column 4, **Table 14-10**) reveals that soil ingestion contributes to 0.002% of the respective TDIs (column 6, **Table 14-10**).
- Oral exposure to the lighter aliphatic fractions is expected to be negligible because they will easily volatilize into the air. The remainder will readily migrate through the soil and biodegrade. As volatilization occurs within minutes to hours, it only represents a potential significant exposure pathway to persons in the immediate vicinity of highly contaminated freshly excavated soil. For our soil ingestion scenario of a child playing in the private garden this is not a relevant exposure scenario.

  Aliphatics in the intermediate carbon number range (*SCAHT note*: the C_{11}-C_{18} range) typically migrate through soil and only a small amount of the product is retained in the top surface layer, which is relevant for the SCAHT risk assessment scenario.

  The longer chain/branched aliphatics tend to sorb to soil or sediment, and remain relatively immobile at the site of release but oral absorption is expected to decrease with molecular weight and branching.

[6] Area of the FID-chromatogram between n-pentane and n-decane, multiplied by the response factor of n-hexane, minus the sum of the BTEX.

- EFSA is concerned about the low biotransformation rates, in particular for some branched- and cyclo-alkanes. Aliphatic hydrocarbons from C_{16}-C_{35} may accumulate in several tissues but the SCAHT assumes that the **additional burden** from soil ingestion during childhood is negligible, particularly because exposure from soil is extremely low compared to dietary exposure (<1%).

Table 14-10: Comparison of exposure from incidental soil ingestion

Fraktion AltV	**Fraktion** TPHCWG	**Exposition via Boden AltV**[a] µg /kg KG/Tag	**TDI (TPHCWG)**[b] µg /kg KG/Tag	**Diätische Exposition**[c] µg /kg KG/Tag	**Exposition via Boden AltV** in % TDI	**Exposition via Boden** in % Diät. Exp.
$C_5 – C_{10}$	$C_6 – C_8$	0.1 für C5-C10	5000	Keine Angaben[d]	0.002 des TDI C6 – C8	
$C_{11} – C_{40}$	$C_9 – C_{16}$	0.1 für C5-C10 10 für C11-C40	100	1187– 3880[c] für C11-C40	0.1 des TDI C9 – C16 10 des TDI C9 – C16	0.003 – 0.008 0.258 – 0.842
	$C_{17} – C_{34}$	10 für C11-C40	2000	1187– 3880[c] für C11-C40	0.5 des TDI C17 – C34	0.258 – 0.842
	$C_{>34}$	10 für C11-C40	20000	1187– 3880[c] für C11-C40	0.05 des TDI >C34.	0.258 – 0.842

[a] Assuming daily ingestion of 250 mg soil, an time weighted average body weight of 12.5 kg and a bioaccessibility of soil derived hydrocarbons of 100%.

[b] data represent TPHCWG TDIs from table 14-6 which are sufficiently similar to the CSO-grouping and are therefore considered relevant for risk assessment. EFSA did not derive ADIs for food grade hydrocarbons because there is a lack of toxicological data on relevant mixtures (of food grade hydrocarbons).

[c] data represent the sums of scenario 1 and 2 in table 14-6.

[d] EFSA considers only C_{10}–C_{50} as food grade hydrocarbons relevant for dietary risk assessment. Most relevant are C_{12}-C_{40}.

Aliphatics compounds are not carcinogenic and have low oral toxicity. The major toxicological effects observed in animals are neurotoxicity and hepatotoxicity.

Hepatotoxicity

- MOSH mixtures with carbon number in the range C10-C13 caused moderate liver cell hypertrophy, and bioaccumulation of MOSH can lead to formation of microgranulomas in liver and mesenteric lymph nodes (MLN).
- The CONTAM Panel did not consider liver cell hypertrophy to be an adverse effect because it was not associated with pathological effects. Instead, hepatic microgranulomas were considered the critical effect because they have been associated with inflammation in rats.
- However, in humans exposed to MOSH, the microgranulomas observed in liver, spleen, lymph nodes and other organs, have not been associated with inflammatory reactions or other adverse consequences and are therefore considered of low toxicological relevance.
- Likewise microgranulomas in mesenteric lymph nodes are considered of low toxicological concern in humans and rats because they are not associated with an inflammatory response or necrosis, do not progress to adverse lesions and available studies did not show any effect on immune functions.

Neurotoxicity

- In general, acute (and reversible) neurotoxicity after inhalation of lighter chain aliphatic fractions is most the relevant toxicological endpoint for humans.

- However, under the SCAHT soil ingestion szenario inhalation from volatized aliphatics is expected to be of low relevance because volatilization occurs on a time scale of minutes to hours and inhalation of released vapors may only be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil.

14.6.2 Uncertainties related to this risk assessment

To estimate the potential health risk from incidental soil ingestion exposure, data have to be compared to existing health-based reference values and the overall background exposure. There are several challenges associated with this approach:

The grouping of aliphatics in the CSO does not match any grouping scheme for risk assessment

- The grouping of the aliphatics according to the Swiss Contaminated Sites Ordinance (CSO) is neither harmonized with the TPHCWG specification for environmental media for which TDIs have been derived nor is it aligned with the classification of food grade mineral hydrocarbons for which a human health risk assessment has been carried out on the basis of a MOE-approach.

Grouping schemes for human health risk assessment of the hydrocarbons are not harmonized

- TPHCWG and ATSDR generally agree that the TPH fractions can be defined by the physico-chemical properties of constituents assuming that fractions with similar physico-chemical properties have similar toxicological properties, though this is not always the case (ATSDR 1999, page 13, first paragraph). They also agree that in practice, when health effects data for petroleum products (mixtures) similar in composition to the defined fractions are not available, data for individual constituents could be used as surrogates, taking into account the potential for toxicologic interactions and for additive effects (ATSDR 1999, p.96).
- In contrast to TPHCWG and ATSDR, EFSA argues that products with the same physico-chemical specification may vary considerably in their composition, depending on the source of the oil and its processing (EFSA 2012, page 3, paragraph 4). It recommends that in the future MOSH (and MOAH), sub-classes should be distinguished based on molecular mass ranges and structure. Two sub-classes were identified based on molecular mass: MOSH up to n-C16 and MOSH from n-C16 to n-C35. Based on the MOSH structure, distinction should be made among n-alkanes, branched alkanes and cyclic alkanes. Additionally, hydrocarbons with structures similar to MOSH, such as poly alpha olefins and oligomeric polyolefins (POSH), should be distinguished from the MOSH (EFSA 2012, page 7, last paragraph).

There is the general lack of more appropriate data for chronic exposure from soil ingestion

- Many toxicological data are derived from inhalations studies and most data refer to subchronic rather than chronic studies.
- Identification and quantification of the individual compounds released to the environment as a consequence of a petroleum spill is difficult.
- Information characterizing the fate of the individual compounds in petroleum mixtures is lacking.

There is a lack of quantitative exposure data besides dietary exposure

- As petroleum derivatives, aliphatic compounds are ubiquitous, and it is nearly impossible to avoid exposure, whether it is through accidents, as managed releases, or as unintended by-

products of industrial, commercial or private actions, e.g. via environmental exposure to contaminated air (e.g. gazoline fuels at the pump), soil (spilled motor oil, asphalt or tires debris), foodstuffs (migration of food contact material, lubricating oil-contaminated grain from harvest machines engines) or drinking water.

- However, the only quantitative exposure data available are from dietary exposure assessment and we do not know what the actual contribution of dietary exposure to the total exposure might be.

14.6.3 SCAHT conclusion

Despite all these shortcomings the SCAHT assumes that a comparison of the incidental exposure from soil ingestion with realistic worst case dietary exposure data for Switzerland (combined dietary exposure from background exposure and bread and rolls consumption see Table 14-6) along with a comparison of TPHCWG derived TDIs provides suffcient information for a health risk assessment.

- Although EFSA concluded that no ADI for MOSH could be established for food grade mineral hydrocarbons (EFSA 2012, p.7, paragraph 2) and none of the existing ADIs was considered adequate for the risk characterisation of the range of MOH present in the background exposure of humans (C_{12}-C_{40} with centres ranging from C_{18}-C_{34} in different foods) the SCAHT uses the TPHCWG derived TDIs to evaluate soil clean up values.
- The TPHCWG derived TDIs were generally derived from exposure levels that were free of observable effects (i.e. NOAELs) in exposed animals (CCME 2008, chapter 3.6, p.3-42 ff) which was criticised by EFSA in 2012. However, in 2008, a review of the evidence on TPH has also been done by the Canadian Council of Ministers of the Environment (CCME) to develop soil quality guidelines for TPH; it was concluded that although various uncertainties remain with the Edwards et al. (1997) analysis, the toxicity reference values provided by the TPHCWG remain valid at the current time and represent the most reasonable published approach for addressing risk from petroleum hydrocarbons (CCME 2008, chapter 3.6, p.3-42 sq).
- The TPHCWG derived TDIs also better reflect the overall protection goal of the Swiss Contaminated Sites Ordinance (CSO) because they are concerned with site contamination and not food grade hydrocarbons. ADIs derived for food grade hydrocarbons refer to refined petroleum products in the form of hydrogenated products (saturated mineral hydrocarbons) only, but disregard potential site contamination with petroleum products containing C-C double and triple bounds.

⇒ **Based on its assessment and taking the current uncertainties into account, the SCAHT concludes that at these threshold values, incidental soil ingestion does not present a major additional health risk and therefore the current threshold values can be kept.**

14.7 Grenzwerte im internationalen Vergleich

Based on a review in the scientific and regulatory literature of national soil remediation regulations in Europe, USA and Canada (e.g. Carlon 2007; CCME 2003; City of Copenhagen 2011), it appears that there is a large heterogeneity between the remediation soil regulations or guidelines for aliphatic compounds across the 13 selected countries (refer to Appendix 1, **Table A1**). Most of these regulations specify the threshold values for "sensitive", "residential" or "garden" soil use.

- Six countries have provisions for aliphatic compounds (A, CAN, CH, CZ, D, I).
- For seven countries (B, E, F, NL, S, UK, USA) no soil remediation values for aliphatic compounds could be identified, but three out of those seven countries have values for mineral oil instead (F: 5000 (total hydrocarbons); NL: 5000 (unspecified); B: 1000 (unspecified).
- Four countries (E, S, UK, USA) appear to have no provisions for aliphatic compounds or mineral oil.

Country	**TPH-Fraktion $C_{<12}$**	**Grenzwert (mg/kg dm)**
CAN	C_6-C_{10}	15000
A	ca. C_5-C_{10}	500
I	$<C_{12}$	10
CH	**C_5-C_{10}**	**5**

Country	**TPH-Fraktion $C_{>10}$**	**Grenzwert (mg/kg dm)**
CAN	$>C_{10}$-C_{16} $>C_{16}$-C_{34} $>C_{34}$	8000 18000 25000
A	ca. $>C_{17}$ ca. C_9-C_{17}	1000 500
CH	**C_{11}-C_{40}**	**500**
D	C_{10} - C_{40}	500
CZ	*unspecified total nonpolar extractable substances*	500
I	$>C_{12}$	50

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ANHANG

Table A.1: International comparison of soil quality standards / soil clean up values for residential land use, modified from Provoost et al (2006, 2008)

Contaminant (mg/kg dm)	Austria[35]	Belgium[1]	Czech Republic[40]	Netherlands	Germany[2]	Italy[36]	France[38]	Spain[39]	Sweden[37]	UK[4,5]	Canada[31]	USA	Switzerland[25]
Inorganic compounds													
Antimony	5	-	-	15	-	10	100	6	-	-	20	27[55], 31[54]	50
Arsenic	50	110	70	55	50	20	37	30	15	20/20	12	19[54]	50
Cadmium	10	6	20	12	20	2	20	5.5	0.4	8[6]/30	10	78[54], 82[55]	20
Chromium total	250[3]	-	500[3]	-	400[3]	150	130[3]	-	-	-	64	-	-
Chromium III	-	300	-	180[56]	-	-	-	1000	120	130/200	-	110000[55]	-
Chromium VI	-	-	-	78[56]	-	2	-	10	5	-	0.4	210[55]	100
Copper	600	400	600	190	-	120	190	310	100	-	63	150[55], 3100[54]	1000[7]
Lead	500	700	300	530	400	100	400	60	80	450/450	140	400[54, 55]	1000[8]
Mercury	10	15	10	10	20	1	7	3	1	8/8	6.6[33]	3[55], 23[10, 54]	2[11]
Nickel	140	470	250	210	140	120	140	470	35	50/75	50	340[55], 1600[54]	1000
Silver	-	-	-	15[27]	-	-	-	-	-	-	-	390[54] 410[55]	500
Zinc	-	1000	2500	720	-	150	9000	650	350	-	200	23000[54],26000[55]	2000[9]
Organic compounds													
PAH	50	-[42]	280[14]	40[28]	10[30]	10[16]	-	-	0.3[20], 20[21]	-	-[34]	-[57]	100[12]
B[a]P	5	1.5	2	-	4	0.1	-	0.2	15	-	0.7	0.1[55] 0.2[54] 0.022-1[53] 0.015-300[57]	10
PCB	1[49]	0.9[43]	5[15]	1	0.8[29]	0.001[18]	-	0.08	0.02[19]	8[48]	1.3	0.2, 0.5[55,19]	1[13]
BTEX	6[50]	-[41]	-	-	-	-	-	-	-	-	-	-	500[24]
Benzene	-	0.5	0.8	1	-	0.1	2.5	1	0.06	0.33	0.5	2[54], 1.2[55]	1
Toluene	-	15	100	130	-	0.5	10	20	10	610	0.8	6300[54], 7500[55]	-
Ethylbenzene	-	5	50	50	-	0.5	50	30	12	350	1.2	7500[54], 7800[54]	-
Xylene(s)	-	15	30	25	-	0.5	10	100	15	720[47]	1	130[55], 12000[54]	-
Mineral oil	-	1000	-	5000	-	-	5000[45]	-	-	-	-	-	-
Hydrocarbons (C5-C40)	500 [51,52] 1000[52]	-	500[44]	-	500[46]	10[17] 50[17]	-	-	-	-	15000[32], 51000[32]	-	5[22] 500[23]

[1] Order of the Flemish Government of 6 March 1999 on the Flemish Regulation for soil remediation (from Carlon 2007)

[2] Bundes-Bodenschutz- und Altlastenverordnung vom 12. Juli 1999 (BBodSchV), Standards applicable as national legislation for 'wirkungspad Boden-Mensch'
[3] Only the value for total chromium is given, without indication of Cr (III) or Cr (VI)
[4] Residential area with vegetable garden
[5] Residential area without vegetable garden
[6] 1/2/8 mg/kg dm related to the soil clean-up standards at pH 6, 7, 8, respectively. The clean-up standard of 8 mg/kg dm was used in this comparison.
[7] 1000/4 related to the soil clean-up standard as total concentration and soluble concentration. The clean-up standard of 1000 mg/kg dm was used in this comparison.
[8] 1000/0.1 related to the soil clean-up standard as total concentration and soluble concentration. The clean-up standard of 1000 mg/kg dm was used in this comparison.
[9] 2000/5 related to the soil clean-up standard as total concentration and soluble concentration. The clean-up standard of 2000 mg/kg dm was used in this comparison.
[10] 23/6.1 describes the chlorinated mercury and organic-mercury. The clean-up standard of 23 mg/kg dm was used in this comparison.
[11] Newly introduced value 2014
[12] Sum of 16 EPA-PAK: Naphthalin, Acenaphthylen, Acenaphthen, Fluoren, Phenanthren, Anthracen, Fluoranthen, Pyren, Benz[a]anthracen, Chrysen, Benzo[a]pyren, Benzo[b]fluoranthen, Benzo[k]fluoranthen, Dibenz[a,h]anthracen, Benzo[g,h,i]perylen, Indeno[1,2,3-c,d]pyren
[13] Sum 6 PCB Congeners x 4.3: Nr. 28, 52, 101, 138, 153, 180
[14] Clean up values are mentioned for 12 individual PAHs: anthracene, benz[a]anthracene, benz[a]pyrene, benz[b]fluoranthene, benz[ghi]perylene, benz[k]fluoranthene, fluoranthene, phenanthrene, chrysene, indeno[1,2,3-cd]pyrene, naphtalene, pyrene. However, a total PAH value is only given for 9 of these PAHs (PAH9, without anthracene, naphtalene and benzo(b)fluoranthene).
[15] Sum PCB congeners 28, 52, 101, 118, 138, 153, 180.
[16] Sum of benz[a]anthracene, benz[a]pyrene, benz[b]fluoranthene, benz[k]fluoranthene, benz[ghi]perylene, chrysene, dibenzo[a]pyrene, dibenzo[a,h]anthracene, indeno[1,2,3-c,d]pyrene, pyrene
[17] Hydrocarbons C<12 (light) 10 mg/kg/ Hydrocarbons C>12 (heavy) 50mg/kg (from Carlon 2007, p.285)
[18] 0.06 was proposed in the revision of the law by National Institute of Health (ISS)
[19] PCB total (detailed congeners not given)
[20] Sum of carcinogenic PAH = benzo(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(a)pyrene, indeno(1,2,3-cd)pyrene and dibenzo(a,h)anthracene). PAHs carcionogenic vs PAH others.
[21] Sum of other PAH = naphthalene, acenapthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene and benzo(ghi)perylene)
[22] Sum aliphatische Kohlenwasserstoffe C5-C10 = sum C5- bis C10-KW: Fläche FID-Chromatogramm zwischen n-Pentan und n-Decan, multipliziert mit dem Response Faktor von n-Hexan, minus sum BTEX
[23] Sum aliphatische Kohlenwasserstoffe C11-C40
[24] Sum 6BTEX: Benzol, Toluol, Ethylbenzol, o-Xylol, m-Xylol, p-Xylol
[25] SR 814.680, Verordnung über die Sanierung von belasteten Standorten (Altlastenverordnung, AltlV) vom 26. August 1998 (Stand am 1. August 2012)
[26] HAP7 non défini pour les sols, utiliser les valeurs par substance: anthracene, benzo(a)anthracene, benzo(k)fluoranthene, chrysene, benzo(a)pyrene, fluoranthene, indeno(1,2,3-cd)pyrene, naphtalene. HAP7 non défini.
[27] No reliable value could be derived; the gven value is refered to by the Ministerial Circular as an Indicative Level for serious soil contamination
[28] Sum of 10 PAH: Naphthalene, Anthracene, Phenanthrene, Fluoranthene, Benz[a]anthracene, Chrysene, Benzo[a]pyren, Benzo[g,h,i]perylene, Benzo[k]fluoranthene, Indeno[1,2,3-c,d]pyrene. Individual vales are not specified
[29] Detailed 6 PCBs not specified; If total PCB is examined, the analysed levels have to be divided through 5

[30] Gemäss Bundes-Bodenschutz- und Altlastenverordnung vom 12. Juli 1999 (BBodSchV), Vorsorgewerte für organische Stoffe, for Humusgehalt > 8% in Boden, 16 EPA-PAK.

[31] Canadian Council of Ministers of the Environment (CCME), Environmental Guideline for Contaminated Site Remediation, November 2003, APPENDIX 5 , Table A7, p.33, Remediation Criteria for other Contaminants in soil.

[32] According to CCME 2003, Appendix 3, p.21, petroleum hydrocarbons – contaminated soil is assessed by four parameters (fractions F1-F4, according to specified ranges of equivalent carbon number; the fractions are further divided in subfractions). For residential soil ingestion,remediation criteria are the same for fine-grained or coarse-grained surface soils: 15000 (F1:C6-C10); 8000 (F2:>C10-C16); 18000 (F3:>C16-C34); 25000 (F4:>C34).

[33] Inorganic mercury

[34] Individual remediation criteria are given for the following individual PAHs: Benzo(*a*)anthracene, Benzo(*b*)fluoranthene, Benzo(*k*)fluoranthene, Benzo(*a*)pyrene, Dibenz(*a,h*)anthracene, Indeno(I,2,3-c,d)pyrene, Naphthalene, Phenanthrene, Pyrene.

[35] Intervention-Value for contaminated soils according to Austrian Standard S 2088-2 (2000-06-01), foreseeing uses for which a direct hazard from oral intake of contaminated topsoil (0-10 cm) cannot be excluded (e.g. residential areas, sport fields, playgrounds) (from Carlon 2007, Table 1, p. 245)

[36] Limit values for surface and subsurface soil according to residential and public use, (from Carlon 2007)

[37] Guideline values for soil for sensitive land use, as given in the Swedish EPA report 4639, (SEPA, 1996) (from Carlon 2007)

[38] VCl sol, usage sensible; valeurs francaises, allemandes et hollandaises

[39] Values of the General Reference Levels (GRL) for metals applicable to Catalonia, http://residus.gencat.cat/en/ambits_dactuacio/sols_contaminats/

[40] Trigger values, Methodical guideline of the Ministry of Environment, Section of ecological damage – criteria of soil and groundwater pollution (from Carlon 2007)

[41] A value is given for each individual B, T, E, X compound but not a single value for the BTEX sum...

[42] Values are given for each of the following PAH: naphtalene, benzo(a)pyrene, phenanthrene, fluoranthene, benzo(a)antracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(ghi)perylene, indeno(1,2,3-cd)pyrene, anthracene, fluorene, dibenz(a,h)anthracene, acenaphtene, acenaphtylene, pyrene; however no single value for the sum of the PAH is given.

[43] Order of the Brussels Capital Government concerning the values for soil and groundwater pollution above which a risk investigation has to be undertaken. Date 9/12/2004, Belgian law gazette 13/01/2005; value for residential areas (from Carlon 2007, p.264)

[44] Nonpolar extractable substances (total)

[45] Hydrocarbures totaux, VCl sol, usage sensible (valeurs hollandaises 1994) (from Carlon 2007, pp.274-275)

[46] Threshold values for depositing of soil in Hamburg, Deposit Klass 0, Hydrocarbons (C10 - C40) (from City of Copenhagen survey 2011, Table A5, p.30)

[47] Soil guidelines values for contaminated soils in London (residential land use): sum of o-xylene (250), m-xylene (240), p-xylene (230) (from City of Copenhagen 2011, p.34)

[48] Soil guidelines values for contaminated soils in London (residential land use): there are no provisions for the NDL-PCBs but only for the sum of the dioxins, furans and DL-PCBs (from City of Copenhagen 2011, p.34)

[49] PCB7 (from City of Copenhagen survey 2011, Table A14, p.40)

[50] Threshold values for soil that is being deposited in Vienna (from City of Copenhagen survey 2011, Table A14, p.40)

[51] Values for remediation of soil in Vienna, sum of hydrocarbon with a boiling point between 30-180 °C (from City of Copenhagen survey 2011, Table A15, p.40)

[52] Values for remediation of soil in Vienna; Hydrocarbon-index with a boiling point between 160-300 °C = 500 mg/kg; Hydrocarbon-index with a boiling point above 300 °C = 1000 mg/kg (from City of Copenhagen survey 2011, Table A15, p.40)

[53] Comparison of residential cleanup standards or goals for 6 US States (mg/kg soil): Connecticut (1), Delaware (0.09), Maryland (0.022), New Jersey (0.2), New York (1), Pennsylvania (0.57) (from Blauvelt RB, Sweet M. 2014. Interstate Comparison of Soil Remediation Standards among Six Mid-Atlantic States, USA. Journal of Environmental Protection, 2014, 5, 811-818).

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[56] Soil Remediation Circular 2009, Soil Intervention Values, Table 1, p. 16, http://www.esdat.com.au/Environmental%20Standards/Dutch/ENGELSE%20versie%20circulaire%20Bodemsanering%202009.pdf. These values are in line with the threshold values for soil remediation reported by the City of Amsterdam for the year 2011 (City of Copenhagen 2011, p.28, Table A1).

[57] Values can be found for individual non carcinogenic PAH in Jennings (2012a) and for individual carcinogenic PAH in Jennings (2012b).

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Addendum to

Risikobeurteilung von Bodenschadstoffen in Haus- und Familiengärten gemäss Anhang 3, Ziffer 2 AltlV für die menschliche Gesundheit

(Version: 24. Januar 2017; Chapter 12, BTEX)

SCAHT

Lothar Aicher

20. September 2018

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1 Executive summary

The Swiss Contaminated Sites Ordinance (CSO)[1] sets a clean up value for benzene at 1 mg/kg soil and for BTEX (mixtures of benzene (B), toluene (T), ethylbenzene (E) and (o-, m-, p-) xylenes (X)), at 500 mg/kg soil, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

In its previous report "Risikobeurteilung von Bodenschadstoffen in Haus- und Familiengärten gemäss Anhang 3, Ziffer 2 AltlV für die menschliche Gesundheit, SCAHT, Lothar Aicher, Nicolas Roth, 24. Januar 2017", SCAHT recommended to keep the current clean up value for benzene (B) but to drop the benzene-tolouene-ethylbenzene-xylene (BTEX) clean up value and to introduce new individual values for T, E and X.

It was the objective of this addendum report to identify individual soil clean up values for T, E and X following the same methodological principles outlined in the original report.

The SCAHT recommends individual soil clean up values of 4, 5 and 9 mg/kg soil for T, E and X respectively. The SCAHT derived these individual soil clean up values based on the most conservative health-based guidance values published by US EPA and/or WHO, applying the SCAHT standard exposure scenario, which assumes a chronic oral exposure of a 12.5 kg child to 250 mg contaminated soil per day and an oral bioavailability of the soil contaminant of 100%.

2 Hazard identification

As indicated in **Table 1,** not all individual mixture components show the same toxicological effects. Like many volatile organic compounds (VOC) all four compounds B, T, E and X are **neurotoxic,** and acute neurotoxicity is the most sensitive non-cancer toxicological endpoint. Neurotoxicity of B, T, E and X is a direct effect of the parent compound, and the effect is additive when mixing the individual compounds.

Only B and E are **carcinogenic** but both are generally considered not mutagenic (e.g. negative responses in most tests at doses showing no overt signs of toxicity). However, there are qualitative and quantitative differences in the carcinogenic profiles of B and E. While B is classified as a human carcinogen, E is classified as a possible human carcinogen. B is gentoxic and is considered to be a non-threshold carcinogen while E is not genotoxic which implies that a threshold mechanism for carcinogenicity might exist. The target organs for carcinogenicity are also different. Only B causes leukemia which can be considered a secondary effect following **hematoxicity and immunotoxicity**. B probably requires metabolic activation to exert its carcinogenic effects. E is not hematotoxic and immunotoxic and does not cause leukemia but other types of cancer including liver, kidney, testis and lung cancer. The mechansism of carcinogenicity of E is likely related to the parent compound and/or reactive metabolites. T and X are not hematotoxic and not carcinogenic.

In general, the **reproductive and developmental effects** of B, T, E and X are often incompletely characterized and studies are often inconclusive due to study limitations including small population size, absence of adequate study design (e.g no multigeneration studies) or concomitant exposure to other substances. However, there is suggestive evidence that B, T and possibly E but not X are reprotoxicants in animals. Most of this information has been derived from inhalation studies; those

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen (AltlV 1998).

positive effects were also confirmed by a limited number of oral studies. In humans, while occupational/epidemiological data are very limited and inconclusive for B and X, there is suggestive evidence for reprotoxic effects of T. No data are available for E. B, T, E and X are all developmental toxicants in animals. However, adverse effects on the developing fetus were only observed at high levels of exposure that are maternally toxic. In humans, it has been shown that the abuse of toluene during pregnancy at high dose can be toxic to the developing fetus; no data are available for E, and very limited or inconclusive evidence exist for B and X.

Table 1: Overview of toxicological endpoints for the individual BTEX components

Please note that: this overview does not consider mixture effects; the majority of data is derived from single substance inhalation studies; if not stated otherwise findings have been observed in humans.

	B	T	E	X
Neurotoxicity	+	+	+	+
Hematotoxicity	+	-	?	-
Immunotoxicity	+[1]	-	-	-
Carcinogenicity	+[1,2]	-	?[3] Possible human carcinogen	-
Genotoxicity	+[2]	-	?	-
Reprotoxicity	? Testicular effects - in vivo	?	? Testicular tumors, uterine and hormonal effects - in vivo	-
Developmental toxicity	+ Fetotox in vivo	+ Fetotox in vivo, humans	+ Fetotox in vivo	+ Fetotox in vivo
Liver	-	-	+ in vivo	+ in vivo
Kidney	-	+	+ in vivo	+ in vivo
Others	-	Irritation Respiratory tract	Irritation Respiratory tract , eyes	Irritation Respiratory tract , eyes, skin

\+ Relevance of toxicological effect for human health established
\- No toxicological effect reported
? Relevance of toxicological effect for human health is inconclusive
[1] Secondary to hematotoxicity
[2] In bone marrow cells and lymphocytes
[3] Not in bone marrow but in kidney (rat), testis (rat), lung (mice), liver (mice)

3 Mixture effects

Multiple metabolic pathways and mechanisms are involved in B, T, E and X toxicity. Metabolism of the four B, T, E, X components is dose-dependent and generally extensive at dose levels that do not saturate the first metabolic step of each compound, which involves CYP450-dependent mixed function oxidases, predominantly CYP2E1 (but also 2B1, 2B6, 1A2). There can also be competition for the available CYP450 sites amongst the parent compounds and their metabolites. Therefore, simultaneous exposure to a BTEX mixture can cause two or more components to compete for enzyme-mediated biotransformation, resulting in an inhibition of the metabolism of at least one of the parent chemicals

or its metabolites. As a consequence, the toxicological profile of a BTEX mixture can vary depending on the percentage content and mixing proportions of the mixture. The threshold for competitive metabolic interaction was estimated to be 20 ppm of each component in humans.

Because hematotoxicity, immunotoxicity and leukemia are benzene specific **no additive effects** are expected in BTEX mixtures. Likewise, carcinogenic effects other than leukemia are ethylbenzene-specific and no additive effects are expected. However, **inhibitory / less than additive effects** have been observed in BTEX mixtures. Toluene for example, decreases the hematotoxicity and carcinogenicity potential of benzene. This can be explained by metabolic saturation. When the individual compounds (here B and T) compete for the same metabolic enzymes, but the available number of CYP450 binding sites is insufficient to bind and metabolize all B and T components, this results in an inhibition of the metabolism of at least one of the parent chemicals or its metabolites and has an impact on the toxicological profile. In the case of B and T, the presence of T in BT mixtures reduces metabolization of B which requires metabolic activation to exert its carcinogenic effects. For quaternary BTEX-mixtures metabolic saturation is expected at at higher concentrations, namely above 20 ppm (mg/kg) for each mixture component. However, there is evidence for no metabolic interaction between TEX mixtures in humans at lower inhaled doses (Marchand et al 2016)[2].

4 Health based guidance values

For the individual BTEX components health-based reference values have been established as indicated in the summary **Table 2**.

[2] Marchand A, Aranda-Rodriguez R, Tardif R, Nong A, Haddad S. Evaluation and modeling of the impact of coexposures to VOC mixtures on urinary biomarkers. Inhal Toxicol. 2016;28(6):260-73. https://www.ncbi.nlm.nih.gov/pubmed/27053005.

Table 2: Selected reference points for BTEX compounds

	Toxicological endpoint	Population or animal, reference study	Reference point (mg/kg/day)	Drinking water guideline (µg/L)[a]	Tolerable intake (µg/kg bw/day)	Reference
B	Carcinogenicity	Leukemia in humans after inhalation exposure	N.A.	10[b]	ILCR = 1 x 10^{-5}	WHO 1993a, 1993b WHO 2011
	Decreased lymphocyte count	Occupational, inhalation study (Rothman et al. 1996)	$BMDL_{ADJ}$: 1.2[c]	N.A.	RfD = 4	USEPA 2003a
T	Hepatotoxicity	Rats oral subchronic (NTP 1990)	LOAEL: 312	700	TDI = 223	WHO 1993a
	Nephrotoxicity Increased kidney weight	Rats oral subchronic (NTP 1990)	$BMDL_{10}$: 238	N.A.	RfD = 80	USEPA 2005
E	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	300	TDI = 97.1	WHO 1993a
	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	N.A.	RfD = 100	USEPA 1991
X	Weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	500	TDI = 179	WHO 1993a
	Weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	N.A.	RfD = 200	USEPA 2003b

[a] Allocating 10% of TDI to drinking water.

[b] The guideline value for benzene in drinking-water was initially recommended in 1984 by WHO based on data for the production of leukemia after inhalation exposure in humans and using a linear multistage extrapolation model and a life-time risk level of 1 in 100 000 (source: WHO 1993b citing WHO 1984).

[c] The Benchmark Dosel Level (BMDL) was derived by route-to-route extrapolation with the assumptions that inhalation absorption was 50% and oral absorption was 100% in the dose range near the benchmark concentration (BMC). $BMDL_{ADJ}$ = 8.2 mg/m^3 x 20 m^3/day x 0.5 ÷ 70 kg = 1.2 mg/kg/day. (N.B: the original BMC was based on a benchmark response of one standard deviation change from the control mean) (USEPA 2003a).

4.1 Benzene

For carcinogenicity assessment, the World Health Organization (WHO) and the EU former Scientific Committee on Food (SCF) have not established TDIs or restriction levels because B is a human carcinogen (IARC 1987, Group 1), therefore no safe level of exposure can be recommended. WHO (1993a) derived concentrations in drinking water of 100, 10 and 1 µg/L, corresponding to excess/incremental lifetime cancer risk (ILCR) of 1 x 10^{-4}, 1 x 10^{-5}, and 1 x 10^{-6}, respectively and recommended a guideline value for drinking water of 10 µg/L (WHO 1984, 2011). Based on leukemia data in humans, the inhalation unit risk range was extrapolated to an oral (drinking water) unit risk range of 4.4 x 10^{-4} to 1.6 x 10^{-3} per mg/L (USEPA 2003a).

For the non-carcinogenic enpoints assessment, USEPA (2003a) derived a Reference dose (RfD) of 4 µg/kg bw/day based on a Benchmark Dosel Level (BMDL) of 1.2 mg/kg/day to account for decreased lymphocyte count in a human occupational epidemiological inhalation study (Rothman et al. 1996). The BMDL was derived by route-to-route extrapolation with the assumptions that inhalation absorption was 50% and oral absorption was 100% in the dose range near the benchmark dose concentration. A comparison analysis based on BMD modeling of data from the National Toxicology Program's experimental animal gavage study (NTP 1986) was also conducted. In addition, comparison

analyses using the lowest-observed-adverse-effect levels (LOAELs) from the Rothman et al. (1996) and NTP (1986) studies were performed. Additionally, oral studies in rodents gave medium supporting evidence for the chosen BMD range (Hsieh et al. 1988; Sabourin et al. 1987, 1989, cited in USEPA 2003a).

4.2 Toluene

WHO (1993) derived a TDI of 223 μg/kg bw/day using a LOAEL for marginal hepatotoxic effects of 312 mg/kg bw/day (5 days/week) in a 13-week corn-oil gavage study (NTP 1990) in mice and applying an UF of 1000 (applied 100x default uncertainty factor to account for inter- and intraspecies extrapolations, and an extra 10x for the short duration of the study and use of a LOAEL instead of a no-observed-adverse-effect level (NOAEL) which could not be identified for chronic effects) (WHO 2011, p. 422; WHO 2000, p. 113). On this basis, a guideline value for drinking water of 700 μg/L (rounded figure) was derived, allocating 10% of the TDI to drinking water and assuming a daily consumption of 2 L water consumption and 60 kg bodyweight (WHO 2011, p.422).

The USEPA (2005) derived an RfD of 80 μg/kg bw/day for increased kidney weight (higher dose range resulting in overt signs of toxicity) in the same 13-week gavage study in rats (NTP 1990), based on a $BMDL_{10}$ of 238 mg/kg bw/day (corresponding to the NOAEL) and applying a UF of 3000 (100x default uncertainty factor, an extra 10x to account for extrapolating from a subchronic study to estimate chronic exposure conditions, and an extra 3x to account for deficiencies in the toluene database). No studies examining the chronic or subchronic effects of oral exposure to T in humans are available.

4.3 Ethylbenzene

A TDI of 97.1 μg/kg bw/day was derived by WHO (1993), from a NOAEL of 136 mg/kg bw/day (5 days/week, conversion factor is x 5/7 days), based on a LOAEL for hepatoxicity and nephrotoxicity at 400 mg/kg bw/day in a limited 6 months study in rats (Wolf et al. 1956), and applying an uncertainty factor of 1000 (this is in line with the USEPA/IRIS 2001 RfD of 100 μg/kg bw/day); on this basis, a guideline value for drinking water of 300 μg/L (rounded figure) was derived, allocating 10 % of the TDI (60kg/2L/day) (WHO 2011, p. 368).

4.4 Xylenes

A TDI of 179 μg/kg bw/day was derived by WHO (1993), from a NOAEL of 250 mg/kg bw/day (5 days/week) based on a decreased body weight and increased mortality at LOAEL of 500 mg/kg bw/day in a 103-week mixed xylenes gavage study in rats (NTP 1986) and applying an uncertainty factor of 1000 (this is line with the RfD of 200 μg/kg bw/day based on the same key study and UF by USEPA 2003b); on this basis, a guideline value for drinking water of 500 μg/L (rounded figure) was derived, allocating 10 % of the TDI to drinking water (WHO 2011, p.462).

5 Exposure

BTEX are widely distributed in the environment; air, water and soil can be contaminated with BTEX through natural or anthropogenic processes. Since BTEX are naturally-occurring compounds in crude oil, BTEX can contaminate surface water, lake water and groundwater in the vicinity of natural (crude) petroleum, coal and gas deposits. Relevant natural sources of BTEX compounds for Switzerland include gas emissions from forest fires. Contamination of soil and groundwater with BTEX from anthropogenic sources typically occurs through atmospheric pollution and industrial effluents, near petroleum and natural gas production sites, petrol stations, and other areas with underground/above-ground petroleum product-containing storage tanks. The primary man-made releases of BTEX compounds are

through atmospheric pollution emissions from motor vehicles and aircraft exhaust, spills (i.e. leaking underground storage tanks) and cigarette smoke.

Once released in the environment, BTEX compounds usually evaporate quickly into the air or can dissolve in aqueous media. Wet and dry deposition may introduce BTEX into the water and soil compartments. BTEX can contaminate the food chain and drinking water supplies. Low concentrations of BTEX can be found in foodstuffs but also in many consumer products (see **Tables 3 and 4**).

Environmental exposure to BTEX for humans occurs mostly via inhalation. For example, it is considered that ca. 99.9% of human exposure to B occurs via inhalation (SCF 1999) and that more than 96% of E in the environment can be expected to be present in air (WHO 2011, p.368).

Smoking is a large source of personal chronic exposure to benzene, and can increase daily exposure dramatically (see **Table 4**). According to a NICNAS (2001) evaluation, based on a value of 50 µg/cigarette, the daily intake of B for an average smoker (17.8 cigarettes per day) is increased by 0.89 mg/day (2001, p.157).

For BTEX, high short-term exposures can occur during refuelling of motor vehicles. Extended travel in motor vehicles with elevated air benzene levels (from combustion and evaporative emissions) can contribute up to 30% to cumulative ambient benzene exposure and associated cancer risk when the travel time is one hour (WHO 2000, p.62). **Tables 3** and **4** below summarize the dietary and non-dietary exposure sources for BTEX compounds.

Table 3: Qualitative overview of main exposure sources for the four individual components

(Source: WHO 2000, 2011)

	Smoking	Combustion, evaporation gasoline	Petroleum Industry	Refuelling tanks of motor vehicles	Traffic, traveling in motor vehicles	Solvent in consumer product	Dietary sources	Reference
B	+++	+++	++	++(+)	++	+	+	WHO 2000, p.62
T	+++	+++	++	++(+)	++	+	+	WHO 2000, p. 112
E	++	+++	+++	++(+)	++	+	+	WHO 2011, p.368
X	+++	+++	++	++(+)	++	+	+	WHO 2011, p.432

SCAHT classification scheme: +++ = large source; ++ = intermediate source; + = low source.

Table 4: Relative importance of BTEX exposure from dietary and non dietary sources

BTEX	Exposure	Source	Pathway	Range of calculated or reported exposures for adults	References
Benzene	Dietary exposure	Food, average	Oral	0.5-2.4 µg/person/day	SCF 1999
		Food, average Food, max	Oral	0.056 µg/kg bw/day 1.149 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,c]	Inhalation	0.29-7.7 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking[d]	Inhalation	1.74-2.10 µg/kg bw/day	ATSDR 2004
		Skin contact	Dermal	*not identified*	
	Total exposure	All [all + smokers][e]		1.15-1.5 µg/kg bw/day [7.46-9.00 µg/kg bw/day]	ATSDR p.276
Toluene	Dietary exposure	Food, average	Oral	7.7 µg/person/day (UK) 0.119 µg/kg bw/day	SCF 1999 Medeiros Vinci et al. 2015[a]
		Food, max	Oral	3.290 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,f]	Inhalation	0.29-74.9 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact		*not identified*	
	Total exposure	All		*not identified*	
Ethylbenzene	Dietary exposure	Food, average	Oral	0.027 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
		Food, max	Oral	0.502 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,g]	Inhalation	0.06-7.4 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact	Dermal	*not identified*	
	Total exposure	All		*not identified*	
Xylenes	Dietary exposure	Food, average	Oral	< 5 µg/person/day (UK) 0.032 µg/kg bw/day[h]	SCF 1999 Medeiros Vinci et al. 2015[a]
		Food, max	Oral	0.945 µg/kg bw/day[h]	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b]	Inhalation	0.23-16.7 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact	Dermal	*not identified*	
	Total exposure	All		*not identified*	

[a] results from the deterministic analysis are shown, which may possibly overestimate the exposure compared to probabilistic anaylsis.

[b] Calculated for adults, based on indoor/outdoor air levels in µg/m^3 from table 3 in the literature review of Demirel et al. 2014 and USEPA/IRIS database, a body weight (bw) of 70 kg and an inhalation rate of 20 m^3/day; ranges are for **benzene**: 1-27 µg/m^3 = 20-400 µg/day /70kg => 0.29-7.7 µg/kg bw/day; for **toluene**: 1-262 µg/m3 = 20-5240 µg/day /70kg => 0.29-74.9 µg/kg bw/day; for **ethylbenzene**: 0.2-26 µg/m^3 = 4-520 µg/day /70kg => 0.06-7.4 µg/kg bw/day; for the sum of **xylenes**: 0.8-58.5 µg/m^3 = 16-1170 µg/day /70kg => 0.23-16.7 µg/kg bw/day.

[c] Mean ambient air levels of benzene in rural + urban areas are ca. 1 µg/m^3 and 5-20 µg/m^3, respectively (WHO 2000, p.62).

[d] Based on a value of 50 µg/cigarette, the daily benzene intake of an average smoker is increased by 0.89 mg per day, the average smoker (32 cigarettes per day) takes in about 1.8 mg benzene per day from smoking (ATSDR p.276). Passive smokers' estimated daily intake averages are 2.10 and 1.74 µg/kg bw/day for women and men, respectively.

[e] Urban women and men smokers intake estimates of 9.00 and 7.46 µg/kg bw/day, respectively (ATSDR p.276).
[f] Mean ambient air concentrations of toluene in rural areas are generally less than 5 µg/m^3, while urban air concentrations are in the range 5-150 µg/m^3 (WHO 2000, p.112).
[g] Values of up to 26 µg/m^3 in air have been reported (WHO 2011, p.368).
[h] estimated for o-xylene.

6 Risk assessment

In a first-tier risk assessment, the SCAHT backcalculates individual soil clean up values T, E and X based on the most conservative health-based guidance values (HBGV), applying the SCAHT standard exposure scenario, which assumes a chronic oral exposure of a 12.5 kg child to 250 mg contaminated soil per day and assuming an oral bioavailability of the soil contaminant of 100%.

6.1 Toluene

The SCAHT backcalculates an individual soil clean-up value for toluene based on the more conservative health-based guidance value, reference dose (RfD) of 80 µg/kg bw/day, derived by USEPA in 2005 (see chapter 5.2).

HBGV	RfD: 80 µg/kg bw/day	
Exposure limit for a 12.5 kg child	12.5*80 µg/12.5kg bw/day	
Exposure limit for 250 mg soil	1000 µg/12.5kg bw/250 mg soil	
SCAHT clean up value for kg soil	1000 µg * 4000 / kg soil	**= 4 g/kg soil**

6.2 Ethylbenzene

The SCAHT backcalculates an individual soil clean-up value for ethylbenzene based on the more conservative health-based guidance value, a tolerable daily intake (TDI) of 97.1 µg/kg bw/day was derived by WHO (1993), (see chapter 5.3).

HBGV	TDI: 97.1 µg/kg bw/day	
Exposure limit for a 12.5 kg child	12.5*97.1 µg/12.5kg bw/day	
Exposure limit for 250 mg soil	1213.75 µg/12.5kg bw/250 mg soil	
SCAHT clean up value for kg soil	1213.17 µg * 4000 / kg soil	**= 4.855 g/kg soil**

6.3 Xylene

The SCAHT backcalculates an individual soil clean up value for xylene based on the more conservative health-based guidance value, A TDI of 179 µg/kg bw/day was derived by WHO (1993) (see chapter 5.4).

HBGV	TDI: 179 µg/kg bw/day	
Exposure limit for a 12.5 kg child	12.5*179 µg/12.5kg bw/day	
Exposure limit for 250 mg soil	2237.5 µg/12.5kg bw/250 mg soil	
SCAHT clean up value for kg soil	2237.5 µg * 4000 / kg soil	**= 8.95 g/kg soil**

6.4 Comparison of HBGV

Based on a review in the scientific and regulatory literature of national soil remediation regulations in Europe, USA and Canada (e.g. Carlon 2007; CCME 2010; City of Copenhagen 2011), it appears that the clean-up value as defined by the Swiss Ordinance on Polluted Soils is, in international comparison (refer to **Annex 1, original report**), the highest for the BTEX mixture, however only Austria besides Switzerland has set a remediation value (**CH: 500;** A: 6 mg/kg dm). The clean up value for benzene as defined by the Swiss Ordinance on Polluted Soils is, in international comparison, in the higher range (USA: 2; USA: 1.2; **CH**, E, NL: **1**; CZ: 0.8; B, CAN: 0.5; UK: 0.33; I: 0.1; S: 0.06 (mg/kg dm). It should be noted that, based on these 13 countries reviewed, Switzerland was found to be the only country to set a clean-up value both for the sum of BTEX and for benzene alone.

Despite the conservative approaches assumed, the SCAHT derived soil clean-up levels for T, E, X are in international comparison up to several orders of magnitude higher than the range of clean-up values for the same compounds T, E, X in other countries (**Table 5**).

However, no information could be identified that would allow a comparison of the dervation of the individual values. In particular, it remains unclear whether or not these values have been established based on analytical considerations, scientific evaluations or have been established as default values. Moreover, no information could be identified to judge whether these values have the same meaning in the different local regulatory contexts and whether they serve the same protection goals e.g. environmental protection versus human safety.

Table 5: The range of clean up values for T, E, X in selected countries:

Compound	**Internat. Soil remediation values**	**SCAHT derived soil clean-up values**
Toluene:	0.5 (Italy) – 610 (UK) (mg/kg dm)	4000 mg/kg soil
Ethylbenzene:	0.5 (Italy) – 350 (UK) (mg/kg dm)	4855 mg/kg soil
Xylenes:	0.5 (Italy) – 720 (UK) (mg/kg dm)	8950 mg/kg soil

6.5 Conclusion

Individual soil clean-up values could be established for T, E and X. The values that have been derived by the SCAHT on the basis of US EPA and/or WHO derived HBGV are approximately 4, 5 and 9 mg/kg soil for T, E and X respectively and are three orders of magnitude higher than the existing clean-up value for benzene of 1 mg/kg soil in the Swiss Contaminated Sites Ordinance (CSO).

A more conservative cut-off value for B in comparison to T, E and X is in line with the toxicological profiles of the compounds. While B is a non-threshold human carcinogen, E is possibly carcinogenic to humans but a threshold level for toxicity is assumed. T and X are not carcinogenic. All compounds are neurotoxic and acute neurotoxicity is the most sensitive effect of all the four compounds. However, acute neurotoxicity is not the most relevant effect to assess the potential health impact from chronic oral exposure to BTEX contaminated soils.

7 Anhang 1: BTEX inklusive Benzol

7.1 Datenblatt

Handlungsbedarf	Ja	Aktueller Sanierungswert von 500 mg BTEX/kg Boden sollte durch individuelle Sanierungswerte für T, E und X ersetzt werden. Ohne Definition von kritischen BTEX-Mischungen kann eine Risikoanalyse nicht durchgeführt werden. Aktueller Sanierungswert von 1 mg Benzol/kg Boden kann beibehalten werden
Gefährdungspotential	Hoch	Akute Neurotoxizität bei B, T, E und X Kanzerogenität bei B und E
Kanzerogen	Ja	Benzol: Einstufung: IARC Gruppe 1, krebserregend im Menschen. Benzol ist ein genotoxisches, klastogenes Humankarzinogen ohne Schwellenwert. Bei wiederholter Exposition kann Benzol vor allem das blutbildende System und das Immunsystem schädigen und wirkt krebserzeugend (hauptsächlich Leukämien). Ethylbenzol: Einstufung: IARC Gruppe 2a wahrscheinlich krebserregend in Menschen, Mechanismus unklar.
Mutagen	Nein	Benzol ist genotoxisch, klastogen aber nicht mutagen. Ethylbenzol ist wahrscheinlich nicht genotoxisch.
Reprotoxisch	Unklar	Befunde zur Reprotoxizität von B, T, E sind unklar. X ist nicht reprotoxisch. Entwicklungstoxizität (Fötotoxizität) in vivo bei B, T, E und X.
Neurotoxisch	Ja	Alle vier Substanzen B, T, E und X sind leicht flüchtige organische Verbindungen, die beim Einatmen neurotoxisch sind; akute Vergiftungen treten erst bei relativ hohen Konzentrationen ein. Es kommt zu Schwindelgefühl, Brechreiz, Benommenheit und Apathie. Schwere Vergiftungen kommt es zu Fieber und Sehstörungen bis hin zu vorübergehender Erblindung und Bewusstlosigkeit.
Andere	Ja	Der sensitivste nicht kanzerogene Endpunkt bei Benzolexposition ist die Schädigung der blutbildenden Organe, was sich in Knochenmarks- und Blutbildveränderungen sowie immuntoxischen Effekten äußert

und schliesslich zu Leukämie führen kann.
Irritationen der Atemwege.

Gesundheitsbasierter Referenzwert

	Toxicological endpoint	Population or animal, reference study	Reference point (mg/kg/day)	Drinking water guideline (µg/L)[a]	Tolerable intake (µg/kg bw/day)	Reference
B	Carcinogenicity	Leukemia in humans after inhalation exposure	N.A.	10[b]	ILCR = 1 x 10^{-5}	WHO 1993a, 1993b WHO 2011
	Decreased lymphocyte count	Occupational, inhalation study (Rothman et al. 1996)	$BMDL_{ADJ}$: 1.2[c]	N.A.	RfD = 4	USEPA 2003a
T	Hepatotoxicity	Rats oral subchronic (NTP 1990)	LOAEL: 312	700	TDI = 223	WHO 1993a
	Nephrotoxicity Increased kidney weight	Rats oral subchronic (NTP 1990)	$BMDL_{10}$: 238	N.A.	RfD = 80	USEPA 2005
E	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	300	TDI = 97.1	WHO 1993a
	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	N.A.	RfD = 100	USEPA 1991
X	weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	500	TDI = 179	WHO 1993a
	weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	N.A.	RfD = 200	USEPA 2003b

Exposition		
Äussere Exposition Boden (250 mg)		Benzol: 1 mg /kg Boden = 250 ng/250 mg Boden = 20 ng/kg KG/Tag (KG: 12.5kg). BTEX: 500 mg /kg Boden = 125 µg/250 mg Boden = 10 µg/kg bw/day (KG: 12.5kg).
Innere Exposition Boden „Bioavailability“		Benzol: konservative Annahme 100% orale absolute orale Bioverfügbarkeit aus dem Boden, also innere Exposition = 20 ng/kg KG/Tag (KG: 12.5kg) BTEX: konservative Annahme 100% orale absolute orale Bioverfügbarkeit aus dem Boden, also innere Exposition = 20 ng/kg KG/Tag (KG: 12.5kg)
Hintergrundexposition Nahrung, Wasser, Luft		Geschätzte Benzolaufnahme über die Nahrung: 0.056-2.4 µg/kg KG/Tag (Kinder 1 - 3 Jahre) Geschätzte Benzolaufnahme über die Luft: Keine Daten, aber die inhalative Exposition ist der Hauptaufnahmepfad für leichtflüchtige organische Substanzen.
Zusätzliches Gesundheitsrisiko durch die direkte Bodenaufnahme im Vergleich zur unvermeidbaren Hintergrundbelastung.	Unwahrscheinlich	Für Benzol ist ein zusätzliches Risko durch das Verschlucken von kontaminiertem Boden trotz der hohen Giftigkeit des Benzols unwahrscheinlichkeit, weil die zu erwartenede Exposition klein im Vergleich zur Hintergrundbelastung ist. Die zusätzliche Belastung für ein 12.5 kg schweres Kind, das täglich 250 mg kontaminierten Boden verschluckt liegt bei 20 ng/kg KG/Tag das entspricht 8% - 36% der geschätzen Aufnahme über die Nahrung für Erwachsene (0.056-2.4 µg/kg bw/day). Bezogen auf das Körpergewicht ist anzunehmen, dass die Belastung über die Nahrung bei Kindern noch höher liegt und der Beitrag durch das Verschlucken von Boden sich entsprechend reduziert. Wenn man weiterhin davon ausgeht, dass die inhalative Exposition der Hauptaufnahmepfad für Benzol ist (bis zu 99,9%), kann eine zusätliches Gesundheitsrisiko als unwahrscheinlich betrachtet werden. Für BTEX, ohne die Definition von kritischen Mischungen, ist eine Risikobeurteilung nicht möglich.
Grenzwert im Vergleich		BTEX-Mischung: **CH: 500**; A: 6 (mg/kg dm) Benzol: USA: 2; USA: 1.2; **CH**, E, NL: **1**; CZ: 0.8; B, CAN: 0.5; UK: 0.33; I: 0.1; S: 0.06 (mg/kg dm) Toluol: 0.5 (I) – 610 (UK), max: 7500 (USA) (mg/kg dm) Ethylbenzol: 0.5 (I) – 350 (UK), max: 7800 (USA) (mg/kg dm) Xylol: 0.5 (I) – 720 (UK), max: 12000 (USA) (mg/kg dm)

Datenlage	Unzureichend	Es gibt keine Studien zur Bioverfügbarkeit von BTEX aus dem Boden im Mensch oder Tier. Es gibt kaum Studien zur Bioverfügbarkeit des einzelsubstanzen B, T, E oder X aus dem Boden. Ohne die Definition von kritischen BTEX-Mischungen kann keine Risikoanalyse für die quarternären Mischungen vorgenommen werden.

7.2 Zusammenfassung

The Swiss Contaminated Sites Ordinance (CSO)[1] sets a clean up value for benzene at 1 mg/kg soil and for BTEX at 500 mg/kg soil, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

According to SCAHT there are currently no sound scientific data which would support a change in the current clean up value for benzene.

- Benzene is hematotoxic, immunotoxic, carcinogenic and genotoxic but not mutagenic; after prolonged exposure, hematotoxicity may lead to aplastic anemia and leukemia. For genotoxic carcinogens we would typically apply the ALARA principle. However, in this case SCAHT assumes that the oral route of exposure is not the major exposure pathway for benzene and ingestion of soil does not create a significant additional health risk.
- For benzene, the additional exposure from direct ingestion of 250 mg contaminated soil is 20 ng/kg bw/day for a child weighing 12.5 kg. Based on this exposure scenario, the SCAHT assumes that the overall contribution from soil ingestion is small compared to the total background exposure and that an additional health risk from direct soil ingestion of benzene-contaminated soil is small.
- In the SCAHT scenario soil ingestion accounts for 8% - 36% of the estimated dietary exposure for adults (range: 0.056-2.4 µg/kg bw/day). No dietary exposure data could be identified for children but compared to adults children are typically exposed to higher doses based on a body weight basis and the contribution from soil ingestion to the overall dietary exposure should be lower for children.
- WHO has defined drinking water guidelines based on estimated excess lifetime cancer risks using data on leukemia from epidemiological studies. It was calculated that a drinking water concentration of 1 µg/L. was associated with an excess lifetime cancer risk of 10^{-6} (WHO 1996, page 4, paragraph 3). Assuming that a toodler with a body weight of 12.5 kg would consume 1 L. water a day, this would translate into an exposure of 80 ng/kg bw/day. In this case soil ingestion would account for 25% of exposure via drinking water and the related excess lifetime cancer risk.
- Anyhow, dietary exposure and exposure from direct soil ingestion is expected to be small in comparison to inhalative exposure for volatile organic compounds (VOCs) like B.

The SCAHT proposes to drop the BTEX clean up value and to introduce new individual values for T, E and X.

BTEX is the sum parameter of benzene (B), toluene (T), ethylbenzene (E) and (o-, m-, p-) xylenes (X), which combine at varying concentrations to form a vast array of BTEX (quaternary) mixtures of often unknown composition. The absence of well-defined BTEX mixtures to which humans can be exposed precludes the quantitative assessment of a potential additional risk from soil ingestion to the background exposure for the following reasons:

- There is a huge number of possible combinations of different concentrations of the four

[1] AltlV, Anhang 3, Ziffer 2: Verordnung über die Sanierung von belasteten Standorten (vom 26. August 1998, Stand am 1. März 2015) für Standorte bei Haus und Familiengärten, Kinderspielplätzen und Anlagen, auf denen Kinder regelmässig spielen (AltlV 1998).

chemicals to which humans can be exposed. Unless mixtures of concern are defined there is no way to compare a BTEX clean up value to the given background exposures to assess a potential additional risk.

- Indeed there is no health-based reference value for the quaternary BTEX mixture which could be used as a reference point for risk assessment. However, health-based reference values have been established for the individual B, T, E, X components.

The toxicological database on BTEX is poor, particularly for oral exposure and mixture effects.

No studies are available that directly characterize health hazards of the quaternary BTEX mixtures. For the four individual chemicals the toxicological profile after inhalation (but not oral) exposure is reasonably well characterized but the potential adverse effects of the interactions between B, T, E and X when present simultaneously in a mixture is poorly understood. Physiologically-based Pharmacokinetic (PBPK) models have been developed to simulate toxicological effects for all different kind of mixtures, yet for inhalation exposure only.

- B, T, E and X are highly volatile organic compounds (VOCs) and inhalation is the most common route of exposure. Neurotoxicity, hematotoxicity, immunotoxicity and carcinogenicity are the critical health effects following human exposure to BTEX.
- **Neurotoxicity of B, T, E and X is a direct effect of the parent compound, and the effect is additive when mixing the individual compounds.** All four individual compounds B, T, E and X are neurotoxic even at low doses after acute oral and inhalation exposure.
- **Hematotoxicity, immunotoxicity and leukemia are benzene specific and no additive effects are expected in BTEX mixtures.**
- **However, inhibitory / less than additive effects have been observed in BTEX mixtures.** Toluene for example, decreases the hematotoxicity and carcinogenicity potential of benzene. This can be explained by metabolic saturation. Metabolism of the four B, T, E, X components is dose-dependent. If the four B, T, E, X compounds are present in low concentrations in the mixture, then they are extensively metabolized. As there are only a limited number of metabolizing enzymes available, simultaneous exposure to higher concentrations of BTEX mixtures can cause two or more components to compete for the same enzyme-mediated biotransformation pathway. This results in an inhibition of the metabolism of at least one of the parent chemicals or its metabolites and has an impact on the toxicological profile.

Despite the fact that no quantitative risk assessment can be conducted for the quaternary BTEX mixture, the SCAHT assumes that an additional health risk from direct soil ingestion is low, because a sufficiently high oral exposure to BTEX from direct soil ingestion to cause permanent toxic effects is unlikely for the following reasons:

- Acute neurotoxicity is the most sensitive toxicological endpoint. Dizziness, vertigo and tremors are expected to be transient but would most likely prevent prolonged exposure to BTEX from soil.
- Moreover, BTEX are VOCs and volatilization occurs on a time scale of minutes to hours. Therefore, inhalation of released vapours may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil.
- BTEX that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (= desorption resistant fraction). Benzene in particular, is a VOC that will not usually be found in high concentrations in surface soils due to loss through volatilization; since B is also fairly mobile in

soil, it will migrate downwards following water movement, typically remaining in subsurface soils or may migrate to the groundwater compartment. The degree of vaporization of VOCs from soils varies between freshly added compounds and aged residues. At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures.

The SCAHT review of the scientific and regulatory literature of national soil remediation regulations reveals that besides Switzerland, Austria is the only country that has set up a remediation value for BTEX. However, Austria has not set a clean up value for benzene alone. Most countries reviewed have established individual remediation values for each of the four B, T, E and X compounds. Germany appears to be the only country that does not specify any clean up values for B, T, E or X in the Federal Soil Protection act and Contaminated Sites Ordinance.

7.3 Gefährdungspotential

BTEX is the sum parameter of benzene (B), toluene (T), ethylbenzene (E) and (o-, m-, p-) xylenes (X). These chemicals are single-ring aromatic hydrocarbons which are classified as volatile organic compounds (VOCs). Because of this high volatility inhalation is the most common route of exposure for these compounds.

While BTEX as such occurs as the quaternary mixture of varying concentrations of B, T, E and X, various combinations of the four chemicals exist, such as binary mixtures (e.g. BE, BT, BX, TE, TX, EX) and ternary mixtures (e.g. BTX, TEX). While the toxicological profile after inhalation exposure of the four individual chemicals is reasonably well characterized, the potential adverse effects of the interactions between B, T, E and X when present simultaneously in a mixture is poorly understood.

No studies are available that directly characterize health hazards and dose-response relationships for exposures to the quaternary BTEX mixtures (ATSDR 2004, page ix, paragraph 2) and there is only limited toxicological information for binary and ternary mixtures.

The health effects information for quaternary BTEX mixtures is a proxy derived from toxicological data of the individual BTEX chemicals and from data on binary component mixtures as well as from some toxicokinetic and mechanistic information that is available from an interaction-based PBPK[2] model of this mixture (ASTDR 2004 page 3, paragraph 1).

PBPK models have been developed to simulate toxicological effects for all different kind of mixtures (ATSDR 2004, chapter 2) but for inhalation exposure only. For oral exposure, no such models exist and therefore route-to-route extrapolations would be required, adding another level of complexity and uncertainty to the modelling approaches.

Likewise, there are extremely limited data for oral chronic exposure to B, T, E and X because inhalation is the most common route of exposure for these compounds. Moreover, the high volatility of the compounds leads to a rapid evaporation from the fed-matrix and challenges dose concentration control in oral exposure scenarios.

7.3.1 Toxicological endpoints

Each of the chemicals is well absorbed, extensively metabolized, and does not persist in the body for long periods of time. **Neurotoxicity, hematotoxicity, immunotoxicity, and carcinogenicity are the critical effects** of concern for human exposure to BTEX. Not all individual mixture components show the same toxicological effects.

- All four compounds B, T, E and X are neurotoxic;
- B is the only hematotoxic compound. Following prolonged exposure hematotoxicity leads to leukemia and immunotoxicity;
- E is possible carcinogenic to humans but not to the bone marrow;
- B, T, E and X data on reproductive and developmental toxicity from occupational exposure and animal studies are inconclusive but suggest some effects at high doses.

Table 12-1 summarizes the major toxicological effects of B, T, E and X. For more in-depth information

[2] Physiologically-based Pharmacokinetic (PBPK) modelling is a mathematical modelling technique for predicting the absorption, distribution, metabolism and excretion (ADME) of chemical substances in humans and animal species.

please refer to the subsequent paragraphs.

Table 12-1: Overview of toxicological endpoints for the individual BTEX components

Please note that: this overview does not take into account mixture effects; the majority of data is derived from inhalation studies; if not stated otherwise findings have been observed in humans.

	B	**T**	**E**	**X**
Neurotoxicity	+	+	+	+
Hematotoxicity	+	-	?	-
Immunotoxicity	+[1]	-	-	-
Carcinogenicity	+[1,2]	-	?[3] Possible human carcinogen	-
Genotoxicity	+[2]	-	?	-
Reprotoxicity	? Testicular effects - in vivo	?	? Testicular tumors, uterine and hormonal effects - in vivo	-
Developmental toxicity	+ Fetotox in vivo	+ Fetotox in vivo, humans	+ Fetotox in vivo	+ Fetotox in vivo
Liver	-	-	+ in vivo	+ in vivo
Kidney	-	+	+ in vivo	+ in vivo
Others	-	Irritation Respiratory tract	Irritation Respiratory tract , eyes	Irritation Respiratory tract , eyes, skin

\+ Relevance of toxicological effect for human health established
\- No toxicological effect reported
? Relevance of toxicological effect for human health is inconclusive
[1] Secondary to hematotoxicity
[2] In bone marrow cells and lymphocytes
[3] Not in bone marrow but in kidney (rat), testis (rat), lung (mice), liver (mice)

7.3.1.1 Neurotoxicity

Acute inhalation or oral exposure to the individual B, T, E, X compounds can produce neurotoxic effects {dizziness, vertigo, tremors, central nervous system (CNS) depression, narcosis, etc}, which are reversible upon cessation of exposure. Neurotoxicity is the most critical non-cancer effect of concern for BTEX mixtures following acute inhalation exposure, because it is expected to occur at the lowest exposure levels.

Observed effects for all four B, T, E, X compounds have been attributed to their liposolubility and direct action on neuronal membranes. This is similar to the way general anesthetic agents work, i.e. either by a disruption of the lipid environment in which membrane proteins function or by direct interaction with the hydrophobic/hydrophilic conformation of proteins in the membranes. Mechanistic aspects are summarized in **Table 12-2** below (refer to section 12.3.2).

Benzene

- Acute neurological effects of B are presumed to result from a direct effect of the parent B compound on CNS cell membranes unrelated to its metabolites. Human data are mostly

associated with overt signs of CNS toxicity, and dose-response data in the lower concentration range are often lacking in humans (ATSDR 2004, appendix A, chapter A3, page 88, paragraph 1).

Toluene

- Chronic exposure to high concentrations of T brings about structural changes in the brain related to lipid compositional changes. Supporting evidence for this hypothesis includes altered phospholipid composition of brain synaptosomes, decreased phospholipid concentrations in the cerebral cortex, and decreased number of neurons in the hippocampus in T-exposed rats (ATSDR 2004, appendix B, chapter B3, page 101, first paragraph). Neurological impairment (e.g. gait and speech abnormalities) and brain atrophy have been observed in humans in several cases of chronic inhalation abuse to T, as well as occular and ear toxicity following inhalation exposure of T. Mechanistic understanding of direct T-induced hearing loss at the molecular and cellular level is limited; recent evidence suggests that T modifies the response of protective acoustic reflexes to loud noises via anticholinergic effects, potentially resulting in increased noise-induced hearing loss (ATSDR 2015, chapter 3.5.2, page 247, second paragraph). It has been postulated that toluene interference with dopaminergic mechanisms of retinal cells or toxic demyelination of optic nerve fibers may be involved in the vision impairment (ATSDR 2015, chapter 3.5.2, page 248, second paragraph).

Ethylbenzene

- Neurotoxic effects of E have been primarily studied *in vitro*, in particular changes in integrity and functionnality of cell membranes of astrocyte in rodents have been described. Membrane-mediated effects resulted in a dose-dependent inhibition of the enzymatic activity of Na^+, K^+-ATPase, and Mg^{2+}-ATPase, which may disturb the ability of the cells to maintain homeostasis. Experiments with rat synaptosome preparations showed that membrane fluidity was increased after exposure to E. ATPase and acetylcholinesterase activity were also decreased, as seen in the astrocyte preparations. There is yet no direct evidence that the interaction of E with astrocytes *in vivo* is the mechanism of neurological effects following acute exposure to high levels of E in humans or in animals (ATSDR 2004, appendix C, chapter C3, page 116, second paragraph). Similarly to T, direct ototoxicity (loss of outer hair cells in the Corti organ) of E after inhalation exposure in rats has also been described (ATSDR 2010, chapter 3.5.2, page 122, first paragraph).

Xylenes

- Acute inhalation exposure to X can cause impaired short-term memory, impaired reaction time, performance decrements in numerical ability, and alterations in equilibrium and body balance in humans experimental studies; case reports and occupational studies together provide suggestive supportive evidence that acute and chronic inhalation exposure to X or solvent mixtures containing X may also be associated with several neurotoxic effects (ATSDR 2004, appendix D, chapter D2, page 125, first paragraph). Ito et al. (2002) suggested that high concentrations of *m*-xylene in the cerebellum increased may increase $GABA_A$ receptor binding activity, and that the increased inhibitory effect of GABAergic neurotransmission in the cerebellum is consistent with the adverse effect of *m*-xylene on motor coordination (ATSDR 2007, chpater 3.5.2, page 154, first paragraph). It is yet unclear whether these represent direct effects of X mediated (via altered cellular membrane integrity, function and homeostasis) or are secondary changes resulting from non-specific CNS depression. Some authors have also suggested that metabolic intermediates, such as arene oxides or methylbenzaldehyde, may be responsible for the toxic effects of X (ATSDR 2004, appendix D, chapter D2, page 128, first paragraph).

7.3.1.2 Hematotoxicity, immunotoxicity & carcinogenicity

For B (only) there is a causal relationship between the development of non-cancer hematological effects, immunotoxicity and the development of leukemia. Benzene can cause hematological effects, which may ultimately lead to aplastic anemia and acute myelogenous leukemia (AML).

- Hematotoxicity is the most noted and characteristic systemic effect resulting from intermediate and chronic B exposure in humans and animals. All of the major types of blood cells are susceptible (erythrocytes, leukocytes, and platelets). In the less severe cases of toxicity, specific deficiencies occur in individual types of blood elements. A common clinical finding is cytopenia, which is a decrease in various cellular elements manifested as anemia, leukopenia, or thrombocytopenia in humans. Benzene-associated cytopenias vary and can involve a reduction in one (unicellular cytopenias) to all three (pancytopenia) cellular elements of the blood (ATSDR 2004, appendix A, chapter A2, page 85-86).

- Prolonged exposure to B can cause severe damage to the bone marrow involving cellular aplasia in humans and animals. This condition, is known as aplastic anemia, in which the bone marrow and the blood stem cells that reside there are damaged. This causes a deficiency of all three blood cell types (pancytopenia), i.e. red blood cells (anemia), white blood cells (leukopenia), and platelets (thrombocytopenia). The term “aplastic“ refers to the inability of the stem cells to generate the mature blood cells (ATSDR 2004, appendix A, chapter A2, page 86).

  Human studies that provide some estimate of levels of exposure indicate that adverse hematological effects occurred at levels >10 ppm and generally not at levels <1 ppm. Adverse hematological effects begin to appear in animals at B concentrations of 10-100 ppm and above. Oral data are essentially limited to findings in intermediate- and chronic-duration animal studies showing that loss of blood elements occurs following exposure to B in drinking water or by gavage at doses as low as 8-25 mg/kg/day (ATSDR 2004, appendix A, chapter A2, page 86, paragraph 1).

- Benzene-induced aplastic anemia can progress to AML, a fast-growing cancer of the blood and bone marrow. In AML, the bone marrow makes many cancerous cells called leukemic blasts. While normal blasts would normally develop into white blood cells that fight an infection, in AML the leukemic blasts do not develop properly and cannot fight infections. These leukemic blasts grow quickly and crowd out the bone marrow, preventing it from making the normal red blood cells, white blood cells, and platelets that the body needs.

- Other health effects of B include immunological changes in humans and animals, which appear to be largely related to decreases in circulating white blood cells (leukocytes) and the ability of lymphoid tissue to produce the mature lymphocytes (lymphocytes are white blood cells that encompass B-cells, T-cells and natural killer cells) necessary to form antibodies (ATSDR 2004, appendix A, chapter A2, page 86, paragraph 2, first sentence).

7.3.1.3 Carcinogenicity and genotoxicity

Benzene

- Benzene is a non threshold carcinogen. The causal relationship between hematological effects and the development of leukemia is well established as indicated by its consensus classification as a human carcinogen by the National Toxicology Program, U.S. Environmental Protection Agency (USEPA Category A), and International Agency for Research on Cancer (IARC Group 1) (ATSDR 2004, page 2).

- Benzene is genotoxic and clastogenic, but not mutagenic. Chromosomal damage in bone marrow cells and lymphocytes are well documented effects of benzene based on findings in

human occupational studies and *in vivo* studies in animals (ATSDR 2004, appendix A, chapter A2, page 86, second paragraph).

- Reactive metabolites appear to play key roles in the development of the clastogenic and carcinogenic effects of B (see **Table 12-2** for a description of the mechanism of action in section 12.3.2). It is generally believed that B metabolites covalently bind to cellular macromolecules (including DNA, RNA and proteins), thereby leading to dysfunction in the bone marrow (including stem, progenitor, and stromal cells) and other tissues. For example, B and its metabolites may induce oxidative DNA damage or interfere with the incorporation of iron into bone marrow precursors, chelates of iron and hydroquinone or 1,2,4-benzenetriol appear to be potent DNA cleaving agents, and hydroquinone may accumulate in bone marrow to act as substrates for myeloperoxidase, forming benzoquinone which is myelotoxic and clastogenic. The relationships between adduct formation and toxicity is not clear, and multiple metabolic pathways and mechanisms are involved in B toxicity and carcinogenicity (ATSDR 2004, appendix A, chapter A3, page 87, paragraph 3 and 4).

Ethylbenzene

- Ethylbenzene is not hematotoxic but does cause carcinogenic effects in other tissues. Results from an oral rat study and an epidemiological study were inconclusive but there was clear evidence of carcinogenic activity from a chronic inhalation study in rats and mice which revealed carcinogenic activity in kidney and testis (rat) and in lung and liver (mice). Ethylbenzene has been classified as possibly carcinogenic to humans based on a recent assessment by IARC (ATSDR 2004, page 2; Huff et al., 2010). The mechanism of carcinogenicity of E has not been entirely elucidated, but is likely related to the parent compound and/or reactive oxidative metabolites in the 4-ethylphenol pathway, rather than the 1-phenylethanol pathway (ATSDR 2010, chpater 3.5.2, page 123, first paragraph).
- Ethylbenzene was not genotoxic in most studies, although some marginal effects have been reported. Workers exposed to low levels of E in a styrene plant showed no increases in sister chromatid exchanges, DNA adduct formation, micronuclei, or DNA single-strand breaks in the peripheral lymphocytes. Micronucleated peripheral erythrocytes were not increased in mice that were exposed to 750 ppm ethylbenzene for 13 weeks. Ethylbenzene was generally not mutagenic in bacteria or yeast cells *in vitro*, and did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster cells. A weak positive response was observed when E was tested for sister chromatid exchanges in human lymphocytes *in vitro*, but only at a concentration that was toxic to the cells. A positive response also was seen in mouse lymphoma cells when E was tested at a near lethal concentration (ATSDR 2004, appendix C, chapter C2, page 115, third paragraph).

Toluene and xylenes

- Toluene and (o-, m-, p-) xylenes (X) are not carcinogenic and not mutagenic. T and X have been categorized as not classifiable as to human carcinogenicity by both EPA and IARC, reflecting the lack of evidence for the carcinogenicity of these two chemicals (ATSDR 2004, page 2).

7.3.1.4 Reprotoxicity and developmental toxicity

In general, the reproductive and developmental effects of B, T, E and X are often incompletely characterized and studies are often inconclusive due to study limitations including small population size, absence of adequate study design (e.g no multigeneration studies) or multiple-exposure to other substances.

There is suggestive evidence that B, T and possibly E but not X are reprotoxicants in animals. Most of this information has been derived from inhalation studies; those positive effects were also confirmed

by a limited number of oral studies. In humans, while occupational/epidemiological data are very limited and unconclusive for B and X, there is suggestive evidence for reprotoxic effects of T. No data are avaialble for E.

B, T, E and X are developmental toxicants in animals. However, adverse effects on the developing fetus were only observed at high levels of exposure that are maternally toxic. In humans, it has been shown that the abuse of toluene during pregnancy at high dose can be toxic to the developing fetus; no data are available for E, and very limited or inconclusive evidence exist for B and X.

Benzene

- There are no inhalation or oral multigeneration animal studies available but there is suggestive evidence of reproductive toxicity in rodents and rabbits from (sub)chronic inhalation studies which showed effects on male reproductive organs (e.g. atrophy/degeneration of testes, decrease in spermatozoa, increase in abnormal sperm forms, etc), particularly in mice following intermediate duration exposure to 300 ppm (ATSDR 2004, appendix A, chapter A2, page 86, second paragraph). There were no ovarian effects in either the rats or the mice treated for 90 days or in the rats treated for 2 years. Mice treated for 2 years exhibited ovarian lesions ranging from atrophy to neoplasia (USEPA 2002, page 79, chapter 4.2.2.1.1, first paragraph). However, the incidence of non-neoplastic lesions was not dose related, which might be an indication of secondary effects to B carcinogenic potential.

  Some occupational data regarding reproductive effects of B in humans exist (e.g. reproductive dysfunction, dysmenorrhea) but evidence is limited and rather weak due to co-exposure to other chemicals, lack of good exposure monitoring data or missing quantitative dose-response information (USEPA 2002, chapter 4.1.2.3, page 44-46).

- Results of developmental toxicity studies in animals indicate that inhalation exposure to high levels of B is fetotoxic and maternally toxic in several species as shown by decreased fetal weight and/or minor skeletal variants. Fetotoxic effects in rodents occurred at B levels ≥ 47 ppm, although there was evidence of transient hematopoietic anomalies in fetuses and offspring of mice exposed to 5-20 ppm B (ATSDR 2004, appendix A, chapter A2, page 86, second paragraph).

  Results regarding developmental toxicity of B in humans are unconclusive. Most studies consisted of small numbers of subjects, lacked important experimental details, and involved (in almost all cases) concomitant exposure to other chemicals, and did not provide monitoring data or quantitative dose-response information (USEPA 2002, chapter 4.1.2.4, page 47-50).

Toluene

- Reproductive toxicity studies in experimental animals found some decreased sperm count in male rats and ultrastructural changes in ovary follicles of female rats but showed no damage at the histological level to the reproductive organs in rats and mice in (sub)chronic oral studies. Also, no evidence for impaired reproductive performance was found in several assays, including a 2-generation study of rats intermittently exposed to up to 2000 ppm T (ATSDR 2004, appendix B, chapter B2, page 99, first paragraph).

  Adverse reproductive effects of T in humans have been suggested especially with repeated inhalation exposure during pregnancy to concentrations above 200 ppm T. Occupational exposure to increasing concentrations of T (8-111 ppm) has been associated with decreased plasma levels of the luteinizing hormone, follicle stimulating hormone and testosterone levels in males. Increased risks of spontaneous abortions and menstrual function were observed in women occupationally exposed to T, or wives of men similarly exposed (Lindbohm et al. 1990; Ng et al. 1992a, 1992b). However, interpretation of these results is limited due to many study limitations and potential confounders.

- Developmental toxicity studies in experimental animals have shown that T exerts fetotoxic effects at exposure levels associated with maternal toxicity. Increased fetal mortality, retardation of growth and altered skeletal development were seen following inhalation exposure during gestation in rats (> 2000 ppm) and rabbits (at 267 ppm). Altered neurobehavioural development was seen following inhalation exposure during gestation and lactation in rats (> 1200 ppm) (ATSDR 2004, appendix B, chapter B2, page 99, first and second paragraphs). Oral exposure of pregnant rats to 650 mg T/kg bw/day resulted in decreased bw, delayed ossification, smaller brain volumes, and decreased forebrain myelination of the offspring. In general, no-effect levels following inhalation exposure ranged from about 133-750 ppm T; however, no developmental effects were observed in pregnant mice exposed by gavage to doses ≥ 1800 mg T/kg bw/day.

  In humans, several reports of birth defects in children born to women who abused T or other organic solvents during pregnancy suggest that high-level (4,000–12,000 ppm) exposure to T during pregnancy can be toxic to the developing fetus, including effects such as microcephaly, central nervous system dysfunction, growth deficiency, cranofacial and limb abnormalities, and reversible renal tubular acidosis.

Ethylbenzene

- Reproductive toxicity studies in experimental animals are limited, and no multigeneration studies are available. In inhalation studies, the only observed reproductive effects were increased incidences of testicular tumors in rats. In oral studies, changes in uterine structure, delayed estrus cycle and reduced hormone levels were observed. For the latter, no dose-reponse could be established.

  In humans, no studies were identified regarding reproductive effects following inhalation, oral or dermal exposure to E (ATSDR 2010, chapter 3.2.1.5 page 69; chapter 3.2.2.5, page 83; chapter 3.2.3.5, page 87).

- Developmental toxicity studies in animals indicate that inhalation exposure to E can produce minimal fetotoxic effects at exposure levels that may or may not induce minimal maternal changes. In both rats and mice anomalies of the skeletton and the urinary tract were reported (ATSDR 2004, appendix C, chapter C2, page 115, second paragraph), as well as increased fetal mortality in rats and rabbits.

  In humans, no studies were identified regarding developmental effects following inhalation, oral or dermal exposure to E (ATSDR 2010, chapter 3.1.2.6, page 70; chapter 3.2.2.6, page 84; chapter 3.2.3.6, page 87).

Xylenes

- The limited data available do not suggest reproductive effects of (mixed) X in experimental animals. A one-generation inhalation study in male and female rats with mixed X showed no reproductive effects. A subchronic inhalation study in male rats did not show changes in hormones levels and no structural changes in testes. Similarly, (sub)chronic oral studies in male and female rats and mice reported no effects on reproductive tissues (ATSDR 2004, appendix D, chapter D2, page 127, second paragraph).

  In humans, information on the reproductive toxicity of X is limited to two studies that found an increased incidence of spontaneous abortions following paternal exposure or maternal exposure. These findings are inconclusive due to study limitations including multiple chemical exposures and small population size.

- Developmental toxicity in experimental animals was shown following inhalation exposure to mixed X or the individual isomers in rats, mice, and rabbits, incl. increased skeletal

abnormalities, delayed ossification, fetal loss, hemorrhages in fetal organs, and decreased fetal body weight; these levels were generally associated with maternal toxicity (350-700 ppm)(ATSDR 2004, appendix D, chapter D2, page 126, third paragraph; ATSDR 2007, chapter 3.5.2, page 156, third paragraph). Neurodevelopmental effects (e.g. neuromotor, learning and memory abilities) were reported in rats at lower gestational inhalation exposure levels (200-500 ppm) that did not induce maternal toxicity. An oral study found that mixed X-induced cleft plate and decreased fetal weight in mice exposed to maternally toxic dose, and a dermal study found changes in brain enzymes levels of rat embryos (ATSDR 2004, appendix D, chapter D2, page 126, third paragraph).

Information on the developmental toxicity of X in humans is limited to a few occupational studies that are inadequate for assessing the relationship between exposure to X and developmental effects due to concurrent exposure to other solvents and small numbers of subjects.

7.3.2 Mechanisms of action of BTEX

Knowledge of the mechanisms of toxicity for the individual BTEX components can help understnand how they might influence each other in mixtures. Modes of action (MoA) are generally well documented for some general (e.g. BTEX neurotoxicity) and specific toxicological endpoints (e.g. B hematotoxicity or X nephrotoxicity).

However, many data gaps still exist, in particular for T and E. For example, the mechanism of carcinogenicity of E has not yet been elucidated, but involves likely the formation of reactive metabolites; mechanistic investigations are being conducted on E-induced lung tumors in mice, including the role of potenially cytotoxic quinine metabolites of E (ATSDR 2010, chapter 3.12.3, page 143, first paragraph).

Table 12-2 summarizes known or postulated mechanisms of toxicity for the toxicological endpoints of each of the four B, T, E, X compounds.

Table 12-2: Overview of known or postulated modes of action for B, T, E and X

(Source: ATSDR 2004, pp. 87-88, 100-101, 116-117, 128-129; ATSDR 2007, pp. 154-157; ATSDR 2010, pp. 240-250; ATSDR 2010, page 122-124; ATSDR 2015, pp. 240-250)

Enpoint	Compound	Mechanism of action
Neurotoxicity	B, T, E, X	Lipophilic parent compound exert direct, narcotic and anaesthetic effects leading to CNS depression and narcosis via changes in: • CNS-cell membrane composition/structure (intercalation into the lipid bilayer) • Membrane integrity (e.g. increased fluidity) • Functionality (barrier, energy transport, matrix for interaction with proteins and enzymes) • Neurotransmitters levels (ACh, GABA, DA)
Carcinogenicity	B	Compensatory proliferative response to anemia via: • Decrease in bone marrow cellularity • Regenerative hyperplasia in the bone marrow, thymus and spleen leading to aplastic anemia and development of AML
Hematotoxicity Clastogenicity	B	Changes in metabolic pathways via: • Covalent binding of reactive metabolites[a] to cellular macromolecules leading to dysfunction • Competition with other chemicals for Cytochrome (CYP) 450 binding sites and subsequent adduct formation • Direct competition between parent compound and metabolites • Induction or inhibition of (Phase II) conjugating enzymes • Synergism between metabolites or GSH-depleting metabolites and oxygen radicals
Pulmonary toxicity	X	Inhibition of pulmonary microsomal enzymes via: • Formation of toxic reactive metabolite (such as methylbenzaldehyde)
Foetal toxicity	X	Decreased progesterone and estradiol levels; Increased microsomal enzyme activity; Increased hormone catabolism
Nephrotoxicity	X, (T?)	Renal tubules and glomeruli injury due to reactive metabolites formation causing: • Irritation • Direct membrane fluidization • Faster cellular turnover (increased urinary levels of β-glucuronidase, albumin, erythrocytes, leukocytes)

[a] known benzene biologically reactive metabolites include: benzene oxide, benzene dihydrodiol, hydroquinone, catechol, benzoquinones, and muconaldehyde.

7.3.3 Mixture effects

As there are no studies available that directly characterize health hazards and dose-response relationships for exposures to quaternary BTEX mixtures (ATSDR 2004, page ix, paragraph 2), PBPK models have been developed to predict ADME characteristics of chemical substances in humans and animal species; those models allow for calculation of human exposure and estimation of the mixture effects of B, T, E and X on human health.

- PBPK analyses from binary exposure studies suggested competitive inhibition of hepatic metabolism as the most plausible mechanism of interaction between individual B, T, E and X compounds (ATSDR, chapter 2.1, page 3).
- The quaternary PBPK model indicates that the competitive inhibitory effect tends to increase with increasing number and concentration of inhibitors (ATSDR, chapter 2.1, page 4). This is illustrated in **Table 12-3** where data from the quaternary mixture PBPK model were compared to blood concentration data of B, T, E and X in rats that have been exposed to mixtures of BTEX at various concentrations: 50 ppm of each BTEX component; 100 ppm of each BTEX component; 100 ppm of B and 50 ppm each of T, E, and X.

- The predicted blood level of B is 39.4% higher from the binary mixture B/T compared to B alone. The addition of the third chemical, E, to the binary mixture resulted in levels of T and B that were increased 26% and 15.7%, respectively, compared to the binary concentrations. Similarly, addition of X to the ternary mixture affected the kinetics of all three chemicals by increasing levels of B, T and E by approximately 7.1%, 5.7% and 9.4%, respectively, compared to the ternary concentrations. The magnitude of the modulation of binary interactions invoked by the addition of another chemical to an existing "network" of binary interactions (i.e., at the binary, ternary, or quaternary level) depends on its inhibition potency and blood concentration.
- With increasing mixture complexity, the blood level of a chemical is increased according to the potency and number of inhibitors, rather than by modification of the inhibition constant for each binary interaction.

Table 12-3: Quaternary PBPK model predictions of hepatic venous blood levels of B, T, E, X

Data were obtained in rat studies after a 4-hour acute inhalation exposure to 100 ppm B alone or combined with 100 ppm of T, E, and/or X.

(Source: ATSDR 2004, page 5, table 2.1)

	Hepatic venous concentration							
	Benzene		Toluene		Ethylbenzene		Xylene	
Mixture components	mg/L	%	mg/L	%	mg/L	%	mg/L	%
B	1.847	—	—	—	—	—	—	—
B + T	2.576	39.4[a]	2.499	—	—	—	—	—
B + T + E	2.981	15.7[b]	3.150	26.0[b]	5.830	—	—	—
B + T + E + X	3.192	7.1[c]	3.328	5.7[c]	6.377	9.4[c]	6.244	—

[a]Percent increase compared to benzene alone
[b]Percent increase compared to binary mixture (B+T)
[c]Percent increase compared to ternary mixture (B+T+E)

7.3.3.1 Toxicokinetics of BTEX mixtures

BTEX compounds distribute easily to lipid-rich and highly vascular tissues such as the brain, bone marrow, liver and kidneys and body fat due to their lipophilicity, are extensively metabolized and are rapidly eliminated from the body, primarily via the urine. Multiple metabolic pathways and mechanisms are involved in B, T, E and X toxicity. Metabolism of the four B, T, E, X components is dose-dependent and generally extensive at dose levels that do not saturate the first metabolic step of each compound, which involves CYP450-dependent mixed function oxidases, predominantly CYP2E1 (but also 2B1, 2B6, 1A2). There can also be competition for the available CYP450 sites amongst the parent compounds and their metabolites. Elimination occurs by e.g. exhalation for the unmetabolized B parent compound and via urine for B, T, E, X metabolites (summarized from ATSDR 2004, pp. 82-83, 95-96, 111-112, 123-124; WHO 2011, pp. 368, 422-423, 433).

⇒ Therefore simultaneous exposure to a BTEX mixture can cause two or more components to compete for enzyme-mediated biotransformation, resulting in an inhibition of the metabolism of at least one of the parent chemicals or its metabolites.

⇒ The threshold for competitive metabolic interaction was estimated to be 20 ppm of each component in humans (ATSDR, page 48, last paragraph). As shown in table 3, competitive metabolic interaction could be measured as increased blood levels of the inhibited parent compound.

As the metabolism of B, T, E and X can comprise several toxification and detoxification (via conjugation) pathways, inhibition of the metabolism can either increase or decrease toxicological effects. Individual metabolic pathways might be changed if oxidation or conjugation enzymes are induced or inhibited in the presence of additional B, T, E, X components and their metabolites. There also may be synergism between metabolites or between glutathione-depleting metabolites and oxygen radicals generated.

- **Additive effects of BTEX mixtures** are expected for neurotoxicity.

  ⇒ The joint neurotoxic action of B, T E and X is expected to be additive at BTEX concentrations below the threshold of ca. 20 ppm of each component for competitive metabolic interaction. BTEX-induced neurotoxicity is not dependent on metabolic activation but is a direct effect of the parent compounds. Because of their lipophilic characteristics the individual B, T, E and X compounds can directly effect the composition/structure, integrity and functionality of the CNS-cell membrane (see also table 2).

- **No additive effects of BTEX mixtures** are expected for toxicological effects that are specific for a single component.

  ⇒ Hematotoxicity and secondary carcinogenic effects on bone marrow and immunotoxicity of the quaternary BTEX mixture are benzene-specific. These effects are not changed in the presence of toluene, ethylbenzene and xylene.

  ⇒ Likewise carcinogenic effects other than leukemia are ethylbenzene-specific. Benzene, toluene, and xylene are unlikely to influence the carcinogenicity of ethylbenzene, at exposure concentrations below approximately 20 ppm of each component, i.e. environmental relevant exposure.

- **Inhibitory effects of BTEX mixtures** have been observed at exposure levels above the threshold for competitive metabolic interaction (metabolic saturation). At higher concentrations of BTEX, the individual compounds compete for the same metabolic enzymes. The available number of CYP450 binding sites is insufficient to bind and metabolize all four BTEX components. This results in increased blood levels for the parent compound (as indicated in table 3) and decreased blood levels of metabolically activated metabolites.

  ⇒ As a consequence of metabolic saturation the hematotoxicity and carcinogenicity potential of B is decreasing in the presence of E, T, and X (ATSDR 2004).

  ⇒ Toluene was found to inhibit the hematological effects of B. Although E and X are also expected to reduce the hematotoxic/carcinogenic potential of benzene due to competitive metabolic interactions, available toxicity data for these pairs of chemicals are inconclusive.

  ⇒ Similarly, there are no binary toxicity data supporting the possible reduction in E carcinogenicity due to competitive metabolic interactions with B, T, and X.

7.4 Gesundheitsbasierter Referenzwert

There is no health-based reference value that has been established for the quaternary BTEX mixture neither for any binary or ternary mixtures of BTEX.

- For the individual BTEX components health-based reference values have been established as indicated in the summary **Table 12-4**. More detailed background information is provided in the subsequent paragraphs.

Table 12-4: Selected reference points for BTEX compounds

	Toxicological endpoint	Population or animal, reference study	Reference point (mg/kg/day)	Drinking water guideline (µg/L)[a]	Tolerable intake (µg/kg bw/day)	Reference
B	Carcinogenicity	Leukemia in humans after inhalation exposure	N.A.	10[b]	ILCR = 1 x 10^{-5}	WHO 1993a, 1993b WHO 2011
	Decreased lymphocyte count	Occupational, inhalation study (Rothman et al. 1996)	$BMDL_{ADJ}$: 1.2[c]	N.A.	RfD = 4	USEPA 2003a
T	Hepatotoxicity	Rats oral subchronic (NTP 1990)	LOAEL: 312	700	TDI = 223	WHO 1993a
	Nephrotoxicity Increased kidney weight	Rats oral subchronic (NTP 1990)	$BMDL_{10}$: 238	N.A.	RfD = 80	USEPA 2005
E	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	300	TDI = 97.1	WHO 1993a
	Hepatotoxicity, Nephrotoxicity	Rats oral subchronic (Wolf et al. 1956)	NOAEL: 136	N.A.	RfD = 100	USEPA 1991
X	Weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	500	TDI = 179	WHO 1993a
	Weight loss, increased mortality	rats oral chronic (NTP 1986)	NOAEL: 250	N.A.	RfD = 200	USEPA 2003b

[a] Allocating 10% of TDI to drinking water.

[b] The guideline value for benzene in drinking-water was initially recommended in 1984 by WHO based on data for the production of leukemia after inhalation exposure in humans and using a linear multistage extrapolation model and a life-time risk level of 1 in 100 000 (source: WHO 1993b citing WHO 1984).

[c] The Benchmark Dosel Level (BMDL) was derived by route-to-route extrapolation with the assumptions that inhalation absorption was 50% and oral absorption was 100% in the dose range near the benchmark concentration (BMC). $BMDL_{ADJ}$ = 8.2 mg/m^3 x 20 m^3/day x 0.5 ÷ 70 kg = 1.2 mg/kg/day. (N.B: the original BMC was based on a benchmark response of one standard deviation change from the control mean) (USEPA 2003a).

Benzene

- For carcinogenicity assessment, the World Health Organization (WHO) and the EU former Scientific Committee on Food (SCF) have not established TDIs or restriction levels because B is a human carcinogen (IARC 1987, Group 1), therefore no safe level of exposure can be recommended.

  However WHO (1993a) derived concentrations in drinking water of 100, 10 and 1 µg/L, corresponding to excess lifetime cancer risk of 1 x 10^{-4}, 1 x 10^{-5}, and 1 x 10^{-6}, respectively and

recommended a guideline value for drinking water of 10 μg/L (WHO 1984, 2011). Based on leukemia data in humans, the inhalation unit risk range was extrapolated to an oral (drinking water) unit risk range of 4.4×10^{-4}-1.6×10^{-3} per mg/L (USEPA 2003a).

- For the non-carcinogenic enpoints assessment, USEPA (2003a) derived a Reference dose (RfD) of 4 μg/kg bw/day based on a Benchmark Dosel Level (BMDL) of 1.2 mg/kg/day to account for decreased lymphocyte count in a human occupational epidemiological inhalation study (Rothman et al. 1996). The BMDL was derived by route-to-route extrapolation with the assumptions that inhalation absorption was 50% and oral absorption was 100% in the dose range near the benchmark dose concentration. A comparison analysis based on BMD modeling of data from the National Toxicology Program's experimental animal gavage study (NTP 1986) was also conducted. In addition, comparison analyses using the lowest-observed-adverse-effect levels (LOAELs) from the Rothman et al. (1996) and NTP (1986) studies were performed. Additionally, oral studies in rodents gave medium supporting evidence for the chosen BMD range (Hsieh et al. 1988; Sabourin et al. 1987, 1989, cited in USEPA 2003a).

Toluene

- WHO (1993) derived a TDI of 223 μg/kg bw/day using a LOAEL for marginal hepatotoxic effects of 312 mg/kg bw/day (5 days/week) in a 13-week corn-oil gavage study (NTP 1990) in mice and applying an UF of 1000 (applied 100x default uncertainty factor to account for inter- and intraspecies extrapolations, and an extra 10x for the short duration of the study and use of a LOAEL instead of a no-observed-adverse-effect level (NOAEL) which could not been identified for chronic effects) (WHO 2011, p. 422; WHO 2000, p. 113). On this basis, a guideline value for drinking water of 700 μg/L (rounded figure) was derived, allocating 10% of the TDI to drinking water and assuming a daily consumption of 2 L and 60 kg (WHO 2011, p.422).
- The USEPA (2005) derived an RfD of 80 μg/kg bw/day for increased kidney weight (higher dose range resulting in overt signs of toxicity) in the same 13-week gavage study in rats (NTP 1990), based on a $BMDL_{10}$ of 238 mg/kg bw/day (corresponding to the NOAEL) and applying a UF of 3000 (100x default uncertainty factor, an extra 10x to account for extrapolating from a subchronic study to estimate chronic exposure conditions, and an extra 3x to account for deficiencies in the toluene database). No studies examining the chronic or subchronic effects of oral exposure to T in humans are available.

Ethylbenzene

- A TDI of 97.1 μg/kg bw/day was derived by WHO (1993), from a NOAEL of 136 mg/kg bw/day (5 days/week, conversion factor is x 5/7 days), based on a LOAEL for hepatoxicity and nephrotoxicity at 400 mg/kg bw/day in a limited 6 months study in rats (Wolf et al. 1956), and applying an uncertainty factor of 1000 (this is in line with the USEPA/IRIS 2001 RfD of 100 μg/kg bw/day); on this basis, a guideline value for drinking water of 300 μg/L (rounded figure) was derived, allocating 10 % of the TDI (60kg/2L/day) (WHO 2011, p. 368).

Xylenes

- A TDI of 179 μg/kg bw/day was derived by WHO (1993), from a NOAEL of 250 mg/kg bw/day (5 days/week) based on a decreased body weight and increased mortality at LOAEL of 500 mg/kg bw/day in a 103-week mixed xylenes gavage study in rats (NTP 1986) and applying an uncertainty factor of 1000 (this is line with the RfD of 200 μg/kg bw/day based on the same key study and UF by USEPA 2003b); on this basis, a guideline value for drinking water of 500 μg/L (rounded figure) was derived, allocating 10 % of the TDI to drinking water (WHO 2011, p.462).

7.5 Exposition

7.5.1 Äussere Exposition

BTEX are widely distributed in the environment; air, water and soil can be contaminated with BTEX through natural or anthropogenic processes. Since BTEX are naturally-occurring compounds in crude oil, BTEX can contaminate surface water, lake water and groundwater in the vicinity of natural (crude) petroleum, coal and gas deposits. Relevant natural sources of BTEX compounds for Switzerland include gas emissions from forest fires. Contamination of soil and groundwater with BTEX from anthropogenic sources typically occurs through atmospheric pollution and industrial effluents, near petroleum and natural gas production sites, petrol stations, and other areas with underground/above-ground petroleum product-containing storage tanks. The primary man-made releases of BTEX compounds are through atmospheric pollution emissions from motor vehicles and aircraft exhaust, spills (i.e. leaking underground storage tanks) and cigarette smoke.

Once released in the environment, BTEX compounds usually evaporate quickly into the air or can dissolve in aqueous media. Wet and dry deposition may introduced BTEX into the water and soil compartments. BTEX can contaminate the food chain and drinking water supplies. Low concentrations of BTEX can be found in foodstuffs (Medeiros Vinci et al. 2015) but also in many consumer products (Lim et al. 2014) (see **Table 12-5**).

Environmental exposure to BTEX for humans occurs mostly via inhalation. For example, it is considered that ca. 99.9% of human exposure to B occurs via inhalation (SCF 1999) and that more than 96% of E in the environment can be expected to be present in air (WHO 2011, p.368).

- Smoking is a large source of personal chronic exposure to benzene, and can increase daily exposure dramatically (see **Table 12-6**). According to a NICNAS (2001) evaluation, based on a value of 50 µg/cigarette, the daily intake of B for an average smoker (17.8 cigarettes per day) is increased by 0.89 mg/day (2001, p.157).
- For BTEX, high short-term exposures can occur during refuelling of motor vehicles. Extended travel in motor vehicles with elevated air benzene levels (from combustion and evaporative emissions) can contribute up to 30% to cumulative ambient benzene exposure and associated cancer risk when the travel time is one hour (WHO 2000, p.62).

Table 12-5 and **Table 12-6** below summarize the dietary and non-dietary exposure sources for BTEX compounds.

Table 12-5: Qualitative overview of main exposure sources for the four individual components

(Source: WHO 2000, 2011)

	Smoking	Combustion, evaporation gasoline	Petroleum Industry	Refuelling tanks of motor vehicles	Traffic, traveling in motor vehicles	Solvent in consumer product	Dietary sources	Reference
B	+++	+++	++	++(+)	++	+	+	WHO 2000, p.62
T	+++	+++	++	++(+)	++	+	+	WHO 2000, p. 112
E	++	+++	+++	++(+)	++	+	+	WHO 2011, p.368
X	+++	+++	++	++(+)	++	+	+	WHO 2011, p.432

SCAHT classification scheme: +++ = large source; ++ = intermediate source; + = low source.

Table 12-6: Relative importance of BTEX exposure from dietary and non dietary sources

BTEX	Exposure	Source	Pathway	Range of calculated or reported exposures for adults	References
Benzene	Dietary exposure	Food, average	Oral	0.5-2.4 µg/person/day	SCF 1999
		Food, average Food, max	Oral	0.056 µg/kg bw/day 1.149 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,c]	Inhalation	0.29-7.7 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking[d]	Inhalation	1.74-2.10 µg/kg bw/day	ATSDR 2004
		Skin contact	Dermal	*not identified*	
	Total exposure	All [all + smokers][e]		1.15-1.5 µg/kg bw/day [7.46-9.00 µg/kg bw/day]	ATSDR p.276
Toluene	Dietary exposure	Food, average	Oral	7.7 µg/person/day (UK) 0.119 µg/kg bw/day	SCF 1999 Medeiros Vinci et al. 2015[a]
		Food, max	Oral	3.290 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,f]	Inhalation	0.29-74.9 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact		*not identified*	
	Total exposure	All		*not identified*	
Ethylbenzene	Dietary exposure	Food, average	Oral	0.027 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
		Food, max	Oral	0.502 µg/kg bw/day	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b,g]	Inhalation	0.06-7.4 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact	Dermal	*not identified*	
	Total exposure	All		*not identified*	
Xylenes	Dietary exposure	Food, average	Oral	< 5 µg/person/day (UK) 0.032 µg/kg bw/day[h]	SCF 1999 Medeiros Vinci et al. 2015[a]
		Food, max	Oral	0.945 µg/kg bw/day[h]	Medeiros Vinci et al. 2015[a]
	Non-dietary exposure	House dust	Oral	*not identified*	
		Ingested soil	Oral	*not identified*	
		Air[b]	Inhalation	0.23-16.7 µg/kg bw/day	Demirel et al. 2014; WHO 2000
		Smoking	Inhalation	*not identified*	
		Skin contact	Dermal	*not identified*	
	Total exposure	All		*not identified*	

[a] results from the deterministic analysis are shown, which may possibly overestimate the exposure compared to probabilistic anaylsis.

[b] Calculated for adults, based on indoor/outdoor air levels in µg/m^3 from table 3 in the literature review of Demirel et al. 2014 and USEPA/IRIS database, a body weight (bw) of 70 kg and an inhalation rate of 20 m^3/day; ranges are for **benzene**: 1-27 µg/m^3 = 20-400 µg/day /70kg => 0.29-7.7 µg/kg bw/day; for **toluene**: 1-262 µg/m3 = 20-5240 µg/day /70kg => 0.29-74.9 µg/kg bw/day; for **ethylbenzene**: 0.2-26 µg/m^3 = 4-520 µg/day /70kg => 0.06-7.4 µg/kg bw/day; for the sum of **xylenes**: 0.8-58.5 µg/m^3 = 16-1170 µg/day /70kg => 0.23-16.7 µg/kg bw/day.

[c] Mean ambient air levels of benzene in rural + urban areas are ca. 1 µg/m^3 and 5-20 µg/m^3, respectively (WHO 2000, p.62).

[d] Based on a value of 50 µg/cigarette, the daily benzene intake of an average smoker is increased by 0.89 mg per day, the average smoker (32 cigarettes per day) takes in about 1.8 mg benzene per day from smoking (ATSDR p.276). Passive smokers' estimated daily intake averages are 2.10 and 1.74 µg/kg bw/day for women and men, respectively.

[e] Urban women and men smokers intake estimates of 9.00 and 7.46 µg/kg bw/day, respectively (ATSDR p.276).

[f] Mean ambient air concentrations of toluene in rural areas are generally less than 5 µg/m^3, while urban air concentrations are in the range 5-150 µg/m^3 (WHO 2000, p.112).

[g] Values of up to 26 µg/m^3 in air have been reported (WHO 2011, p.368).

[h] estimated for o-xylene.

7.5.2 Innere Exposition

For BTEX, SCAHT applies the TIER 2-strategy as outlined in the methodology section

There are basically no information on oral bioavailability from dietary or other sources for the quaternary BTEX mixture, and many data gaps exist in humans for the four individual components as well. Nonetheless, collectively, available data suggest that oral absorption is relatively high and may be even complete depending on the B, T, E, X compound. This is also supported by evidence in laboratory animals (section 12.5.2.1).

There are no studies in humans that have investigated the impact of soil on the oral bioavailability of the quaternary mixture or any of the four individual B, T, E, X compounds (section 12.5.2.2), and similar studies in experimental animals are scarce (section 12.5.2.3). Despite the very limited evidence, these studies suggest that ingestion of soil-bound BTEX compounds may be similar or even greater that BTEX alone. It could be inferred that ingestion of BTEX adsorbed to soil matrices may be comparable as well to BTEX from dietary sources. This would support a more conservative approach to the RAF and the use of a 100% RAF value (section 12.5.2.4), which is further justified by the limited evidence from these studies.

In conclusion, considering a conservative dietary oral bioavailability of 100% in humans and a RAF of 100% to account for the higher uncertainty of the database, SCAHT uses an absolute oral bioavailability from soil of 100% for its risk assessment.

7.5.2.1 Oral bioavailability from food and/or water from dietary studies and other sources

Specific ADME/toxicokinetics information in humans is lacking for the quaternary BTEX mixture, and available oral absorption data for each of the individual B, T, E, X components are limited. Collectively, human data suggest that oral absorption for B, T, E, and X is high or nearly complete. There is also reasonable evidence from animal studies (rodents, rabbits) suggesting that absorption for B, T, E, and X is high and may be complete via ingestion (72%-100%). BTEX chemicals are generally well absorbed via inhalation (between 50-60%, see **Table 12-8**). Volatilization occurs on a time scale of minutes to hours. Therefore, inhalation of released vapors may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil. Dermal absorption occurs to a much lesser extent.

- *Benzene (ATSDR 2004; MASS DEP 1992; NICNAS, 2001; USEPA, 2002)*

  In humans, although only limited data are available on absorption of benzene by the oral route, accidental or intentional poisoning case studies indicate that benzene is readily absorbed (not quantified) (ATSDR 2004; USEPA 2002, citing Thienes and Haley, 1972). USEPA (2003a) has used an oral absorption of 100% for benzene for use in health risk assessment. Only a few experimental animal studies could be identified. Data suggest that oral doses of benzene are extensively absorbed (ca. 80-90% in rabbits, Parke and Wiliams 1953; not quantified in rats, Turkall et al., 1988), nearly competely absorbed (>97% in rats and mice, Sabourin et al 1987) or completely absorbed (100% in rabbits, Sabourin et al 1986 cited by MASS DEP 1992).

- *Toluene (ATSDR 2015; Health Canada, 2014; MASS DEP, 1992; USEPA, 2005)*

  In humans, only one study by Baelum et al. (1993) was identified which found that gastrointestinal absorption was complete in human volunteers after oral administration of

toluene at 2 mg/min via a 3-hour gastric tube. Experimental animal studies suggest high oral absorption, yet slow in rats (not quantified, Pyykko et al 1977; Sullivan and Conolly 1988), nearly complete (99%, Turkall et al 1991) or virtually complete in rabbits following a single oral exposure (ca. 88%-98%, Smith et al 1954).

- *Ethylbenzene (ATSDR 2010; Health Canada, 2014; MASS DEP, 1992)*

  No studies were located regarding the absorption of ethylbenzene in humans following oral exposure (ATSDR 2010). Animal studies indicate that ethylbenzene is quickly and efficiently absorbed by the oral route. Recovery estimates range from ca. 72%-92% in rabbits (El Masry et al., 1956) to 84% in a second study (Climie et al., 1983) following a single oral dose. In the Faber et al. (2006) study, ethylbenzene was detected at 0.49, 3.51 and 18.28 mg/L in maternal blood of rats 1 hour after the last of four daily administrations of ethylbenzene by gavage, corresponding to a total dose of 26, 90 and 342 mg/kg bw/day, respectively. Since important kinetic information is missing in that study, gastrointestinal absorption cannot be estimated.

- *Xylenes (ATSDR, 2007; Health Canada, 2014; MASS DEP 1992; USEPA, 2003)*

  For humans, ATSDR (2007) and Health Canada (2014) reported up to 90% oral absorption for xylenes (studies not further specified). Several experimental animal studies were identifed. Ogata et al. (1980) reported that the absorption of xylene in human volunteers (oral ingestion of 40 mg/kg bw) was at least 34% for o-xylene and 53% for m-xylene, based on the recovery of urinary metabolites. Bray et al. (1949) found ca. 80-90% oral absorption of xylenes in rabbits following oral gavage. Rat studies (Turkall et al., 1992; Kaneko et al., 1995) showed rapid and extensive uptake via the oral route through the detection of parent material in blood or metabolites in the urine.

⇒ **Based on these data, SCAHT uses a conservative estimate of 100% for the oral bioavailability of BTEX in children.**

7.5.2.2 Oral bioavailability from *in vivo* soil ingestion studies in humans

No studies have been located in the literature either for the quaternary BTEX mixture or its individual components.

7.5.2.3 Oral bioavailability from *in vivo* soil ingestion studies in experimental animals

No studies have been located in the literature either for the quaternary BTEX mixture. Three studies were identified for benzene, toluene and xylenes (Turkall et al., 1988, 1991, 1992) (Health Canada, 2014; USEPA, 2002; MASS DEP 1992) (see **Table 12-7**).

- Turkall et al. (1988) evaluated the oral bioavailability of soil-adsorbed radiolabelled-benzene in male and female rats via oral gavage (5% in aqueous suspension of gum acacia) of radiolabelled-benzene alone or adsorbed to sandy or clay soil. They found that the oral bioavailability of radiolabelled-benzene was slightly but not significantly increased by adsorption to clay soil. Adsorption of benzene to soil apparently increased the rate of gastrointestinal absorption, as the peak plasma benzene concentrations were higher in both soil treatments, and the time to peak was reduced in the sandy soil. Further metabolism and excretion data support the fact gastrointestinal absorption was apparently rapid and efficient, even in the presence of soil.
- Turkall et al. (1991) evaluated the impact on gastrointestinal absorption of radiolabelled-toluene alone or adsorbed on two types of soil (sandy soil and clay soil) in male rats, following oral gavage (aqueous suspension in gum acacia). They found that >99% of a single dose was

eliminated in the urine or expired air, indicating near-total absorption of the exposure dose. Both soils reduced the peak plasma concentration of radioactivity, while sandy soil also reduced the time to reach peak vs toluene alone. However, neither soil altered the area under the plasma radioactivity-time curve (AUC) vs toluene alone. Thus oral absorption efficiency of soil-bound toluene was not changed compared to toluene alone even though sandy soil delayed the absorption of toluene.

- Turkall et al (1992) evaluated the oral bioavailability of soil-adsorbed *m*-xylene in male and female rats via oral gavage (5% in aqueous suspension of gum acacia) of radiolabelled-m-xylene alone or adsorbed to sandy or clay soil. Adsorption to clay soil did not produce a biologically significant difference from m-xylene administered alone. Sandy and clay soil-adsorbed xylenes demonstrated significantly longer absorption half-lives, while sandy soil produced a shorter elimination half-life vs *m*-xylene alone in female rats. Increased bioavailability of sandy soil-adsorbed *m*-xylene in females was evidenced by a significantly increased (+75%) area under the plasma concentration time curve (AUC). Neither of the soils altered the maximum plasma concentration, the rate at which xylene-derived radioactivity was absorbed or eliminated, or the AUC in male rats.

Table 12-7: Impact of clay soil and sandy soil on B, T and X oral bioavailability compared to the individual compounds adminisitered alone in the Turkall experiments

Compound	Effect of sandy soil on oral absorption	Effect of clay soil on oral absorption	References
B	+, male rat	++, male rat	Turkall et al. 1988
T	∅, male rat	∅, male rat	Turkall et al. 1991
X	++, female rat ∅, male rat	∅, female rat ∅, male rat	Turkall et al. 1992

+: increased; -: decreased; ∅: unchanged (no effect)

The bioaccessibility from ingested soil and further absorption of volatile organic chemicals (VOC) such as B, T, E, X compounds depends largely on the desorption and solubilization processes from the soil matrix through the action of gastric and/or intestinal fluids.

- Significant differences in oral bioavailability are expected between freshly applied compounds at high concentrations, and aged residues present at low concentrations. These differences have been attributed to differences in partitioning between the soil and fluids within the gastrointestinal tract. These aspects however were not considered by Turkall et al.
- The BTEX bioavailability from dermal exposure is expected to be minimal, due to volatilization that occurs at the surface of the skin (NEPI 2000, p. vi). Absolute dermal absorption from soil have been estimated to be between < 0,1-8% for B, 3-12% for T and X, and 3-20% for E (NRC 2003, pp. 69-70) (see **Table 12-8**).

⇒ **While the Turkall experiments provide only very limited evidence, they suggest that soil did not reduce B, T, X oral absorption but rather increase or had no significant effect on their oral bioavailability compared to B, T, X alone. Therefore, it could be inferred that ingestion of soil-bound B, T, E, X compounds may be similar to BTEX from dietary sources. This would support a more conservative approach to the RAF (see section 12.5.2.4 below).**

7.5.2.4 Relative bioavailability from soil: use of the Relative Oral Adjustment Factor (RAF)

One possible way to estimate the relative bioavailability of BTEX in soil compared to food or water, is to use the RAF approach proposed by the USEPA, as outlined in the Methodology section. A

conservative default medium-specific RAF value of 1.0 (100%) has been proposed for each of the four B, T, E and X componens by the US Massachusetts Department of Environmental Protection (MASS DEP 1992; NRC 2003, Table 2.1 pp. 69-70) (see **Table 12-8**).

⇒ **These RAF values were based on laboratory dietary animal studies in rats and rabbits which showed nearly or virtually complete oral absorption rates for each individual B, T, E, X compound alone. For B, T and X there was further indication that adsorption to a soil matrix was comparable or even greater than the compound given alone[3].**

⇒ **SCAHT takes a conservative approach and assumes a 100% oral bioavailability in humans. Taking into account a proposed relative oral absorption factor of 1.0 (100%) (NRC 2003), the absolute oral bioavailability from soil for BTEX is 100%. This means that in the present case, internal exposure equals external exposure.**

Table 12-7: Absolute and relative oral bioavailabilities for B, T, E, X compounds

(Source: NEPI 2000, p.8; NRC 2003, pp.69-70, Table 2-1; MASS DEP 1992)

BTEX	Absolute inhalation[a] bioavailability	Absolute oral bioavailability[b]	Absolute dermal Bioavailability from soil[c]	Relative Oral Bioavailability from soil[d]	Absolute oral bioavailability from soil[e]
B	50%	suggested default 100%	0.05-8%	suggested default 100%[f]	100%
T	50%		3-12%		
E	60%		3-20%		
X	60%		3-12%		

[a] As established in experimental animal studies (source: ATSDR 2004; NEPI 2000; USEPA 2003a, see note c in Table 12-4.

[b] Gastrointestinal absorption in experimental animal studies (rodents, rabbits) following oral gavage ranges between 72%-100%, depending on the individual B, T, E, X compound (see section 12.5.2.1).

[c] Absolute bioavailability of the compound in soil via the dermal route (NRC 2003, pp. 69-70, table 2-1).

[d] Relative absorption factor, equals the relative bioavailability of the compound (i.e. in soil vs in the medium used in the toxicity study) (NRC 2003, pp.69-70, table 2-1)

[e] The absolute oral bioavailability from soil is calculated using the absolute oral bioavailability found from animal studies (72-100%, suggested default 100%), adjusted by a relative oral absorption factor of 1 (100%) to account for reduced oral bioavailabilty from soil.

[f] Proposed default values by the Massachusetts Department of Environmental Protection (MASS DEP 1992, Appendix C-13 to C-15, C-55 to C56, C97 to C98, C105 to C106). Justification has been provided, and is

[3] **RAF for benzene**: set based on experimental data showing virtually complete (100%) oral absorption (Sabourin et al. 1986; Parke and Wiliams, 1953) and the indication that absorption of benzene from soil is slightly increased compared to benzene alone (Turkall et al. 1988). **RAF for toluene:** set based on the indication that (i) oral absorption efficiency of soil adsorbed toluene was not changed from that of the pure compound, even though absorption was delayed in time by the presence of sandy soil (Turkall et al. 1991); and (ii) rabbit studies indicated 100% absorption efficiency by the oral route (Smith et al., 1954; El Masry et al., 1956). **RAF for ethylbenzene:** extrapolated from in vivo experimental studies (El Masry et al. 1956; Climie et al. 1983) but set at 100% since it was considered that oral absorption was underestimated by not controlling for respiratory volatilization following oral absorption. **RAF for xylenes**: extrapolated based on limited excretion data specifying that more than 98% of an oral dose of p-xylene was absorbed and excreted as metabolites in urine and expired air of the rabbit (Bray et al., 1949). The Turkall et al. (1992) study, not available yet at that time, would support a conservative RAF of 100%.

summarized in footenote 3, page 261 of the present report.

7.5.2.5 Summary of the in vitro bioaccessibility information

BTEX are widespread contaminants of the soil subsurface. The bioaccessibility of BTEX from the soil matrix will be highly dependent on the soil exposure to the atmosphere, the contact time between the BTEX and the soil, the soil organic matter content and BTEX concentrations. Since BTEX are highly volatile, reasonably water soluble and tend to biodegrade rapidly, they are not persistent in soils (NRC 2003, p. 134).

- For example, B will not usually be found in high concentrations in surface soils due to rapid loss through volatilization; since B is fairly mobile in soil, it will migrate downwards following water movement, typically remaining in subsurface soils or may migrate to the groundwater compartment (NEPI 2000, p. vi, third paragraph; NICNAS 2001, chapter 8.2.3, p.28).
- BTEX that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (= desorption resistant fraction) (NEPI 2000, p. 50). The degree of volatilization of VOCs from soils also varies greatly between freshly added compounds and aged residues. At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures (Farrell and Reinhard, 1994).
- Huesemann et al. (2005) found that leaching of BTEX in aged soils contaminated with crude oil (> 20,000 mg/kg) was not affected by soil properties or aging but rather was governed by the equilibrium dissolution of these hydrocarbons from the crude oil coating the soil particles.

No data on bioaccessibility were identified in the scientific literature for the quaternary BTEX mixture in soils, and very limited data are available for the four individual B, T, E, X components. This paucity of data may be explained by the high volatility of these compounds and the fact that there has been little or no testing of the oral bioavailability of aged VOC residues due to the difficulty in determining the amount of contaminant contained in an aged soil sample (NEPI 2000, p. 50).

⇒ Salanitro et al. (1997) reported that 40-95% BTEX spiked into a soil sample were volatilised during the preparation of the soil matrix. Other authors report that 50%-85% of BTEX may be lost within the first 30 minutes of analysis in open test system experiments (http://contamsites.landcareresearch.co.nz/btex_details.htm). Similarly, Wang et al. (2014) did not detect benzene in BTEX contaminated soil samples.

7.6 Risikoabschätzung

7.6.1 Benzene

For genotoxic carcinogens such as B, we would typically apply the ALARA ("as low as reasonably achievable") principle. However, in the present case, SCAHT assumes that the oral route of exposure is not the major exposure pathway. Therefore, SCAHT concludes that an additional health risk from direct ingestion of B-contaminated soil is low.

The Swiss Contaminated Sites Ordinance (Altlv 1998) sets a clean up value for B at 1 mg/kg soil, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

At the current clean up level, an accidental (daily) ingestion of 250 mg B-contaminated soil by a 12.5 kg child would contribute to an additional exposure of 20 ng/kg bw/day for B (assuming a conservative 100% absolute oral bioavailability from soil).

There are only a few data on background exposure estimates for the general population, against which the additional B uptake from direct soil ingestion can be compared to (see **Table 12-6**). The data vary widely and the SCAHT cannot assess the robustness and reliability of these data. Dietary exposure estimates for B range from 0.056 - 2.4 µg/kg bw/day reflecting the uncertainty associated with dietary exposure assessments. The data from different studies would suggest that dietary exposure to B has been reduced over the years.

- Despite all the uncertainties, the additional exposure from direct soil ingestion to B (20 ng/kg bw/day) is well below any estimate for dietary exposure (0.056 -2.4 µg/kg bw/day)

Dietary exposure and exposure from direct soil ingestion seems to be small in comparison to inhalation exposure.

- For B in particular, it is considered that ca. 99.9% of human exposure occurs via inhalation (SCF 1999). **Table 12-6**, which lists exposure estimates from different sources, does not support this claim. This might partly be due to the fact that data listed in **Table 12-6** have been consolidated from different international and often historical sources, which have used different methods to estimate exposure. However, the SCAHT considers it reasonable to assume that inhalation is the major route of exposure for high volatility compounds like benzene.

⇒ **There are currently no sound scientific data which would support a change in the current clean up value for benzene.**

7.6.2 Quaternary BTEX-mixtures

The Swiss Contaminated Sites Ordinance (AltlV 1998) set a clean up value for the sum of BTEX at 500 mg/kg, for sites in private gardens and allotments, children's playgrounds and other facilities where children play regularly.

At the clean up level, an accidental (daily) ingestion of 250 mg BTEX-contaminated soil by a 12.5 kg child would contribute to an internal additional exposure of 10 µg/kg bw/day for the whole BTEX mixture (assuming a conservative 100% absolute oral bioavailability from soil).

⇒ The SCAHT concludes that a quantitative risk assessment cannot be conducted for the quaternary BTEX-mixture because there are an almost infinite number of possible combinations of different concentrations of the four chemicals to which humans can be exposed.

A focus on mixtures of potential concern would be necessary for more quantitative evaluations. Unless

those mixtures of concern are defined there is no way to compare the BTEX clean up value to given background exposures to assess a potential additional risk.

In the absence of well-defined mixtures of concern the SCAHT does not see an additional value in keeping a clean up value for the quaternary BTEX mixture but recommends to establish individual clean up values for B, T, E and X.

- This would be in line with the most common practice. Our review of the scientific and regulatory literature of national soil remediation regulations reveals that besides Switzerland, Austria is the only country that has set up a remediation value for BTEX. However, Austria has not set a clean up value for benzene alone. Most countries reviewed have established individual remediation values for benzene, toluene, ethylbenzene and xylenes. Germany appears to be the only country that does not specify any clean up values for B, T, E or X in the Federal Soil Protection act and Contaminated Sites Ordinance (BBodSchV 1999).

Neurotoxicity, hematotoxicity, immunotoxicity, and carcinogenicity are the critical effects of concern for human exposure to BTEX with acute neurotoxicity being the most sensitive toxicological endpoint. Dizziness, vertigo and tremors are expected to be transient but would most likely prevent prolonged exposure to BTEX from soil.

- BTEX are VOCs and volatilization occurs on a time scale of minutes to hours. Therefore, inhalation of released vapors may be a significant exposure pathway to persons in the immediate vicinity of highly contaminated excavated soil.
- BTEX that remain on the soil after several hours exposure to the atmosphere can be quite resistant to mobilization and stick to soil particles near the ground surface (i.e. desorption resistant fraction). However, since B is fairly mobile in soil, it is expected to follow the water movement downwards and remains in the soil subsurface or migrate further down to the groundwater compartment (NEPI 2000, NICNAS 2001).
- The degree of volatilization of VOCs from soils is assumed to vary between freshly added compounds and aged residues. The SCAHT scenario focuses on potential human health effects from aged residues. Freshly applied residues e.g. from leaking underground storage tanks are not considered.
- At low adsorbed phase concentrations, aged residues are released several orders of magnitude slower than freshly applied compounds at ambient temperatures. Furthermore, significant differences in oral bioavailability are expected between freshly applied compounds present at high concentrations, and aged residues present at low concentrations (NEPI 2000).

⇒ **Despite the fact that no quantitative risk assessment can be conducted for the quaternary BTEX-mixture, the SCAHT assumes that an additional health risk from direct soil ingestion is low, because a sufficiently high oral exposure to BTEX from direct soil ingestion to cause intransient toxic effects is unlikely.**

7.7 Grenzwerte im internationalen Vergleich

Based on a review in the scientific and regulatory literature of national soil remediation regulations in Europe, USA and Canada (e.g. Carlon 2007; CCME 2010; City of Copenhagen 2011), it appears that the clean up value as defined by the Swiss Ordinance on Polluted Soils is in international comparison (refer to **Annex 1**):

- The highest for the BTEX mixture, however only Austria besides Switzerland has set a remediation value (**CH: 500;** A: 6 mg/kg dm)
- In the higher range for benzene (USA: 2; USA: 1.2; **CH**, E, NL: **1**; CZ: 0.8; B, CAN: 0.5; UK: 0.33; I: 0.1; S: 0.06 (mg/kg dm)

It should be noted that, based on this 13 countries reviewed, Switzerland was found to be the only country to set a clean up value both for the sum of BTEX and benzene alone.

In the other hand, all the other countries reviewed except A, D and CH have established remediation values for T, E and X.

Germany appears to be the only country that does not specifiy any clean up values for B, T, E or X in the Federal Soil Protection act and Contaminated Sites Ordinance (BBodSchV 1999).

The range of clean up values are the following, excluding USA (refer to **Annex 1**):

- Toluene: 0.5 (I) – 610 (UK) (mg/kg dm)
- Ethylbenzene: 0.5 (I) – 350 (UK) (mg/kg dm)
- Xylenes: 0.5 (I) – 720 (UK) (mg/kg dm)

Further information on BTEX regulatory guidance values in the US can be found in Jennings (2009).

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Human Health Risk Assessment of PCDDs, PCDFs and dl-PCBs for remediation of soil for sites in private gardens and allotments

in the frame of the Contaminated Sites Ordinance

(CSO, Annex 3, chapter 2)

SCAHT

Lothar Aicher, Nicolas Roth

06. March 2019

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Abbreviations

AhR	Aryl hydrocarbon Receptor
ALARA	As Low As Reasonably Achievable
BAG	Bundesamt für Gesundheit (FOPH, Swiss Federal Office of Public Health)
CADM	Concentration- and age-dependent model
CONTAM	EFSA Panel on Contaminants in the Food Chain
CSO	Contaminated Site Ordinance (AltV, Altlastenverordnung)
CYP	Cytochrome P450
DLCs	Dioxin-Like Compounds
dl-PCBs	Dioxin-Like PolyChlorinated Biphenyl congeners
EFSA	European Food Safety Authority
EHDI	Estimated Human Daily Intake
EMPA	Eidgenössisches Material Prüfungsamt (Swiss Federal Laboratories for Materials Science and Technology)
EU SCF	Scientific Committee on Food of the European Commission
GAHP	Global Alliance on Health and Pollution
GD	Gestational day
GEMS/Food	Global Environment Monitoring System/Food Contamination Monitoring and Assessment Program
HBGV	Health Based Guidance Value
HHRA	Human Health Risk Assessment
IARC	International Agency for Research on Cancer
I-TEF	International Toxic Equivalents
K-Wert	Konzentrationswert (concentration value)
LB	Lower Bound
LOAEL	Lowest Observed Adverse Effect Level
NABO	Nationale Bodenbeobachtung (swiss soil monitoring network)
NATO/CCMS	NATO Committee on the Challenges of Modern Society
ndl-PCBs	Non-Dioxin-like PolyChlorinated Biphenyl congeners
NOAEL	No Observed Adverse Effect Level

P95	95th percentile
PBPK	Physiologically Based Pharmacokinetic Modelling
PCDDs	PolyChlorinated Dibenzo-p-Dioxin congeners
PCDFs	PolyChlorinated DibenzoFuran congeners
POD	Point of Departure
POPs	Persistent Organic Pollutants
PTMI	Provisional Tolerable Monthly Intake
RBA	Relative BioAvailability
RfD	Reference Dose
SSL	Soil Screening Level
TCDD	2,3,7,8-TetraChloroDibenzo-p-Dioxin
t-TDI	Temporary TDI
TDI	Tolerable Daily Intake
TEFs	Toxic Equivalency Factors
TEQ	Toxic Equivalent Quotient
TSH	Thyroid Stimulating Hormone
TWI	Tolerable Weekly Intake
UBA	Umweltbundesamt (German Federal Environmental Agency)
UB	Upper Bound
UF	Uncertainty Factor
UK TDS	United Kingdom Total Diet Study
US EPA	United States Environmental Protection Agency
VBBo	Verordnung über die Belastung des Bodens
WHO	World Health Organization
WHO/JECFA	Joint FAO/WHO Expert Committee on Food Additives
WHO-TEQs	TEQ calculated based on TEFs set by the World Health Organization in 1997 and 2005.
XRE	Xenobiotic Response Element

1 Objectives and scope of the evaluation

In its previous human health risk assessment (HHRA) for remediation of soil for sites in private gardens and allotments, according to annex 3, chapter 2, Contaminated Sites Ordinance (CSO, AltV) on non-dioxin-like polychlorinated biphenyls (ndl-PCBs), SCAHT recommended that soil clean-up values should also be determined for dioxin-like polychlorinated biphenyls (dl-PCBs) and polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) (Aicher and Roth, 2017) because these organochlorine compounds are highly toxic environmental persistent organic pollutants (POPs) covered by the Stockholm Convention.

Currently, the CSO, Annex 3, chapter 2 lists no concentration values (Konzentrationswert, K-Wert) for 2,3,7,8-TCCD alone, or the mixture of PCDDs, PCDFs with or without dl-PCBs or for dl-PCBs alone. It only lists a soil clean up value for the sum of six ndl-PCBs (Nr. 28, 52, 101, 138, 153, 180). In contrast, the Swiss Regulation on soil contamination (VBBo) lists only soil clean-up values for the mixture of PCDDs and PCDFs without dl-PCBs of 100 ng I-TEQ/kg soil but does not further specify the PCDD and PCDF congeners included in the mixture. The VBBo lists no adequate soil clean-up value for dl-PCBs. The soil clean-up value for playgrounds and private gardens of 1 mg I-TEQ/kg soil refers to a PCB mixture of six ndl-PCBs and one dl-PCB. The one dl-PCB (Nr. 118) is a mono-ortho dl-PCB-congener with a low Toxic Equivalency Factor (TEF). The six ndl-PCBs are the same as the six ndl-PCBs listed in the CSO.

It was the objective of the present work to conduct a HHRA for PCDDs, PCDFs and dl-PCBs to determine soil clean-up values for these compounds.

2 Methodology

2.1 Risk characterization

2.1.1 Data base

As the number of scientific publications on toxicological issues is constantly growing and scientific issues are often discussed controversially, the SCAHT bases its human health risk assessment (HHRA) on the results of risk assessments of internationally recognized bodies and authorities, as appropriate.

2.1.2 Tiered assessment approach

To efficiently assess human health risks from exposure to pollutants in the soil, SCAHT proposes a multi-step process. In the first step, standard assumptions are used for specific exposure assessment parameters, which allow basic statements on the possible health risk of individual pollutants. In order to support decision-making in the context of risk management, these assumptions can be modified in further steps as part of a refined scenario planning. In a first step, it is assumed that oral exposure is the most relevant pathway for contaminants from the soil.

2.1.3 The health assessment paradigm

The assessment of the health risk from direct uptake of pollutants from soil is based on the general principles of risk assessment. A possible health risk is estimated by comparing the hazard potential of a pollutant with the exposure to the substance concerned. The identification of a possible hazard to human health is carried out in the context of toxicological (i.e. experimental animal) and / or epidemiological studies.

2.1.4 Integrated approach to exposure and risk assessment

The health assessment method of the SCAHT is based on a single substance assessment with a partially integrative approach. For each individual pollutant, the extent of exposure due to the ingestion of contaminated soils is compared with the unavoidable background burden on humans from pollutants in the environment. Possible sources of exposure to pollutants in everyday life are breathing air, food and drinking water. For infants, the intake of pollutants via house dust may be a relevant exposure pathway. The burden of house dust usually correlates with the burden of soil in family gardens. By taking into account the background burden, the additional health risk from ingestion of contaminated soils can be weighted compared to the health risk posed by the unavoidable pollution of the environment. This weighting allows a prioritization of possible risk minimization measures with regard to their protective effect on human health. Soil remediation measures will only make a significant contribution to minimizing the health risk if the health risk of ingestion of soil is high compared to the health risk posed by intake of the pollutants through food and respiratory air.

2.1.5 Protection goal is children

The protection goal of the SCAHT risk assessment is children. Children are particularly vulnerable to direct uptake of pollutants from the soil. In addition, they can be particularly sensitive to possible pollutants. This situation must be taken into account in the risk assessment of pollutants and in the establishment of Health-Based Guidance Values (HBGV). Whether an additional safety factor should be considered for children, is controversial. The SCAHT does usually not consider the introduction of an additional safety factor in its risk assessment. Extrapolation factors ("safety factors") are already being used to derive an HBGV from toxicological data, which take into account individual differences in sensitivity to toxic effects within the human population such as the greater sensitivity of children, the elderly and the sick. In addition, toxicological data on reproductive and developmental toxicity are often available that take into account a particular sensitivity in childhood. Furthermore, the SCAHT exposure estimation assumptions take into account the specific situation of the children. For example, on a body weight basis, children may eat 3 to 4 times more compared to an adult. In addition, their diet is limited to a smaller range of foods that may be less or more strained than adults. The SCAHT therefore only evaluates child-specific data for estimating background exposure to food, if available. Notes on particularly critical toxicological endpoints, such as the possible negative effects of exposure to foreign substances during the first stages of life with regard to later development are taken into account separately in the recommendation of risk minimization measures by the SCAHT.

2.1.6 Use of standard exposure assumptions for tiered risk assessment

As in the previous HHRA in the context of re-evaluation of the soil clean-up values listed in the Contaminated Site Ordinance (CSO) Annex 3, chapter 2 (Aicher and Roth, 2017), a set of standard exposure assessment factors applies. By default, the SCAHT performs a risk assessment for toddlers aged 1-3 years with a time-weighted averaged body weight of 12.5 kg. The SCAHT assumes a daily combined intake of 250 mg soil and dust per day. This is fairly in line with the upper estimates recommended by USEPA in the latest revision of its chapter 5 on soil and dust ingestion (US EPA 2017, *Update for Chapter 5 of the Exposure Factors Handbook*), where it is recommended to use combined soil and dust ingestion estimates of 200 mg at the upper 95th percentile for the general population similarly for the age bin 1 to < 2years old, 2 to<6 years old and 1 to <6 years old; recommended central tendency estimates for the general population are 90 mg, 60 mg, and 60-100 mg for the same age bins (see Table 16 / 5-1). Soil and dust ingestion rates have also been calculated by Wilson et al (2013) using a probabilistic activity pattern modeling approach. Mean and 95th percentile values for toddlers (7th months to 4 years old) were 61 and 204 mg/day respectively. The 250 mg ingestion rate was initially defined through a consultation between SCAHT and the US EPA (2014).

3 Fact sheet

Required action	Yes	Currently, the Contaminated Site Ordinance (CSO, AltV), Annex 3, chapter 2 lists no concentration values (Konzentrationswert, K-Wert) for 2,3,7,8-TCCD (Seveso dioxin) alone, or the mixture of polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) with or without dioxin-like polychlorinated biphenyls (dl-PCBs). SCAHT considers it necessary to introduce a concentration value for the sum of the toxicologically most relevant 7 PCDDs, 10 PCDFs and 12 dl-PCBs because these organochlorine compounds are highly toxic environmental Persistent Organic Pollutants (POPs) covered by the Stockholm Convention. These compounds accumulate in the environment and their half-lives in the human body is estimated to be more than 7 years. **SCAHT assumes that soils contaminated with a maximum of 14 ng WHO_{2005} TEQ PCDD/DFs and dl-PCBs/kg do, per se, not present a health risk for toddlers, who ingest 250 mg contaminated soil per day, 365 days per year. This assumption does not consider exposure from sources other than soil.** The new TWI of 2 pg WHO_{2005} TEQ/kg bw/week (which translates into a TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw/day) which was derived by the EFSA CONTAM panel in November 2018 (and is 7-times lower than the one previously derived by the SCF in 2001) is already exceeded by the estimated unavoidable dietary background exposure, which in turn leaves no room for additional exposure from ingestion of contaminated soil. Therefore, the soil concentration value should follow the ALARA principle. **If based on an integrated risk assessment approach, considering unavoidable dietary background exposure, SCAHT would recommend to introduce a concentration value for the sum of the toxicologically most relevant PCDDs, PCDFs and dl-PCBs of 1.4 ng WHO_{2005} TEQ/kg soil. This recommendation is based on a conservative approach to risk assessment.** A soil concentration value of 1.4 ng WHO_{2005} TEQ/kg soil would equate to 10% of the TDI, assuming a 1-3 year old child with a time-weighted average body weight of 12.5 kg, a daily incidental ingestion of 250 mg contaminated soil over three years and 100% bioavailability of PCDD/Fs and dl-PCBs from soil. SCAHT assumes that an additional exposure accounting for 10% of the TDI is probably not associated with a significant increase in the health risk.
Hazard potential	High	PCDDs, PCDFs and dl-PCBs are of low acute toxicity.

		After chronic exposure, PCDDs, PCDFs and dl-PCBs exert a range of toxic effects at low doses, including immunotoxicity, developmental and neurodevelopmental effects, changes in thyroid and steroid hormones and reproductive function and cancer. Developmental effects are among the most sensitive health end-points, making children, particularly breastfed infants, the population most at risk. The biological and toxic effects of PCDDs, PCDFs and dl-PCBs are similar and mediated by the activation of the AhR.
Carcinogen	Yes	PCDDs, PCDFs and dl-PCBs are not genotoxic carcinogens and it is assumed that there is a threshold mechanism of carcinogenesis, involving the AhR. 2,3,7,8-TCDD, 2,3,4,7,8-PCDF and 12 dl-PCBs have been classified by IARC as a "*known human carcinogens*" (IARC class 1). Other PCDDs and PCDFs are "*not classifiable as to their carcinogenicity to humans"* (IARC class 3).
Mutagen	No	PCDDs, PCDFs and dl-PCBs do not affect genetic material which implies that there is a level of exposure below which cancer risk would be negligible.
Reprotoxic	Yes	Chronic exposure to PCDDs, PCDFs and dl-PCBs is linked to impairment of the development, the endocrine system and reproductive functions. Developmental effects are among the most sensitive health end-points, making children, particularly breastfed infants, the population most at risk.
Neurotoxic	Yes	Long-term exposure to PCDDs, PCDFs and dl-PCBs is linked to impairment of the neurodevelopment.
Others	Yes	PCDDs, PCDFs and dl-PCBs are of low acute toxicity. Short-term exposure of humans to high levels of PCDDs, PCDFs and dl-PCBs may result in skin lesions, such as chloracne and patchy darkening of the skin, and altered liver function. Chronic exposure to high levels of PCDDs, PCDFs and dl-PCBs is linked to impairment of the immune system.
Health based guidance values		

		HBGV	**Conversion to TDI**

<table>
<tr><td></td><td></td><td>
<table>
<tr><td>2018</td><td>EFSA CONTAM</td><td>TWI = 2.0 WHO_{2005} TEQs pg/kg bw/wk</td><td>ca. 0.3 pg WHO_{2005} TEQ/kg bw/d</td></tr>
<tr><td>2012</td><td>US EPA</td><td>RfD_{oral}: 0.7 pg WHO_{2005} TEQs/kg bw/d</td><td>0.7 pg WHO_{2005} TEQ/kg bw/d</td></tr>
<tr><td>2001</td><td>WHO/JECFA</td><td>PTMI: 70 pg WHO_{1997} TEQs/kg bw/month</td><td>2.3 pg WHO_{1997} TEQ/kg bw/d</td></tr>
<tr><td>2001</td><td>EU SCF</td><td>TWI: 14 WHO_{1997} TEQs pg/kg bw/wk</td><td>2 pg WHO_{1997} TEQ/kg bw/d</td></tr>
<tr><td>1998</td><td>WHO</td><td>TDI: 1–4 I-TEQs pg/kg bw/d</td><td>1-4 I-TEQ pg/kg bw/d</td></tr>
<tr><td>1990</td><td>WHO</td><td>TDI: 10 I-TEQs pg/kg bw/d</td><td>10 I-TEQ pg/kg bw/d</td></tr>
</table>
Over time HBGVs (TDI, RfD_{oral}, TWI, PTMI) have been consistently lowered. The common feature of the HBGVs derived by different organizations is that the values were derived only from non-carcinogenic endpoints. WHO does not consider carcinogenic effects to be critical in the derivation of HBGVs.

PCDDs, PCDFs and dl-PCBs are not genotoxic carcinogens and it is assumed that there is a threshold mechanism of carcinogenesis, involving the AhR. WHO argues that the tolerable intake guidance value based on the most sensitive non-cancer end-points (developmental effects, reprotoxicity) is protective for PCDDs, PCDFs and dl-PCBs carcinogenicity because it is already very low.
</td></tr>
<tr><td>Exposure</td><td></td><td></td></tr>
<tr><td>External exposure to soil
(250 mg)</td><td></td><td>Currently, the Contaminated Site Ordinance (CSO) Annex 3, chapter 2 lists no soil clean-up values for PCDDs, PCDFs and dl-PCBs.</td></tr>
<tr><td>Internal exposure to soil
„Bioavailability“</td><td></td><td>The SCAHT assumes a relative bioavailability (RBA) for PCDDs, PCDFs and dl-PCBs in soil of 100% because of the limited number of soil samples for which RBA data are available, to cover variability across soil types and for dioxin mixtures of varying composition.

This approach is probably conservative because:

• In 2011, a US EPA report on bioavailability was peer reviewed by three subject matter experts, who agreed that the relative bioavailability of PCDDs and PCDFs in soil is less than 100%. However, two of the reviewers agreed that there were too few studies data to support a nationally-applicable value for RBA <</td></tr>
</table>

		100%. The third reviewer recommended a RBA value of 75%, arguing that the few studies which have been carried out have consistently shown RBA of around 50%. • EMPA cites case studies where soil dioxin concentrations of up to 100'000 ng I-TEQ/kg dry matter did not result in significant increases in blood fat levels in children and therefore concludes that exposure to highly contaminated soil does not present a substantial additional body burden.
Background exposure Diet, drinking water, air		More than 90% of the exposure for the general population to PCDDs, PCDFs and dl-PCBs is through (fatty) foods, mainly meat and dairy products, fish and shellfish. Toddlers (1-3 years) and "other children" are the most exposed groups, with an exposure for the sum of 29 PCDDs, PCDFs and dl-PCBs for toddlers between 0.68 (mean, min. LB) and 5.94 (P95, max. UB) pg WHO_{2005} TEQ/kg bw per day.
Addition health risk From direct soil ingestion in comparison to unavoidable background exposure		In a Swiss study conducted by the Swiss soil monitoring network (NABO) soil dioxin and PCB values were measured across Switzerland (Schmid et al., 2005; EMPA 2009). The total levels for the sum of 15 PCDD/Fs were between 1.1–11 ng I-TEQ/kg. If we assume that the 1.1–11 ng I-TEQ/kg measured for the sum of 15 PCDD/Fs represents only 45% of the 29 toxicologically most relevant PCDD/Fs and dl-PCBs, their total level can roughly be estimated to be 2.45–24.4 ng TEQ/kg soil (disregarding any differences between I-TEQ and WHO_{1995}TEQ). At the lower level of 2.45 ng TEQ/kg soil measured by NABO, a toddler with a time-weighted average body weight of 12.5 kg, who incidentally ingests 250 mg contaminated soil per day would be exposed to ca. 0.05 pg/kg bw/day (2.45/4000*12.5= 0.049) which is 6-times below the TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day. At the higher level of soil contamination of 24.4 ng TEQ/kg soil, exposure would be ca. 0.5 pg/kg bw per day (24.4/4000*12.5=0.488) which is above the TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw/day. *Nota Bene*: Contribution from soil ingestion would in some cases be a relevant exposure pathway even when compared to dietary exposure for toddlers which is well above the TDI and which ranges from 0.68–5.94 pg WHO_{2005} TEQ/kg bw/day.
Data base		The toxicological database for 2,3,7,8-TCDDs is most complete in comparison to other PCDDs, PCDFs and dl-PCBs. There are few studies on oral bioavailability of PCDDs, PCDFs and dl-PCBs from soil. In the environment, PCDDs, PCDFs and dl-PCBs are always present as chemical mixtures in varying compositions. There is no "typical chemical mixture" for human health risk assessment.

4 Executive Summary

Currently, the Contaminated Site Ordinance (CSO, AltV), Annex 3, chapter 2 lists no concentration values (Konzentrationswert, K-Wert) for dioxin 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) alone, or the mixture of polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) with or without dioxin-like polychlorinated biphenyls (dl-PCBs).

SCAHT considers it necessary to introduce a concentration value for the sum of the toxicologically most relevant PCDDs, PCDFs and dl-PCBs because these organochlorine compounds are highly toxic environmental Persistent Organic Pollutants (POPs) covered by the Stockholm Convention. These compounds accumulate in the environment and their half-lives in the human body is estimated to be more than 7 years (Poiger et al., 1986).

PCDDs, PCDFs and dl-PCBs are of low acute toxicity but after chronic exposure exert a range of toxic effects at low doses. Short-term exposure of humans to high levels of PCDDs, PCDFs and dl-PCBs may result in skin lesions, such as chloracne and patchy darkening of the skin, and altered liver function. Long-term exposure is linked to impairment of the immune system, development and neurodevelopment, the endocrine system and reproductive functions. Some PCDDs, PCDFs and dl-PCBs have been classified by IARC as a "*known human carcinogens*" (class 1). However, PCDDs, PCDFs and dl-PCBs do generally not affect genetic material, which implies that there is a level of exposure below where cancer risk would be negligible. Developmental effects are among the most sensitive health end-points, making children, particularly breastfed infants, the population most at risk. Health-based guidance values are derived based on non-cancer endpoints such as developmental and fertility effects overserved in animals and/or humans.

Different organizations have undertaken Human Health Risk Assessments (HHRA) of PCDDs, PCDFs and dl-PCBs and derived health-based guidance values (HBGVs). Over the years HBGVs were set consistently lower. The most recent HBGV was derived by the EFSA Panel on Contaminants in the Food Chain (EFSA CONTAM panel) in 2018. A new Tolerable Weekly Intake (TWI) of 2 pg WHO_{2005} TEQ/kg bw per week (which translates into a Tolerable Daily Intake TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day) was derived based on impaired semen quality observed in epidemiological studies (Russian Children's Study). The new TWI is 7-times lower than the one previously derived by the Scientific Committee on Food of the European Commission (EU SCF) in 2001.

1. **Based on the newest and lowest TDI derived so far, SCAHT assumes that soils contaminated with a maximum of 14 ng WHO_{2005} TEQ PCDD/DFs and dl-PCBs/kg do, per se, not present a health risk for toddlers, who ingest 250 mg contaminated soil per day, 365 days per year, because at this soil concentration value the TWI/TDI is not exceeded. This assumption does not consider exposure from sources other than soil.**

   However, SCAHT recommends that the derivation of a soil concentration value should consider the ALARA principle, because the EFSA estimated dietary exposure (which accounts for most of the human exposure) for toddlers, is already well above the health-based guidance value (TWI/TDI).

   For the sum of the 29 toxicologically relevant PCDD/Fs and dl-PCBs, the highest exposures were calculated for the age classes toddlers and other children. For toddlers, dietary exposure was estimated to be between 0.68 (mean, min. LB) and 5.95 (P95, max. UB) pg WHO_{2005} TEQ/kg bw per day. This leaves no room for additional exposure from incidental soil ingestion when compared to the TDI of ca 0.3 pg WHO_{2005} TEQ per day. Therefore, the soil-based concentration value for PCDDs, PCDFs and dl-PCBs should follow the ALARA principle ("*As Low As Reasonably Achievable*").

2. **Based on an integrated risk assessment approach and considering unavoidable**

background exposure, SCAHT would recommend to introduce a single concentration value for the sum of the toxicologically most relevant PCDDs, PCDFs and dl-PCBs of 1.4 ng WHO_{2005} TEQ/kg soil. This recommendation is based on a conservative approach to risk assessment.

A soil concentration value of 1.4 ng WHO_{2005} TEQ/kg soil would equate to 10% of the TDI. SCAHT assumes that an additional exposure accounting for 10% of the TDI is probably not associated with a significant increase in the health risk particularly because the impact of the uncertainties related to individual assumptions made on the risk assessment is high and the risk assessment is considered to be conservative.

The soil concentration value for the sum of PCDDs, PCDFs and dl-PCBs is based on a TWI that was primarily driven by the most sensitive toxicological endpoint (impaired semen quality) in the most sensitive study (Russian Children's Study). However, in this study the most critical toxicological endpoint was related to PCDDs and PCDFs but not dl-PCBs. Therefore, setting a soil concentration value for the sum of PCDDs, PCDFs and dl-PCBs based on a TWI that was primarily driven by a toxicological endpoint related to PCDDs and PCDFs only would be seen to be conservative.

PCB-126 is the dl-PCB contributing most to the current dietary intake of PCDD/Fs and dl-PCBs and therefore dominates the TEQ level. In vitro studies with human cells, suggest that PCB-126 is much less potent in humans than suggested by the WHO_{2005} TEF of 0.1. The uncertainty in the relative potency of PCB-126 in humans, seems high and overall, the assessment is likely to be conservative.

Assuming a 100% bioavailability for PCDD/Fs and dl-PCBs from soil seems conservative, because there are indications that at least for some soils it could be as low as 50%.

A continuous daily ingestion of contaminated soil over three years represents a worst-case scenario which might only be relevant for a small group of toddlers.

3. **SCAHT does not recommend to introduce individual concentration values for PCDDs, PCDFs and dl-PCBs, neither a separate value for PCDDs and PCDFs, nor a separate value for dl-PCBs.**

   This is justified by the following reasons: (i) in the environment PCDDs, PCDFs and dl-PCBs are always present as chemical mixtures, albeit in varying compositions; (ii) PCDDs, PCDFs and dl-PCBs exert similar toxic effects; and (iii) binding to the aryl hydrocarbon receptor (AhR) is the common key initiating event; and (iv) the combined effect of complex PCDDs, PCDFs and dl-PCBs mixtures are considered additive. Although the toxic potency of the individual PCDDs, PCDFs and dl-PCBs varies greatly, Toxic Equivalency Factors (TEFs) have been developed to compare the toxicity of the various chemicals and to allow the combined effect of PCDDs, PCDFs and dl-PCBs to be assessed. TEFs express the concentrations of other PCDDs, PCDFs and dl-PCBs as a concentration equivalent to the most toxic dioxin 2,3,7,8-TCDD**.** For individual PCDDs, PCDFs or dl-PCBs, the 2,3,7,8-TCDD toxic equivalent quotient (2,3,7,8-TCDD TEQ) is the product of its concentration in an environmental mixture and its corresponding TEF. For a mixture of PCDDs, PCDFs and dl-PCBs the total TEQ is the sum of the individual 2,3,7,8-TCDD TEQs. This TEF/TEQ-approach provides a means for determining the toxicity of a mixture of PCDDs, PCDFs and dl-PCBs, in the absence of individual toxicity data. The method also supports the regulation of PCDDs, PCDFs and dl-PCBs as a group, instead of regulating each compound individually.

4. **SCAHT also recommends to identify the fraction of the total TEQ attributable to 2,3,7,8-TCDD (for which uncertainty is relatively low) and the one attributable to the sum of 29 PCDDs,**

PCDFs and dl-PCBs (for which uncertainty is somewhat higher).

This is justified by the following reasons: (i) 2,3,7,8-TCDD is used as the index substance in the TEF-approach; (ii) 2,3,7,8-TCDD is one of the most toxic dioxins; and (iii) the toxicological database on 2,3,7,8-TCDD is the most advanced in comparison to other PCDDs, PCDFs and dl-PCBs.

5. **SCAHT finally recommends to identify the fraction of the total TEQ attributable to the sum of the 12 dl-PCBs, although their toxicological potency is well below PCDDs and PCDFs.**

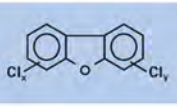
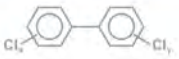
   The driver for this would be practical risk management considerations. Whereas PCDDs and PCDFs are natural contaminants, PCBs are not natural substances. PCDDs and PCDFs often represent diffuse sources of contamination, being naturally occurring by-products of combustion and various industrial processes that can travel long distances in the air. On the other hand, PCBs are exclusively anthropogenic chemicals that were manufactured in the past (with PCDFs as by-products), and whose manufacture is prohibited nowadays under the Stockholm Convention on POPs. However, PCB release into the environment still occurs. The large-scale disposal of electrical equipment and waste can be regarded as a point source of PCB contamination.

5 Introduction

The term 'dioxins' in principle refers to a group of 75 polychlorinated dibenzo-p-dioxin (PCDD) and 135 polychlorinated dibenzofuran (PCDF) congeners (**table 1**). However, only 7 of the 75 PCDD and 10 of the 135 PCDF congeners are thought to be of toxicological relevance for humans. The most toxic 'dioxin' is 2,3,7,8-tetrachloro-dibenzo-p-dioxin (2,3,7,8-TCDD) (**figure 1**). There is also a subset of polychlorinated biphenyls (PCBs) with dioxin-like properties, so-called dioxin-like polychlorinated biphenyls (dl-PCBs). They are referred to as dl-PCBs (UBA, 2017; EFSA, 2015; Chapter 1) or co-planar PCBs (EFSA, 2015; Chapter 1; BAG, 2008). Theoretically, there are 209 possible PCB congeners with 1 to 10 chlorine atoms (**table 1**); of these, there are 12 congeners which have dioxin-like toxic properties (dl-PCBs) namely the four non-ortho (PCB no: 77, 81, 126, 169) and the eight mono-ortho PCBs (PCB no: 105, 114, 118, 123, 156, 157, 167, 189) (table 3) with at least four chlorine atoms. The four non-ortho PCBs, with chlorine atoms only in meta- and para-positions (at least tetra-substituted PCB in the lateral positions) (PCB no: 077, 081, 126, 169) are more toxic than the eight mono-ortho PCBs (PCB no: 105, 114, 118, 123, 156, 157, 167, 189). The non-ortho PBC 126 is the most toxic dl-PCB (table 3, BAG, 2008; UBA 2017).

The environmental behavior and the toxicity of PCDDs, PCDFs and dl-PCBs is driven by the degree of chlorination. The physical and chemical properties such their density, fat solubility (lipophilia) and environmental persistence is increasing as the degree of chlorination increases. At the same time their volatility, water solubility and chemical reactivity is decreasing.

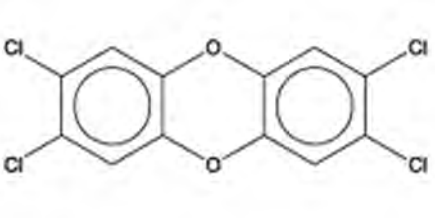
Table 1: Structure of PCDDs, PCDFs and dl-PCBs and their toxicological relevant congeners.

Name	Struktur	Anzahl Kongenere [1]	[2]
Polychlorierte Dioxine (PCDD)		75	7
Polychlorierte Furane (PCDF)		135	10
Polychlorierte Biphenyle (PCB)		209	12

[1] Anzahl theoretisch möglicher Kongenere
[2] Zahl der Kongenere mit hoher Toxizität

(Source: BAG, 2008)

Figure 1: "Seveso-Poison" - 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD)



(Source: de Souza Pereira, 2004)

6 Hazard

Human exposure to polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (dl-PCBs) has been associated with a range of toxic effects, including immunotoxicity, developmental and neurodevelopmental effects, changes in thyroid and steroid hormones, reproductive function and cancer. Developmental effects are the most sensitive health end-point, making children, particularly breastfed infants, the population most at risk (WHO, 2010).

6.1 Non-cancer effects

6.1.1 Acute effects

PCDDs, PCDFs and dl-PCBs are of low acute toxicity. Acute toxic effects in humans are only expected at very high doses e.g. by poisoning or accidents (UBA, 2017). Short-term exposure to high levels of PCDDs, PCDFs and dl-PCBs in occupational settings or following industrial accidents may cause skin lesions known as chloracne, which is persistent (WHO, 2010; BAG, 2008).

By far most toxicity studies have been performed using 2,3,7,8-tetrachlorodibenzo-p-dioxin. Acute effects of single high dose dioxin toxicity studies include wasting syndrome, associated with a severe weight loss and massive liver damage and metabolic disturbance, which can lead to death after several days to weeks (UBA, 2017; BAG, 2008).

6.1.2 Chronic effects

Longer-term environmental exposure causes a range of toxicity, including immunotoxicity, developmental and neurodevelopmental effects, and effects on thyroid and steroid hormones and reproductive function. The most sensitive life stage is considered to be the fetus or neonate. So far, guidance values have been based on reproductive and developmental effects (and not on carcinogenic effects).

6.2 Cancer

PCDDs, PCDFs and dl-PCBs are not genotoxic carcinogens but many of them are classified as human carcinogens (**table 2**). It is considered that the mechanism of carcinogenesis involves the AhR, meaning that there is a threshold for carcinogenicity[1].

The International Agency for Research on Cancer (IARC) classified 2,3,7,8-TCDD as carcinogenic to humans (Group 1) (IARC, 2017: IARC monograph, sup 7, 69 100F, 2012), and PCDDs other than

[1] Cancer is a complex multistep process, which can be divided into three phases: tumour initiation, promotion and progression. Different mechanism can lead to cancer. They can be grouped as genotoxic and non-genotoxic processes. Genotoxic substances cause DNA damage within a cell causing mutations[1], which may lead to cancer if not repaired correctly. While genotoxicity is often confused with mutagenicity, all mutagens are genotoxic but not all genotoxins are mutagenic.

For genotoxic carcinogens (that interact with DNA), it is commonly assumed that a small number of molecular events may evoke changes in a single cell that can lead to uncontrolled cellular proliferation and eventually to a clinical diagnosis of cancer. This toxicity of carcinogens is referred to as being "non-threshold" which implies that exposure levels without any risk for carcinogenic effects cannot be identified. For all carcinogens that do not directly damage DNA, there is a threshold level of exposure, or dose, below which no cancer results. Such substances, that are only carcinogenic after a certain level of exposure is achieved, are called threshold carcinogens.

2,3,7,8-TCDD unclassifiable as to carcinogenicity in humans because there is no evidence at present that it causes cancer in humans (Group 3) (IARC monograph, sup 7, 69, 1997). In addition, in 2012 IARC upgraded its 1997 classification for 2,3,4,7,8-pentachlorodibenzofuran from Group 3 to Group 1 (IARC monograph, 100F, 2012). Other PCDFs are classified in Group 3 (IARC monograph, 69, 1997). In 2016, all 12dl-PCBs where upgraded to Group 1 (IARC monograph, 100F, 2012) (IARC monographs).

Table 2: IARC cancer classification of PCDDs, PCDFs and dl-PCBs

CAS no	Agent	Group*	Volume	Year
001746-01-6	2,3,7,8-Tetrachlorodibenzo-para-dioxin	1	Sup 7, 69, 100F	2012
	Polychlorinated dibenzo-para-dioxins (other than 2,3,7,8- tetrachlorodibenzo-para-dioxin)	3	69	1997
057117-31-4	2,3,4,7,8-Pentachlorodibenzofuran (NB: Overall evaluation upgraded to Group 1 based on mechanistic and other relevant data)	1	100F	2012
	Polychlorinated dibenzofurans	3	69	1997
	Polychlorinated biphenyls, dioxin-like, with a Toxicity Equivalency Factor (TEF) according to WHO (PCBs 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, 189) (NB: Overall evaluation upgraded to Group 1 with strong supporting evidence from other relevant data)	1	107	2016

*Group 1: carcinogenic to humans; Group 3: not classifiable as to their carcinogenicity to humans

Agents Classified by the IARC Monographs, Volumes 1–119

http://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf

6.2.1 Experimental animal studies

Experimental animal studies indicate carcinogenicity in a range of species with multiple sites of tumors.

6.2.2 Epidemiology

Epidemiological studies in occupational settings also indicate human carcinogenicity at multiple sites.

Some of the most relevant epidemiological studies are from the 1976 Seveso cohort. The Seveso disaster was an industrial accident that occurred on July 10, 1976, in a small chemical manufacturing plant north of Milan/Italy. It resulted in the highest known exposure to 2,3,7,8-TCDD in residential populations, which gave rise to numerous scientific studies.

More recently the Russian Children's Study, a longitudinal, prospective children's cohort study designed to examine the association of dioxins, furans, polychlorinated biphenyls (PCB), arsenic, and lead on growth and pubertal development among 500 boys in Chapaevsk, Russia, confirmed that higher peripubertal serum TCDD concentrations and PCDD TEQs were associated with poorer semen parameters (EFSA, 2018; abstract).

6.3 AhR-mediated mechanism of toxicity

PCDDs, PCDFs and dl-PCBs have a range of biological effects; in particular, they can (UBA, 2017):

- Impact protein biosynthesis for metabolic enzymes of the cytochrome P450 family;
- Impact growth factors and cell differentiation factors and disturb normal cell signalling which could explain carcinogenic and teratogenic effects;
- Stimulate the release of growth-stimulating oncogenes which may explain their tumour-promoting properties;
- Block oestrogen receptors in the nucleus, which explains why female test animals are more sensitive to 2,3,7,8-TCDD than males;
- Inhibit the immune system; and
- React with intermediary metabolism receptors affecting the thyroid hormone thyroxine.

The biological and toxic effects of PCDDs, PCDFs and dl-PCBs are similar and are mediated by the activation of the Aryl Hydrocarbon Receptor (AhR) (EFSA, 2015; Chapter 1), a cellular protein involved in the regulation of biological responses to planar aromatic (aryl) hydrocarbons. It is a ligand-activated transcription factor which is located in the cytosol. It is normally inactive and bound to several co-chaperones (UBA, 2017). Upon ligand binding to PCDDs, PCDFs and dl-PCBs, the compound-AhR-complexes can move to the cellular nucleus and binds to specific base sequences, the so-called xenobiotic responsive elements (XRE). This leads to an increased transcription of genes which are under control of the XRE into the corresponding m-RNAs and finally to an increased biosynthesis of the corresponding proteins modifying cell function (de Souza Pereira, 2004, page 935, left column).

The mode of action of PCDDs, PCDFs and dl-PCBs is mainly based on the spatial and chemical similarity to the natural ligand of the AhR. Binding to and activation of the AhR is greatly favored by the 2,3,7,8-chlorine substitution; the PCDDs, PCDFs and dl-PCBs molecules encompass a rectangle, which fits to the ligand binding domain of the AhR (de Souza Pereira, 2004, page 935, left column). The greater the similarity of a given PCDDs, PCDFs or dl-PCB with the natural ligand of the AhR and the stronger the binding to the receptor, the stronger the effect of the compound. This is also the reason for the different toxicity equivalents of the different PCDDs, PCDFs and dl-PCBs (UBA, 2017).

Through interaction with the AhR, PCDDs, PCDFs and dl-PCBs can disturb the cellular balance leading to a disruption in normal cell function, cell growth and cell differentiation that ultimately causes adverse health effects. One important and well-defined interaction is the induction of the monooxygenase isozymes cytochrome P450 1A1 (CYP1A1) and P450 1A2 (CYP1A2). The induction of CYP1A1 and 1A2 is one of the most common indicators of AhR activation used in cellular bioassays and in in vivo studies (de Souza Pereira, 2004, page 935, left column). The toxicokinetic behavior of PCDDs, PCDFs and dl-PCBs in humans (and other primates) depends on three major properties: lipophilicity, metabolism and binding to the CYP1A2 in the liver. Lipophilicity controls the absorption and partitioning of PCDDs, PCDFs and dl-PCBs. Metabolism acts as the rate-limiting step of elimination and thus bioaccumulation. The induction of CYP1A2, like CYP1A1, is controlled by the AhR, and promotes the hepatic sequestration of these substances by the liver (de Souza Pereira, 2004, page 935, right column).

6.4 Hazard based approaches for mixture risk assessments: PCDDs, PCDFs and dl-PCBs

6.4.1 Mixture Toxicity Assessment: the TEF/TEQ-approach

In the environment, PCDDs, PCDFs and dl-PCBs are always present as chemical mixtures, albeit in varying compositions. PCDDs, PCDFs and dl-PCBs exert similar toxic effects: the combined effect of complex PCDDs, PCDFs and dl-PCBs mixtures are considered additive because they are mediated by the AhR (EFSA, 2015; Chapter 1).

The toxic potency of the individual PCDDs, PCDFs and dl-PCBs varies greatly (**table 3**). Therefore, Toxic Equivalency Factors (TEFs) have been developed to compare the toxicity of the various chemicals and to allow the combined effect of PCDDs, PCDFs and dl-PCBs to be assessed. TEFs express the concentrations of other PCDDs, PCDFs and dl-PCBs as a concentration equivalent to the most toxic dioxin 2,3,7,8-TCDD**.**

The index compound, 2,3,7,8-TCDD, is assigned a TEF of 1. PCDDs, PCDFs and dl-PCBs which are less toxic than 2,3,7,8-TCDD have TEFs below 1. For example, 1,2,3,4,7,8- hexachloro-dibenzo-p-dioxin is considered one tenth as toxic as TCDD and has therefore been given a TEF of 0.1.

TEFs are most appropriate for dioxin exposures via the oral exposure route. Generally, the ingestion pathway for 2,3,7,8-TCDD drives human health risk assessment (HHRA) and the TEFs can be used for evaluating the risk posed by the ingestion of soil, sediments, water, and food contaminated with 2,3,7,8-TCDD and PCDDs, PCDFs and dl-PCBs (CLU-IN.ORG, 2013). TEFs can be used for all effects mediated through AhR-binding by PCDDs, PCDFs and dl-PCBs, including cancer and non-cancer effects.

Underlying assumptions of the TEF method include: a) the toxicokinetics and the toxicodynamics of 2,3,7,8-TCDD and other PCDDs, PCDFs and dl-PCBs are similar; b) the dose-response curves of 2,3,7,8-TCDD and other PCDDs, PCDFs and dl-PCBs are similarly shaped; c) the AhR mediates most if not all of the biologic and toxic effects of 2,3,7,8-TCDD and other PCDDs, PCDFs and dl-PCBs; and d) the kinetics and potency of various PCDDs, PCDFs and dl-PCBs are generally similar between species.

The TEFs of the 2,3,7,8-substituted PCDDs and PCDFs and dl-PCBs related to 2,3,7,8-TCDD according to NATO/CCMS, WHO (1997) and WHO (2005) are listed in **table 3**. Over time, toxicity equivalency factors have been determined by different organizations and updated with new findings from different studies. An initial list was developed by the North Atlantic Treaty Organization in joint with the Committee on the Challenges of Modern Society (NATO/CCMS), these TEFs are called international TEFs (I-TEFs). This list focused on PCDDs, PCDFs. WHO further developed the list in 1997 to include the 12 dl-PCBs. The latest classification comes from the WHO in 2005.

In 2018 the CONTAM Panel noted that in the Russian Children's Study, no association was observed for dl-PCB- TEQ or the sum-TEQ of PCDD/Fs and dl-PCBs which might be explained by observations from in vitro studies with human cells, showing that PCB-126 is much less potent in humans than suggested by the WHO_{2005}-TEF of 0.1. PCB-126 is the dl-PCB contributing most to the current intake of PCDD/Fs and dl-PCBs, but also in the serum of boys from the Russian Children's Study (EFSA 2018, Page 7, para 6, last sentences). Based on these findings a reevaluation of the TEFs is indicated.

Table 3: TEFs for Human Health Risk Assessment of PCDDs, PCDFs and dl-PCBs

Name	Kürzel	I-TEF [2;3]	WHO_{97}-TEF [4]	WHO_{05}-TEF [5]
2,3,7,8-TC-Dibenzo-p-Dioxin	DD048	1	1	1
1,2,3,7,8-PeC-Dibenzo-p-Dioxin	DD054	**0.5**	1	1
1,2,3,4,7,8-HxC-Dibenzo-p-Dioxin	DD066	0.1	0.1	0.1
1,2,3,6,7,8-HxC-Dibenzo-p-Dioxin	DD067	0.1	0.1	0.1
1,2,3,7,8,9-HxC-Dibenzo-p-Dioxin	DD070	0.1	0.1	0.1
1,2,3,4,6,7,8-HpC-Dibenzo-p-Dioxin	DD073	0.01	0.01	0.01
OC-Dibenzo-p-Dioxin	DD075	**0.001**	0.0001	**0.0003**
2,3,7,8-TC-Dibenzofuran	DF083	0.1	0.1	0.1
1,2,3,7,8-PeC-Dibenzofuran	DF094	0.05	0.05	**0.03**
2,3,4,7,8-PeC-Dibenzofuran	DF114	0.5	0.5	**0.3**
1,2,3,4,7,8-HxC-Dibenzofuran	DF118	0.1	0.1	0.1
1,2,3,6,7,8-HxC-Dibenzofuran	DF121	0.1	0.1	0.1
1,2,3,7,8,9-HxC-Dibenzofuran	DF124	0.1	0.1	0.1
2,3,4,6,7,8-HxC-Dibenzofuran	DF130	0.1	0.1	0.1
1,2,3,4,6,7,8-HpC-Dibenzofuran	DF131	0.01	0.01	0.01
1,2,3,4,7,8,9-HpC-Dibenzofuran	DF134	0.01	0.01	0.01
OC-Dibenzofuran	DF135	**0.001**	0.0001	**0.0003**
3,3',4,4'-Tetrachlorobiphenyl	PCB077		0.0001	0.0001
3,4,4',5-Tetrachlorobiphenyl	PCB081		0.0001	**0.0003**
3,3',4,4',5-Pentachlorobiphenyl	PCB126		0.1	0.1
3,3',4,4',5,5'-Hexachlorobiphenyl	PCB169		0.01	**0.03**
2,3,3',4,4'-Pentachlorobiphenyl	PCB105		0.0001	**0.00003**
2,3,4,4',5-Pentachlorobiphenyl	PCB114		0.0005	**0.00003**
2,3',4,4',5-Pentachlorobiphenyl	PCB118		0.0001	**0.00003**
2',3,4,4',5-Pentachlorobiphenyl	PCB123		0.0001	**0.00003**
2,3,3',4,4',5-Hexachlorobiphenyl	PCB156		0.0005	**0.00003**
2,3,3',4,4',5'-Hexachlorobiphenyl	PCB157		0.0005	**0.00003**
2,3',4,4',5,5'-Hexachlorobiphenyl	PCB167		0.00001	**0.00003**
2,3,3',4,4',5,5'-Heptachlorobiphenyl	PCB189		0.0001	**0.00003**

Abweichungen zu den WHO_{97}-TEF sind fett markiert

(Source: BAG, 2008)

6.4.2 Toxic Equivalent (TEQ) calculations

The TEQ-approach provides a means for determining the toxicity of a mixture of PCDDs, PCDFs and dl-PCBs, in the absence of individual toxicity data. The method also supports the regulation of PCDDs, PCDFs and dl-PCBs as a group, instead of regulating each compound individually.

- **For individual PCDDs, PCDFs or dl-PCBs**, the 2,3,7,8-TCDD toxic equivalent quotient (2,3,7,8-TCDD TEQ) is the product of its concentration in an environmental mixture and its corresponding TEF.
- **For a mixture of PCDDs, PCDFs and dl-PCBs** the total TEQ is the sum of the individual 2,3,7,8-TCDD TEQs.

The formula for calculating the exposure concentration for n PCDDs, PCDFs and dl-PCBs in a mixture, in 2,3,7,8-TCDD TEQ, is reproduced below (**equation 1**). Exposure to the ith individual PCDD, PCDF, or dl-PCB compound is expressed in terms of an equivalent exposure of 2,3,7,8-TCDD by computing the product of the concentration of the individual compound (C_i) and its assigned TEF_i. TEQ is then calculated by summing these products across the PCDDs, PCDFs and dl-PCBs present in the mixture.

This means that the TEF approach is based on the concept of dose addition, under which it is assumed that the toxicokinetics and toxicodynamics for all PCDDs, PCDFs and dl-PCBs are similar, and that the PCDDs, PCDFs and dl-PCBs act by a common toxic mode of action (i.e. for all PCDDs, PCDFs and dl-PCBs, effects are mediated through AhR-binding). Further, this approach assumes that toxicological interactions do not occur among the PCDDs, PCDFs and/or dl-PCBs within the environmental mixtures being assessed (e.g., synergism and antagonism do not occur) (CLU-IN.ORG, 2013).

Equation 1: TEQ calculation for exposure levels of *n* PCDDs, PCDFs and dl-PCBs in a mixture

$$TEQ = \sum_{i=1}^{n} (C_i \times TEF_i)$$

- C_i *Individual TCDD or DLC concentration in environmental media.*
- TEF_i *Toxicity Equivalence Factor assigned for TCDD or the DLC.*
- TEQ *TCDD toxicity equivalence.*

DLC = Dioxin like compounds = PCDDs, PCDFs and dl-PCBs.

Nota Bene: the TEFs used in the European Union (EU) legislation, by the European Food Safety Authority (EFSA) and by a number of other authorities are those set by the World Health Organization (WHO); therefore, the resulting TEQs are referred to as WHO-TEQs (EFSA, 2015, Chapter 1).

7 Health-Based Guidance Values

7.1 Historical development of HBGVs

As indicated in **table 4**, different organizations have undertaken Human Health Risk Assessments (HHRA) of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (dl-PCBs), and further derived HBGVs (EFSA, 2018; chapter 1.3.3, pages 23-27). They are mainly based on 2,3,7,8-TCDD data but the conclusions have then been extended to cover other PCDDs, PCDFs and dl-PCBs as well, based on the assumption that the toxic effects are mediated by the Aryl Hydrocarbon Receptor (AhR).

Over the years HBGVs were set consistently lower and epidemiological data were given preference when deriving HBGVs. All derived HBGVs are very low (pg-range). At the higher end the EU SCF, and WHO/JECFA HBGVs are very similar (2 and 2.3 pg WHO_{1998} TEQ/kg bw per day, respectively) just as at the lower end the US EPA recommended value for 2,3,7,8-TCDD of 0.7 pg/kg bw per day resembles the most recent EFSA CONTAM recommended value of 0.3 pg/kg bw per day.

Table 4: Historical development of HBGVs

Chronology	Organization	Health-based Guidance Value (HBGV)	Conversion to TDI
1990	WHO	TDI: 10 pg I-TEQs/kg bw/d	10 pg I-TEQ/kg bw/d
1998	WHO	TDI: 1–4 pg I-TEQs/kg bw/d	1-4 pg I-TEQ/kg bw/d
2001	EU SCF	TWI: 14 WHO_{1997} TEQs pg/kg bw/wk	2 pg WHO_{1997} TEQ/kg bw/d
2001	WHO/JECFA	PTMI: 70 pg WHO_{1997} TEQs/kg bw/month	2.3 pg WHO_{1997} TEQ/kg bw/day
2012	US EPA	RfD_{oral}: 0.7 pg WHO_{2005} TEQs/kg bw/d	0.7 pg WHO_{2005} TEQs/kg bw/d
2018	EFSA CONTAM	TWI = 2.0 WHO_{2005} TEQs pg/kg bw/wk	0.3 pg WHO_{2005} TEQ/kg bw/day

In 2015, EFSA examined the approaches taken by different organizations so far for establishing HBGVs in their risk assessment on dioxins and dl-PCBs (EFSA, 2015). Major differences in the HHRA approaches were related to:

- **Use of animal versus epidemiological studies as key studies.**

  EU SCF and WHO/JECFA based the derivation of the HBGV on experimental animal studies, the US EPA selected human data.

  In 2001 EU SCF and WHO/JECFA discussed human studies in which subtle neurobehavioral effects and changes in circulating hormone levels in newborn infants and children were reported to be associated with their mothers' exposure to dioxins and/or PCBs, but these studies were considered as not being critical in the derivation of the tolerable intake. Reproductive effects were considered as the most critical effects. Studies of both rats and humans showed a decreased sperm quality, the effect in rats was observed after in utero exposure and in humans after exposure during childhood. EU SCF and WHO/JECFA gave higher priority to results obtained after in-utero exposure because it also covers early exposure during embryonic and fetal development. Therefore, they favored animal data over epidemiological studies. EU SCF and WHO/JECFA concluded that the critical studies for derivation of HBGV were animal studies (**table 6**), and the most critical effects were adverse effects in the reproductive system observed in developmental toxicity studies in rats (**table 6**).

- **Use of different uncertainty factors (UF) to compensate for missing NOAEL.**

  To extrapolate from a LOAEL to a NOAEL in a pivotal study an UF of 3 was applied by the EU SCF and JECFA as the LOAEL observed in a pivotal study was considered to be close to the NOAEL observed in another animal study which was however not considered to be pivotal. In the same context US-EPA applied an UF of 10 for extrapolation from a LOAEL in the absence of a NOAEL.

  The EU Scientific Committee on Food (EU SCF) has derived a Tolerable Daily Intake (TDI) for PCDDs, PCDFs and dl-PCBs of 2 pg WHO_{1997} TEQ/kg bw per day mainly based on adverse effects in the reproductive system observed in developmental toxicity studies in rats treated with 2,3,7,8-TCDD (**table 6**). The EU SCF used both the no-observed-adverse-effect level (NOAEL) for decreased anogenital distance from the study provided by Ohsako et al. (2001) and the lowest-observed-adverse-effect level (LOAEL) for decreased sperm production and altered sexual behavior in male offspring from the study provided by Faqi et al. (1998) in deriving a tolerable intake for 2,3,7,8-TCDD, using a body burden approach to calculate the equivalent estimated human daily intakes (EHDIs). To compensate for the lack of a clear NOAEL for the critical toxicological endpoint

of decreased sperm production and altered sexual behavior in male offspring reported by Faqi et al. (1998) EU SCF introduced an additional uncertainty factor of only 3, arguing that the LOAEL in the key studies was close to a NOAEL observed in another animal study which however, was not considered as a key study. In contrast, the US EPA routinely applies a default uncertainty factor of 10 for extrapolation from a LOAEL in the absence of a NOAEL.

The Joint FAO/WHO Expert Committee on Food Additives (WHO/JECFA) also in 2001 established a provisional tolerable monthly intake (PTMI) of 70 pg WHO_{1997} TEQ/kg bw for PCDDs, PCDFs and dl-PCBs. Converted to a tolerable daily intake, this equates to a dose of 2.3 pg WHO_{1997} TEQ/kg bw/day, comparable with the group TDI of 2.0 pg WHO_{1997} TEQ/kg bw/day from EU SCF, and the basis for its derivation is similar. JECFA calculated the same average maternal and fetal body burdens as those established by EU SCF after a single dose (Ohsako et al., 2001) and repeat doses of 2,3,7,8-TCDD to pregnant rats. The Committee assessed the same studies as EU SCF and concluded that a tolerable intake could be established for 2,3,7,8-TCDD on the basis of the assumption that there is a threshold for all effects, including cancer. Thus, they considered the studies summarized in table 6 to determine the NOAELs and LOAELs, which were provided by the studies of Ohsako et al. (2001) and Faqi et al. (1998) respectively. Following toxicokinetic conversion, these studies give maternal body-burden LOAELs and NOAELs for effects on male offspring of 25 ng/kg bw and 13 ng/kg bw, respectively. WHO/JECFA used the same rationale as the EU SCF to conclude that an uncertainty factor of 9.6[2] should be applied to the LOAEL or 3.2 to the NOAEL, resulting in a range of PTMIs from 40-100 pg per kg bw per month. The Committee chose 'the mid-point of this range' 70 pg per kg bw per month as the PTMI.

- **Use of different modeling approaches to derive critical effect levels.**

  The EU SCF and WHO/JECFA applied a body burden one-compartment kinetics approach to derive an HBGV from rat data, whereas US EPA applied more complex PBPK modelling of blood levels estimated from epidemiology studies. Overall, this resulted in the reference dose set by US-EPA (0.7 pg/kg bw per day) being threefold lower than the EU SCF TWI (14 pg WHO_{1997} TEQ/kg bw, or 2 pg/kg bw per day converted to a tolerable daily basis) or the JECFA PTMI (70 pg WHO_{1997} TEQ /kg bw/month, or 2.3 pg WHO_{1997} TEQ/kg bw per day converted to a tolerable daily basis).

  In the most recent evaluation, the EFSA CONTAM panel used refined toxicokinetic models. The models evaluated in the EFSA 2018 assessment were the rat and human models previously published by Emond and colleagues (Emond et al., 2006, 2017) and the so-called concentration- and age-dependent model (CADM), developed by Carrier et al. (1995), further optimized by Aylward et al. (2005) and adapted by Ruiz et al. (2014) to include a growth curve and a breastfeeding period (EFSA 2018; Chapter 2.2.1.1, page 30, third paragraph).

7.1.1 WHO 1998

The WHO held a consultation in May 1998 on the assessment of the health risk of dioxins and re-evaluation of the existing tolerable daily intake (TDI) (WHO, 1998). At that stage, the TDI was 10 pg I-TEQ/kg bw per day, established during a WHO meeting in 1990. WHO considered a number of animal studies with TCDD published since then as the basis for the new TDI, showing a range of effects in rats or monkeys, including neurobehavioral toxicity, immunotoxicity, reproductive toxicity and endometriosis. The accumulated amount of TCDD in the animal rather than the administered dose was taken as the starting point for the extrapolation of toxicity across species. Therefore, the animal body burdens corresponding to these effects were estimated, however, without providing any further details on the calculations. These body burdens ranged from 28 to 73 ng/kg bw (**table 5**). These levels served

[2] Applying an UF of 3 for no-observed-adverse-effect level (NOAEL) to LOAEL extrapolation and a factor of 3.2 for interindividual variation in toxicokinetics within the human population

as a reference point for the calculation of the chronic daily intake which would be expected to lead to similar body burdens in humans. The estimated daily intakes (EDIs) were calculated with the aid of a one-compartmental kinetic model, based on the following equation:

Equation 2: **One compartmental kinetic model-based estimation of human daily intake**

intake (ng/kg bw per day) 1⁄4 (body burden (ng/kg bw) x ln(2)) / ($t_{1/2}$(days) x f)

Taking the animal body burdens shown in **table 5**, an elimination half-life ($t_{1/2}$) in humans of 7.5 years and an assumed fraction absorbed from food (f) to be 0.5, an EDI range of 14–37 pg TCDD/kg bw per day was calculated. Applying a composite uncertainty factor (UF) of 10, the EDI range then resulted in a **TDI of 1–4 pg TEQ/kg bw per day (rounded figures).**

Table 5: Critical adverse effects observed in animal studies used by WHO to derive a TDI

Study	Endpoint	Exposure (LOAEL)	Body burden[(a)] (ng/kg bw)	Related human EDI[(e)] (pg/kg bw per day)
Schantz and Bowman (1989)	Rhesus monkey, neurobehavioural toxicity in offspring (decreased learning)	~ 160 pg/kg bw per day	42[(b),(d)]	21
Gray et al. (1997a), Mably et al. (1992a)	Rat, decreased sperm count in offspring	64 ng/kg bw[(c)]	28[(d)]	14
Gray et al. (1997b)	Rat increased genital malformations in offspring	200 ng/kg bw[(c)]	73	37
Gehrs et al. (1997), Gehrs and Smialowicz (1999)	Rat immune suppression in offspring	100 ng/kg bw[(c)]	50	25
Rier et al. (1993)	Rhesus monkey, endometriosis	~ 160 pg/kg bw per day	69[(b)]	35

Body burdens of TCDD were estimated from the applied oral doses

bw: body weight; EDI: estimated daily intake; LOAEL: lowest-observed-adverse-effect level; TCDD: 2,3,7,8-tetrachlorodibenzo-p- dioxin; TDI: tolerable daily intake.

(a): Increment to background, reported to be 4 ng/kg (TEQ) for rats and mice.

(b): Body burden at time of delivery.

(c): Single oral dose.

(d): Maternal body burden.

(e): Estimated chronic Daily Intake.

Regarding the dietary exposure, WHO indicated a daily intake of PCDD/Fs in the order of 1–3 pg I-TEQ/kg bw per day for a 60-kg adult based on the available information derived from food surveys from industrialized countries. This value would be greater by a factor of 2–3 if dl-PCBs were to be considered. WHO recognized that ‘certain subtle effects may be occurring in some sections of the general populations of industrialized countries at current intake levels (2–6 I-TEQ pg/kg bw per day for PCDD/Fs) and body burdens (4–12 I-TEQ ng/kg bw), but found it tolerable on a provisional basis as these reported subtle effects were not considered overtly adverse and there were questions as to the contribution of non-dioxin-like compounds to the observed effects’.

7.1.2 EU SCF 2001

In 2000, the EU SCF published its opinion on the risk assessment of dioxins and dl-PCBs in food, which was then updated in 2001 (EU SCF, 2001). The EU SCF took as a basis the WHO (1998) assessment but also considered studies published since then. Human studies were also evaluated but, as in the previous WHO evaluations, were not used for deriving an HBGV. Starting with the same critical animal toxicity studies as selected by WHO (**table 5**), EU SCF explicitly recalculated animal lowest- observed-adverse-effect level (LOAEL) body burdens in the rat and the monkey, with corresponding estimated human daily intakes (EHDIs) ranging from 12.5 to 37 pg TCDD/kg bw. Applying an UF of 3 for no-observed-adverse-effect level (NOAEL) to LOAEL extrapolation and a factor of 3.2 for interindividual variation in toxicokinetics within the human population resulted in a TDI ranging from 1 to 3 pg/kg bw per day (TEQ, rounded figures). It was concluded that the lower end of the range, i.e. 1 pg/kg bw per day, was to be considered as a temporary TDI (t-TDI). Recognizing that the compounds like TCDD and related compounds have very long half-lives in the human body, the EU SCF found it more appropriate to express the t-TDI on a weekly rather than a daily basis, thereby arriving at a t-TWI of 7 pg/kg bw per week (TEQ).

However, new studies revealed a particular sensitivity of the gestation day 15 (GD15) rat embryo to TCDD (Faqi et al., 1998; Ohsako et al., 2001). Furthermore, studies by Hurst et al. (2000a,b) revealed a relatively high exposure of the fetus after a single acute maternal GD15 dose when compared to a chronic maternal exposure. This was corrected by applying a factor of 2.6 on a single GD15 dose when estimating the corresponding maternal animal body burden (**table 6**). For example, using 60% absorption of the 64 ng/kg LOAEL of the Mably et al. (1992) study resulted in a corresponding maternal body burden of 64 x 0.6 = 38.4 ng/kg bw following treatment with a single high dose. However, a 2.6-fold higher maternal body burden, i.e. 100 ng/kg bw, is required to obtain the same exposure of the embryo after chronic exposure. In a similar way, body burdens were calculated for the other studies.

Based on these body burdens and using the same assumptions as WHO (1998) on absorption from food (50%) and human half-life (7,5 years), the EU SCF calculated an EHDI of 10 pg/kg bw per day for the body burden (NOAEL) estimated for the Ohsako et al. (2001) study. Applying an UF of 3.2 for interindividual differences in toxicokinetics, then resulted in a TDI of 3 pg/kg bw per day. For the Faqi et al. (1998) study, applying an UF of 3 x 3.2 on the EHDI derived from the estimated body burden (LOAEL) resulted in a **TDI of 2 pg/kg bw per day** (TEQ). As the latter study was performed with the most sensitive rat strain (Wistar), 2 pg/kg bw per day (TEQ) was considered as the TDI. Again, recognizing that TCDD and related compounds have very long half-lives in the human body, the EU SCF found it more appropriate to express the TDI on a weekly rather than a daily basis, thereby arriving at a **tolerable weekly intake (TWI) of 14 pg/kg bw per week** (TEQ). The designation ‘temporary’ was removed from the TWI because the new studies provided a firm basis for the evaluation of the pivotal rat toxicity studies.

Table 6: Key studies used by EU SCF and WHO/JECFA to derive HBGVs

Study	Endpoint	NOAEL	LOAEL	Estimated maternal steady state body burden[a] (ng/kg b.w.)	Associated EHDI (pg/kg b.w./day)
Mably et al. (1992)	Holzman rats: Decreased sperm count in male offspring		64 ng/kg b.w. single bolus dose by gavage	100[b]	50
Gray et al. (1997)	Long Evans rats: Accelerated eye opening and decreased sperm count in male offspring		50 ng/kg b.w. single bolus dose by gavage	80[b]	40
Faqi et al. (1998)	Wistar rats: Decreased sperm production and altered sexual behaviour in male offspring		Maintenance of 25 ng/kg b.w. by subcutaneous injections	40[b]	20
Ohsako et al. (2001)	Holzman rats: Decreased anogenital distance in male offspring	12.5 ng/kg b.w. single bolus dose by gavage		20[c]	10
			50 ng/kg b.w. single bolus dose by gavage	80[c]	40

b.w.: body weight; GD: gestational day; LOAEL: lowest-observed-adverse-effect level; NOAEL: no-observed-adverse-effect level.
(a): Increment over background. Estimated background body burden from feed in rats is approximately 4 ng TEQ/kg b.w. (assumed to be due to background contamination of the feed).
(b): Composite value resulting from pseudo steady state body burden and acute body burden on GD 15.
(c): Maternal body burden at GD 16.

(Source: estimated steady state body burdens of 2,3,7,8-TCDD and associated estimated human daily intakes (EHDI) at NOAEL and LOAELs in key studies adapted from EU SCF, 2001).

The EU SCF based its exposure assessment on the occurrence data compiled by the Scientific Cooperation (EU SCOOP) Task 3.2.5., which included national food contamination data and dietary exposure assessments from ten European countries. The average dietary intake estimates of PCDD/Fs for adults of various European countries ranged from 0.4 to 1.5 pg I-TEQ/kg bw per day, and of dl-PCBs ranged from 0.8 to 1.5 pg PCB-TEQ/kg bw per day. The PCB-TEQs in this exposure assessment were calculated with the PCB-TEFs published by Ahlborg et al. (1994). As a result, the total dietary intake of PCDD/Fs and dl-PCBs was estimated to range from 1.2 to 3.0 pg WHO-TEQ/kg bw per day. The EU SCF concluded that a considerable proportion of the European population would exceed the group TWI of 14 pg WHO-TEQ/kg bw, noting that exceeding it slightly does not necessarily mean that there is an appreciable risk to the health of individuals, but exposure above this tolerable weekly intake leads to an erosion of the protection embedded in the group TWI.

7.1.3 JECFA 2001

In 2001, JECFA evaluated the risk associated with the presence of dioxins and coplanar PCBs in food (FAO/WHO, 2002). JECFA took into account the previous WHO (1998) evaluation and new studies published afterwards. The Committee chose the same critical studies as the EU SCF (2000, 2001), i.e. the study by Faqi et al. (1998) and the study by Ohsako et al. (2001) but used both studies to derive an HBGV. However, it decided to use a factor of 1.7 instead of 2.6 to correct for the single dose instead of chronic treatment in these studies resulting in lower reference points. It subsequently applied the same 'safety' factors of 3 and 3.2 as the EU SCF (2000, 2001). JECFA, however, considered that the tolerable intake should be assessed over a period of at least 1 month, and therefore, established provisional

tolerable monthly intakes (PTMIs) of 40 and 100 pg WHO_{1997}-TEQs/kg bw, from which the midpoint of **70 pg WHO_{1997} TEQs/kg bw was chosen as the PTMI**. JECFA estimated the dietary intake of PCDD/Fs using the GEMS/Food regional diets, and national food consumption data. Estimates using the later consumption data were considered more reliable. For PCDD/Fs, the median estimates ranged from 33 to 42 pg WHO_{1997} TEQ/kg bw per month, while for dl-PCBs it ranged from 9 to 47 pg WHO_{1997} TEQ/kg bw per month.

7.1.4 US EPA 2012

In 2012, the US-EPA published its reanalysis of key issues related to dioxin toxicity, focusing on the non-cancer endpoints (US-EPA, 2012). It established an oral reference dose (RfD) of 0.7 pg TCDD/kg bw per day, defining the oral RfD as 'an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime'. The US-EPA evaluated human and experimental animal studies, and based the risk assessment on data from two studies on the adverse effects in the cohort exposed as a result of the Seveso (Italy) incident in 1976 (see **table 7**). It was shown that men exposed in childhood showed a reduced sperm count and motility (Mocarelli et al., 2008). TCDD levels were measured in blood taken from the boys within one year after the incident. The study indicated a LOAEL of 68 pg/g fat which was used as one of the points of departure (POD). The other POD was based on elevated levels of thyroid-stimulating hormone (TSH) observed in 3-day-old neonates born to mothers from Seveso exposed during the incident (Baccarelli et al., 2008). In this case, TCDD concentrations measured in maternal blood were used to establish a LOAEL of 235 pg/g fat for the effect on TSH in the neonates. The maternal blood samples were taken 16.5 to 22 years after the incident, and TCDD levels higher than 10 pg/g fat were extrapolated to the time of conception. For TSH levels in blood of neonates, a benchmark of 5 IU/mL established by WHO for medical follow-up for potential congenital hypothyroidism was used as a cut-off. Using a physiologically based pharmacokinetic (PBPK) model for humans, the daily TCDD exposures leading to these critical blood concentrations in either boys or mothers were derived. In the case of the boys, it was argued by US-EPA that it was unclear whether the effects on sperm were due to the peak in the blood just after the incident, or the average blood levels during the years before the boys reached the age of 10 (on average 3.5 years). Therefore, both the initial peak level of TCDD and the level some years after the incident were estimated and the average taken as the POD. For both the effects on sperm and TSH, the PBPK model showed that the levels corresponding to the PODs would be obtained with a continuous daily intake of 20 pg/kg bw per day. An UF of 30 (10 to derive a NOAEL and 3 for intraspecies differences) was used to derive the above-mentioned oral RfD of 0.7 pg/kg bw per day. TCDD is considered as the index chemical for other PCDD/Fs and dl-PCBs, using the TEFs to derive the TEQ level. US-EPA did not estimate the exposure to PCDD/Fs and dl-PCBs.

Table 7: Key studies used by US EPA, 2012 to derive HBGVs

Study	LOAEL/NOAEL (pg/kg b.w. per day)	Critical effects observed
Alaluusua et al. (2004)	406[a] (NOAEL)	Dental effects in adults exposed to TCDD in childhood
Baccarelli et al. (2008)	20[b] (LOAEL)	Elevated TSH in neonates; exposure *in utero*
Mocarelli et al. (2008)	20[c] (LOAEL)	Decreased sperm count and motility in men exposed to TCDD in childhood

b.w.: body weight; LOAEL: lowest observed adverse effect level; NOAEL: no observed adverse effect level; TCDD: 2,3,7,8-tetrachlorodibenzo-p-dioxin; TSH: thyroid-stimulating hormone.

(a): Mean of peak exposure (655 pg/kg b.w. per day) and average exposure over 10-year critical window (156 pg/kg b.w. per day).

(b): Maternal exposure corresponding to neonatal TSH concentration exceeding 5 µU/mL.

(c): Mean of peak exposure (32 pg/kg b.w. per day) and average exposure over 10-year critical window (0.80 pg/kg b.w. per day).

7.1.5 EFSA CONTAM 2018

In 2018 the EFSA Panel on Contaminants in the Food Chain (CONTAM) set a new TWI for PCDDs, PCDFs and dl-PCBs in food of 2 pg WHO_{2005} TEQ/kg bw per week which equates to 0.3 pg WHO_{2005} TEQ /kg bw per day, a value that is 7-times lower than the HBGV previously established by the EU SCF in 2001. The main reasons for decreasing the HBGV were the availability of new epidemiological data (Russian children's study) application of more refined modelling techniques for predicting internal human exposure and different selection criteria for selecting the most relevant animal studies.

The EFSA CONTAM HHRA is driven by epidemiological data, considering the most recent epidemiological data from the Russian children's study (Mínguez-Alarcón et al., 2017). The Russian Children's Study is a longitudinal, prospective children's cohort study designed to examine the association of dioxins, furans, polychlorinated biphenyls (PCB), arsenic, and lead on growth and pubertal development among 500 boys in Chapaevsk, Russia. The study confirmed that higher peripubertal serum TCDD concentrations and PCDD TEQs were associated with poorer semen parameters (EFSA, 2018; abstract). Peripubertal boys at 8 to 9 years of age, and their mothers, were recruited between 2003 and 2005. The boys were followed until 21 years of age and provided semen samples to assess markers of fertility in relation to early life environmental exposures. In the Russian Children's Study, an association between decreased sperm concentrations and increasing serum levels of TCDD, PCDD-TEQ and PCDD/F-TEQ was observed. A NOAEL serum level for PCDD/Fs of 7.0 pg WHO_{2005} TEQ/g fat at age 9 years was selected, based on the median level in the lowest quartile (EFSA 2018, summary, page 7, fourth paragraph).

A toxicokinetic model was used to estimate the daily intake leading to a serum level of 7.0 pg WHO_{2005}-TEQ/g fat at the age of 9 years in boys, taking into account breastfeeding for 12 months by mothers with similar exposure. In the calculations, the twofold higher dietary exposure of toddlers and other children was taken into account. The model includes the concentration-dependent distribution between the liver and body fat, the degradation in the liver and the direct loss via lipids in the faeces. It was estimated that a level in human milk of 5.9 pg TEQ/g fat, resulting from the constant exposure of mothers to 0.25 pg TEQ/kg bw per day, and subsequent exposure via food to 0.5 pg TEQ/kg bw per day, would result in the NOAEL serum level of 7.0 pg WHO2005-TEQ/g fat at the age of 9 years (EFSA, 2018; summary, page 7, fifth paragraph).

Taking the uncertainties into account, a TWI of 2 pg WHO_{2005} TEQ/kg bw per week was established. The CONTAM Panel decided to base the HBGV on a weekly basis since this is not expected to result in a critical increase in levels in serum (EFSA 2018, summary, page 7, sixth paragraph).

EFSA CONTAM used animal data for supporting evidence. However, concerning adverse effects in experimental animals, the CONTAM Panel selected only those studies that could potentially show effects at lower body burdens than the one used as basis for the tolerable weekly intake (TWI) set by the Scientific Committee on Food (EU SCF) in their assessment in 2001 (lowest-observed-adverse-effect level (LOAEL) of 40 ng/g bw). The CONTAM Panel decided to focus on studies in which only TCDD had been dosed to the animals. The studies on rodents confirmed that developmental effects were seen at body burdens in a similar range as those that were the basis for the previous risk assessment by the EU SCF. In rats the adverse effects at such low body burdens were reduced sperm production (LOAEL body burden 25 ng/kg bw), delayed puberty development (LOAEL body burden 42–50 ng/kg bw), altered bone parameters (no-observed-adverse-effect level (NOAEL) body burden 28 ng/kg bw) and hepatopathy (NOAEL body burden 26 ng/kg bw). In mice, the lowest extrapolated body burden at the NOAEL was 9 ng/kg bw, based on embryo loss. Studies in primates treated during gestation and lactation showed dental effects and effects on sperm concentration at high dose (EFSA, 2018; summary, page 5, second paragraph).

8 Exposure

8.1 Background information

8.1.1 Environmental sources

PCDDs and PCDFs have never been intentionally produced, but their formation is to some degree technically unavoidable. Any source of organic materials in the presence of chlorine will generate PCDDs and PCDFs during combustion. PCDDs and PCDFs can be generated by natural events, such as volcanic eruptions and forest fires but they may also be generated as impurities in industrial chlorine chemistry products such as the manufacture of chlorophenols and phenoxy herbicides, chlorine bleaching of paper pulp and smelting. PCDDs and PCDFs are also generated through the incineration of waste (domestic, industrial and hospital) at low to moderate temperatures; guidance has been developed to identify and quantify releases from various incineration processes. The use of modern incineration technology destroys PCDDs, PCDFs, whereas inadequate incineration creates them (WHO, 2010).

8.1.2 Anthropogenic sources

PCBs are not natural substances. They were previously produced in large quantities because they have excellent technical characteristics. They are chemically and thermally stable and are good electrical insulators. Therefore, they have been widely used in oils for capacitors, transformers and as lubricants in the last century. They have also been used in flame retardant paints and as softeners in permanently elastic jointing materials. Until 1990, more than one million tons were produced worldwide, of which almost half have entered the environment. Although today PCB manufacture is prohibited under the Stockholm Convention on POPs, their release into the environment still occurs from improper disposal of old equipment, leaky landfills and the like. Therefore, PCBs can still reach the environment and thus the food chain (BAG, 2008).

8.1.3 Environmental fate

PCDDs, PCDFs and dl-PCBs are ubiquitous and although formation of these chemicals is local, environmental distribution is global because these compounds can travel long distances in the air. PCDDs, PCDFs and dl-PCBs persist in the environment and accumulate in biological systems especially in fat tissue (UBA, 2017). The environmental behavior and the toxicity of PCDDs, PCDFs and dl-PCBs is driven by the degree of chlorination. The physical and chemical properties such their density, fat solubility (lipophilia) and environmental persistence is increasing as the degree of chlorination increases. At the same time their volatility, water solubility and chemical reactivity is decreasing.

8.1.4 Inhalation exposure

Entry into the air is heavily regulated through strict emission restrictions for combustion plants and production bans. Therefore, levels of PCBs, PCDDs and PCDFs in air are generally very low, except in the vicinity of inefficient incinerators. However, atmospheric deposit of even small amounts of PCDDs, PCDFs and dl-PCBs can contaminate water sources, aquatic sediments and soils.

8.1.5 Exposure from contaminated soil

Whether or not ingestion of contaminated soil presents a health risk largely depends on the bioavailability of PCBs, PCDDs and PCDFs in soil. In 2010, US EPA published a report titled “Bioavailability of Dioxins in Soil and Soil-Like Materials” which presents a summary of the published

literature and analysis of the available data regarding the relative bioavailability (RBA)[3] of PCDDs and PCDFs in soil. In 2011, this report was peer reviewed by three subject matter experts (US EPA, 2011). There was consensus among the three reviewers that the relative bioavailability of PCDDs and PCDFs in soil is less than 100%. There was also agreement that congener chlorine content will influence the RBA of the congeners. Two of the three reviewers agreed that there were too few studies data to support a nationally-applicable value for RBA for use in risk assessments and therefore no RBA-value < 100% could be recommended. The third reviewer recommended assigning a national RBA value of 75% as a compromise, arguing that the few studies which have been carried out have consistently shown RBA of around 50% (US EPA, 2011). EMPA cites case studies from the scientific literature where soil dioxin concentrations of up to 100'000 ng I-TEQ/kg dry matter did not result in significant increases in blood fat levels in children and therefore concludes that exposure to highly contaminated soil does not present a substantial additional body burden (EMPA, 2009[4]). As a first tier approach the SCAHT applies a conservative approach and uses an RBA of PCDDs, PCDFs and dl-PCBs in soil of 100% because of the limited number of soil samples for which RBA data are available, to cover variability across soil types and for PCBs, PCDDs and PCDFs mixtures of varying composition.

8.1.6 Dietary exposure

Concentrations of PCBs, PCDDs and PCDFs in drinking-water and surface water are also very low, because they are poorly soluble in water. Although dietary exposure to PCBs, PCDDs and PCDFs has declined substantially in the last three decades because of emission controls and the discontinuation of production and use of dl-PCBs (EFSA, 2015; Chapter 1), they are still ubiquitous in the environment today and they continue to be a matter of public concern. Most human exposure is through ingestion of contaminated food with fatty foods, such as dairy products, some fish, meat and shellfish showing higher concentrations. PCDDs, PCDFs and dl-PCBs persist in fatty tissue, with typical half-lives in humans in excess of 7 years (WHO, 2010).

8.2 Dietary exposure assessments

In its 2018 report EFSA estimated the chronic dietary intake based on dietary surveys for 68 population groups across 17 European Member States, covering seven age classes (**table 8**). Exposure to the sum of PCDD/Fs and dl-PCBs was estimated considering occurrence data for the period 2008–2010.

The UB average exposure (calculated with WHO_{2005}-TEFs, UB and LB was similar) ranged from 0.57 to 2.54 pg TEQ/kg bw per day (see table 8, Germany National Nutrition Survey II, mean in adolescents = 0.57; Finland DIPP, mean = 2.54 in toddlers) across dietary surveys, while the 95th percentile was between 1.2 and 9.9 pg TEQ/kg bw per day (see table 8, Hungary National Repr Surv, P95 in elderly = 1.2; Spain enKid, P95 = 9.9 in toddlers). **Toddlers and "Other children" were the age groups with the highest exposure** (average estimates ranging from 1.08 to 2.54 pg TEQ/kg bw per day) (see table

[3] Bioavailability is the amount of a contaminant absorbed into the body following skin contact, ingestion or inhalation. Relative bioavailability of a contaminant in soil is how much of a contaminant is absorbed from soil as compared to how much of that contaminant is absorbed from a reference exposure medium (e.g., food, water) that relates back to the toxicity value of the contaminant.

[4] Bodenbelastung: In der Umgebung des Stahlwerks liegen die meisten Werte bei 1 bis 2 ng I-TEQ/kg Trockensubstanz (TS); der höchste Messwert liegt bei 24.1 ng I-TEQ/kg TS. In einer gesamtschweizerischen Untersuchung von Dioxinen und PCB in Böden wurden Werte im Bereich von 1.1 to 11 ng I-TEQ/kg TS gemessen (Schmid et al., 2005). Im Vergleich dazu sind die meisten Messwerte in der Umgebung des Stahlwerks unauffällig; einige wenige liegen deutlich aber nicht massiv über den im Mittelland typischen Werten. In ähnlich gelagerten, in der Fachliteratur beschriebenen Fällen mit um mehrere Grössenordnungen höheren Bodenkonzentrationen (bis 100'000 ng I-TEQ/kg TS) konnte bei Kindern und weiteren besonders betroffenen Personen keine signifikante Erhöhung der Dioxingehalte im Blutfett beobachtet wer-den. Damit dürfte über diesen Aufnahmepfad auch in der vorliegenden Expositionssituation keine wesentliche Zusatzbelastung erfolgen.

8, Netherlands VCP kids, mean = 1.08 in "Other children"; Finland DIPP, mean = 2.54 in toddlers). Infants were less exposed than Toddlers and Other Children, with an estimated mean dietary intake of around 1.1 pg TEQ/kg bw per day (see table 8, Bulgaria, NUTRICHILD, mean = 1.17; Italy, INRANSCAI 2005 06, mean = 1.08), noting that human milk consumption was not taken into account in the estimation. **With these estimates, the percentage of individuals exposed above the EU SCF TWI of 14 pg TEQ/kg bw defined in 2001 was between 1.0 and 52.9%.**

'Fish and seafood' was the food category which contributed most (30–75%) to the total UB exposure in Adolescents, Adults, Elderly and Very Elderly population groups, followed by 'Meat and meat products' (9–34%) and/or 'Milk and dairy products' (7–25%). In Infants and Toddlers, the major contributor was the category 'Milk and dairy products' (28–50%), followed in Infants by 'Foods for infants and young children' (22–31%) and in Toddlers by 'Fish and seafood products' (11–36%) or 'Meat and meat products' (10–34%). In Other Children, the exposure profile varied, with 'Milk and dairy products', 'Meat and meat products' and 'Fish and other seafood products' as major contributors depending on the country surveyed (EFSA, 2018; pages 191-192).

Table 8: EFSA estimated dietary exposure to PCDDs, PCDFs and dl-PCBs for 2008-2010

Country	Survey acronym	N[(a)]	Mean[(b)]	P95[(c)]	Perc [IC_{95}][(d)]
		Infants			
Bulgaria	NUTRICHILD	860	1.17	3.0	16 [13.6; 18.5]
Italy	INRAN SCAI 2005 06	16	1.08	5.9	6.3 [0.2; 30.2]
		Toddlers			
Belgium	Regional Flanders	36	1.77	3.5	30.6 [16.4; 48.1]
Bulgaria	NUTRICHILD	428	2.53	5.8	53 [48.3; 57.8]
Finland	DIPP	497	2.54	8.0	38.8 [34.5; 43.1]
Germany	DONALD 2006	92	1.84	4.9	26.1 [17.5; 36.3]
Germany	DONALD 2007	85	1.54	3.3	17.6 [10.2; 27.4]
Germany	DONALD 2008	84	1.59	4.3	20.2 [12.2; 30.4]
Italy	INRAN SCAI 2005 06	36	2.34	5.1	44.4 [27.9; 61.9]
Netherlands	VCP kids	322	1.25	2.6	11.5 [8; 15]
Spain	enKid	17	2.44	9.9	52.9 [27.8; 77.0]
		Other children			
Belgium	Regional Flanders	625	1.52	4.8	18.9 [15.8; 21.9]
Bulgaria	NUTRICHILD	433	2.33	6.3	43.9 [39.2; 48.6]
Czech Republic	SISP04	389	2.27	8.1	28 [23.6; 32.5]
Denmark	Danish Dietary Survey	490	1.95	4.3	32.7 [28.5; 36.8]
Finland	DIPP	933	2.49	6.5	42.8 [39.6; 45.9]
Finland	STRIP	250	1.27	3.6	18.8 [14; 23.6]
France	INCA2	482	2.37	5.3	52.9 [48.4; 57.4]
Germany	DONALD 2006	211	1.32	3.5	12.3 [7.9; 16.8]
Germany	DONALD 2007	226	1.29	2.9	11.9 [7.7; 16.2]
Germany	DONALD 2008	223	1.39	3.8	13 [8.6; 17.4]
Greece	Regional Crete	839	1.23	4.5	16.7 [14.2; 19.2]
Italy	INRAN SCAI 2005 06	193	2.15	5.7	26.4 [20.2; 32.6]
Latvia	EFSA TEST	189	1.13	3.8	12.2 [7.5; 16.8]
Netherlands	VCP kids	957	1.08	2.2	7 [5.4; 8.6]
Spain	enKid	156	2.03	7.0	28.8 [21.7; 36]

Spain	NUT INK05	399	2.27	7.0	32.6 [28; 37.2]
Sweden	NFA	1,473	1.29	3.3	15.3 [13.4; 17.1]
		Adolescents			
Belgium	Diet National 2004	584	0.65	2.3	6 [4.1; 7.9]
Cyprus	Childhealth	303	0.78	2.9	12.2 [8.5; 15.9]
Czech Republic	SISP04	298	1.67	5.8	19.1 [14.7; 23.6]
Denmark	Danish Dietary Survey	479	1.06	2.3	7.9 [5.5; 10.4]
France	INCA2	973	1.26	3.0	15.2 [13; 17.5]
Germany	National Nutrition Survey II	1011	0.57	1.6	3.3 [2.2; 4.4]
Italy	INRAN SCAI 2005 06	247	1.36	4.3	15.4 [10.9; 19.9]
Latvia	EFSA TEST	470	0.73	2.0	5.3 [3.3; 7.3]
Spain	AESAN FIAB	86	1.27	3.3	14 [7.4; 23.1]
Spain	enKid	209	1.41	5.4	15.3 [10.4; 20.2]
Spain	NUT INK05	651	1.31	4.0	16.9 [14; 19.8]
Sweden	NFA	1,018	0.81	2.3	7.7 [6; 9.3]
		Adults			
Belgium	Diet National 2004	1,304	0.82	2.8	9.2 [7.6; 10.8]
Czech Republic	SISP04	1,666	1.11	3.9	13.6 [11.9; 15.2]
Denmark	Danish Dietary Survey	2,822	0.95	2.0	5 [4.2; 5.8]
Finland	FINDIET 2007	1,575	1.12	3.7	17.3 [15.5; 19.2]
France	INCA2	2,276	1.18	2.6	13 [11.6; 14.4]
Germany	National Nutrition Survey II	10,419	0.79	2.9	8.9 [8.3; 9.4]
Hungary	National Repr Surv	1074	0.77	1.9	4 [2.8; 5.2]
Ireland	NSIFCS	958	0.89	2.2	7.2 [5.6; 8.8]
Italy	INRAN SCAI 2005 06	2,313	1.21	4.2	16.5 [15; 18]
Latvia	EFSA TEST	1,306	0.86	3.1	11.5 [9.8; 13.2]
Netherlands	DNFCS 2003	750	0.57	1.4	2.3 [1.2; 3.3]
Spain	AESAN	410	1.33	4.5	14.9 [11.4; 18.3]
Spain	AESAN FIAB	981	1.64	4.4	26.2 [23.4; 28.9]
Sweden	Riksmaten 1997 98	1,210	0.92	2.3	7.3 [5.8; 8.7]
United Kingdom	NDNS	1,724	0.75	2.0	5.2 [4.1; 6.2]
		Elderly			
Belgium	Diet National 2004	518	0.99	3.6	12.5 [9.7; 15.4]
Denmark	Danish Dietary Survey	309	1.19	2.6	11.3 [7.8; 14.9]
Finland	FINDIET 2007	463	1.43	4.6	26.3 [22.3; 30.4]
France	INCA2	264	1.28	2.9	17 [12.5; 21.6]
Germany	National Nutrition Survey II	2,006	0.92	3.5	12.8 [11.3; 14.3]
Hungary	National Repr Surv	206	0.59	1.2	1 [0; 2.3]
Italy	INRAN SCAI 2005 06	290	1.07	3.6	14.1 [10.1; 18.1]
		Very elderly			
Belgium	Diet National 2004	712	0.95	3.5	12.1 [9.7; 14.5]
Denmark	Danish Dietary Survey	20	1.49	4.0	15 [3.2; 37.9]
France	INCA2	84	1.20	2.8	14.3 [7.6; 23.6]
Germany	National Nutrition Survey II	490	1.01	3.8	13.9 [10.8; 16.9]
Hungary	National Repr Surv	80	0.61	1.2	1.3 [0.03; 6.8]
Italy	INRAN SCAI 2005 06	228	0.77	2.5	7.5 [4; 10.9]

(a): number of subjects. (b): mean exposure. (c): P95: 95th percentiles of exposure. (d): percentage of individuals with an exposure above the TWI with its corresponding 95% confidence interval. **Reminder: in case of too few observations (less than 60 observations for the 95th percentile), the estimation of high percentiles may be biased and must consequently be interpreted cautiously.**

(Source: EFSA, 2012; Estimated dietary exposure in pg WHO_{2005} TEQ/kg b.w. per day)

8.2.1 EFSA 2018 dietary exposure assessment

Chronic dietary exposure was estimated across Europe. A total of 35 dietary surveys, carried out in 17 different Member States, were selected for the EFSA 2018 dietary exposure assessment (EFSA 2018, chapter 3.3.1, page 184). To estimate the chronic human dietary intake, two exposure assessments were carried out:

(i) taking into account the occurrence values of the samples with all the 29 PCDD/F and dl-PCB congeners (**assessment group A**), and

(ii) taking into account the occurrence values of samples with the 17 PCDD/F congeners only, excluding the 12 dl-PCBs (**assessment group B**).

The difference between the lower bound (LB) and upper bound (UB) estimations across all age classes was small for both exposure assessments (**table 9** and **table 10**). The highest exposures to the sum of PCDD/Fs and DL‑PCBs (29 congeners) and to the sum of PCDD/Fs (17 congeners) were estimated for the age classes Toddlers and Other Children, and were about twofold higher than in Adolescents and Adults (**table 9** and **table 10**).

- **Assessment group A (EFSA 2018, chapter 3.3.1, page 184) (table 9).**

  For the sum of PCDD/Fs and dl-PCBs (29 congeners: Assessment group A), the highest exposures were calculated for the age classes toddlers and other children.

  The mean LB exposure across age groups and surveys ranged from 0.30 (in adolescents) to 2.12 (in toddlers) pg WHO_{2005} TEQ/kg bw per day. The mean UB exposure ranged from 0.39 (in adolescents) to 2.57 (in toddlers) pg WHO_{2005} TEQ/kg bw per day.

  At the 95-percentile exposure, the LB range across age groups and surveys was from 0.76 (in elderly) to 6.02 (in other children) pg (WHO_{2005} TEQ/kg bw per day and at the UB from 0.93 (in elderly) to 6.63 (in other children) pg WHO_{2005} TEQ/kg bw per day.

  Median of the mean exposure ratios of PCDD/Fs and dl-PCBs between either Toddlers and Adults, or Other Children and Adults, calculated for those surveys that included these age classes, were, respectively, 2.2 and 1.9.

  Dietary exposure in specific groups of the population, namely pregnant and lactating women (each represented with one survey), were within the range of exposure estimates for the adult population. The LB mean exposure was 0.70 and 0.99 pg WHO_{2005} TEQ/kg bw per day, while UB mean exposure was 0.82 and 1.12 pg WHO_{2005} TEQ/kg bw per day for pregnant women and lactating women, respectively. Regarding the P95 exposure, LB estimate was 1.99 and 3.43 pg WHO_{2005} TEQ/kg bw per day, while the UB was 2.20 and 3.64 pg WHO_{2005} TEQ/kg bw per day for the pregnant women and lactating women, respectively.

Table 9: Assessment group A - dietary exposure to the 29 PCDD/Fs and dl-PCBs

Age class[a]	N	Mean dietary exposure (pg WHO_{2005}-TEQ/kg bw per day)					
		Minimum[b]		Median[b]		Maximum[b]	
		LB	UB	LB	UB	LB	UB
Infants[c]	6	0.44	0.66	0.65	0.93	1.16	1.42
Toddlers	10	0.68	0.88	1.25	1.53	2.12	2.57
Other children	18	0.56	0.71	1.15	1.39	2.01	2.45
Adolescents	17	0.30	0.39	0.66	0.79	1.27	1.50
Adults	17	0.42	0.49	0.64	0.76	1.11	1.30
Elderly	14	0.39	0.52	0.67	0.77	1.27	1.37
Very elderly	12	0.43	0.57	0.64	0.73	1.21	1.32

Age class[a]	N	95th percentile dietary exposure (pg WHO_{2005}-TEQ/kg bw per day)					
		Minimum[b]		Median[b]		Maximum[b]	
		LB	UB	LB	UB	LB	UB
Infants[c]	5	1.38	1.89	1.96	2.45	2.81	3.28
Toddlers	7	2.02	2.38	2.75	3.19	5.05	5.94
Other children	18	1.52	1.73	3.10	3.47	6.02	6.63
Adolescents	17	0.91	1.07	1.93	2.08	4.06	4.34
Adults	17	0.94	1.18	1.94	2.08	2.87	3.11
Elderly	14	0.76	0.93	2.13	2.38	3.61	3.82
Very elderly	9	0.84	1.04	1.90	2.13	2.55	2.78

EFSA 2018, chapter 3.3.1, pages 184-185, table 42

- **Assessment group B (EFSA 2018, chapter 3.3.1, page 185) (table 10).**

  The highest exposures were calculated for the age classes Toddlers and Other Children.

  For the sum of PCDD/Fs (17 congeners: Assessment group B), the mean LB exposure across age groups and surveys ranged from 0.11 (in adolescents) to 0.92 (in toddlers) pg WHO_{2005} TEQ/ kg bw per day and the mean UB exposure range was 0.17 (in adolescents) to 1.28 (in toddlers) pg WHO_{2005} TEQ/kg bw per day.

  At the 95-percentile exposure, the LB range across age groups and surveys was from 0.30 (in adolescents) to 1.76 (in toddlers) pg WHO_{2005} TEQ/kg bw per day and at the UB from 0.43 (in adolescents) to 2.42 (in toddlers) pg WHO_{2005} TEQ/kg bw per day.

  Similarly, as for Assessment group A, dietary exposure in specific groups of the population, namely pregnant and lactating women (each represented with one survey), were within the range of exposure estimates for the adult population. The LB mean exposure was 0.28 and 0.29 pg WHO_{2005} TEQ/kg bw per day for pregnant women and lactating women, respectively, while UB mean exposure was 0.39 pg WHO_{2005} TEQ/kg bw per day in both surveys. Regarding the P95 exposure, LB estimate was 0.86 and 0.99 pg WHO_{2005} TEQ/kg bw per day, while the UB was 0.99 and 1.08 pg WHO_{2005} TEQ/kg bw per day for them, pregnant women and lactating women, respectively.

The difference between LB and UB estimates was generally found to be small for both assessment groups, indicating that the uncertainty due to left-censored data is minor.

Table 10: Assessment group B - dietary exposure to the 17 PCDD/Fs

Age class[a]	N	Mean dietary exposure (pg WHO_{2005}-TEQ/kg bw per day)					
		Minimum[b]		Median[b]		Maximum[b]	
		LB	UB	LB	UB	LB	UB
Infants[c]	6	0.18	0.35	0.28	0.47	0.47	0.70
Toddlers	10	0.28	0.45	0.51	0.75	0.92	1.28
Other children	18	0.21	0.34	0.40	0.59	0.89	1.25
Adolescents	17	0.11	0.17	0.24	0.34	0.48	0.68
Adults	17	0.14	0.20	0.25	0.34	0.36	0.51
Elderly	14	0.19	0.26	0.23	0.31	0.42	0.52
Very elderly	12	0.20	0.27	0.23	0.31	0.39	0.50

Age class[a]	N	95th percentile dietary exposure (pg WHO_{2005}-TEQ/kg bw per day)					
		Minimum[b]		Median[b]		Maximum[b]	
		LB	UB	LB	UB	LB	UB
Infants[c]	5	0.57	0.95	0.70	1.04	1.06	1.44
Toddlers	7	0.67	1.02	0.89	1.20	1.76	2.42
Other children	18	0.47	0.72	0.99	1.31	1.75	2.27
Adolescents	17	0.30	0.43	0.58	0.80	1.30	1.62
Adults	17	0.41	0.50	0.57	0.72	0.97	1.12
Elderly	14	0.35	0.52	0.69	0.85	1.29	1.37
Very elderly	9	0.38	0.55	0.69	0.83	0.87	1.03

EFSA 2018, chapter 3.3.1, pages 185-186, table 43

8.2.2 Exposure of infants through breastfeeding estimated by the EFSA CONTAM panel

For the exposure assessment of breastfed infants below 6 months of age, a median age of three months was selected, equivalent to a body weight of about 6.1 kg, with an estimated average daily milk consumption of about 0.8 L and a high consumption of 1.2 L. The median occurrence levels were taken from the milk pools collected in European countries and analyzed within the WHO-field-study 2014/2015 (EFSA 2018, page 177, table 41). For breastfed infants with average human milk consumption, the daily exposure to PCDD/Fs, dl-PCBs and sum of PCDD/Fs and dl-PCBs was estimated to be 19.1, 14.5 and 32.9 pg WHO_{2005} TEQ/kg bw, respectively. For breastfed infants with high human milk consumption, the daily exposure to PCDD/Fs, dl-PCBs and sum of PCDD/Fs and dl-PCBs was estimated to be 28.6, 21.7 and 49.3 pg WHO_{2005} TEQ/kg bw, respectively.

8.2.3 Previously reported dietary exposure assessments

Several international bodies have estimated the dietary exposure to PCDD/Fs and dl-PCBs while performing their risk assessments related to the presence of these compounds in food (EFSA 2018, page 191 to second paragraph of page 192).

- The WHO (1998) estimated a daily intake of PCDD/Fs in the order of 1–3 pg I-TEQ/kg bw per day for a 60 kg adult based on the available information derived from food surveys from industrialized countries. It was indicated in this report that this value would be greater by a factor of 2–3 if dl-PCBs were to be included in the estimations.
- JECFA assessed the dietary intake of PCDD/Fs using the Global Environment Monitoring System/Food Contamination Monitoring and Assessment Program (GEMS/Food) regional diets, and national food consumption data. For PCDD/Fs, the median estimates ranged from 33 to 42 pg WHO_{1997} TEQ/kg bw per month, while for dl-PCBs it ranged from 9 to 47 pg WHO_{1997} TEQ/kg bw per month (FAO/WHO, 2002).

- The EFSA estimated the dietary intake of PCDD/Fs and dl-PCBs in its two technical reports on the monitoring of these compounds in food and feed (EFSA, 2010a,b; 2012).

⇒ **Comparing the estimates from period 2008–2010 used in the EFSA 2018 risk assessment with previous estimates in 2002–2004 (data not shown), a statistically significant decrease of between 16.6% and 79.3% was observed across the different population groups. This decrease may be attributable to the effects of the European risk management measures to reduce the exposure of the European population, but could also in part be due to improvements in the analytical methods and sampling designs of the monitoring programs over the years (EFSA, 2018, page 191, second last paragraph).**

Since then, studies on dietary exposure to PCDD/Fs and dl-PCBs in several European countries have been published. For example, Bramwell et al. (2017) reported on the 2012 UK Total Diet Study (UK TDS) and estimated the dietary exposure by combining the occurrence data with the total consumption for each food group derived from 4-day food diaries kept by approximately 500 adult participants for the period 2011–2012. The average UB dietary exposure (in WHO_{2005} TEQs) was estimated to be 0.52 pg TEQ/kg bw per day.

The same authors also carried out a Duplicate Diet Study in which 24-h duplicate diet samples were collected from 10 adult volunteers living in the UK in the period 2011–2012 (Bramwell et al., 2017). The average UB exposure estimate was in this case 0.27 pg TEQ/kg bw per day. The food groups with the greatest contribution to the exposure were 'Fish and seafood', 'Meat' and 'Milk and dairy'.

In France, for its second Total Diet Study that analyzed samples purchased between 2007 and 2009 (ANSES, 2011), the occurrence data were combined with the consumption data from the French Individual and National Food Consumption Survey (INCA 2). The daily mean (range) exposure (in WHO_{1997} TEQs) was estimated at 0.47 (0.39–0.51) pg TEQ/kg bw per day for adults and 0.76 (0.70–0.85) pg TEQ/kg bw per day for children (3–6 years old). In both age categories, the main contributors to the dietary exposure were butter and fish (both around 20%) followed by cheese (around 14%) and meat (around 10%). Mean exposure among women of childbearing age was 0.46 pg TEQ/kg bw per day (ANSES, 2011).

⇒ In conclusion, the mean UB exposure range for the different age groups in the EFSA 2018 risk assessment (0.39–2.57 pg WHO_{2005} TEQ/kg bw per day; see table 9: mean dietary exposure, min UB in adolescents = 0.39; mean dietary exposure, max UB in toddlers = 2.57) is in good concordance with the chronic human PCDD/F and dl-PCB dietary intake estimated by EFSA in its 2012 technical report (0.57–2.54 pg WHO_{2005} TEQ/kg bw per day; see table 8, Germany National Nutrition Survey II, mean in adolescents = 0.57; Finnland DIPP, mean = 2.54 in toddlers) (EFSA, 2012) based on occurrence data from the sampling years 2008–2010.

⇒ Compared to 1.2–9.9 pg WHO_{2005} TEQ/kg bw per day listed in the EFSA 2012 report (see table 8, Hungary National Repr Surv, P95 in elderly = 1.2; Spain enKid, P95 = 9.9 in toddlers), the 95th percentile UB dietary PCDD/F and dl-PCB exposure in the EFSA 2018 opinion is slightly lower with 1.04– 6.63 pg WHO_{2005} TEQ/kg bw per day.

⇒ **These new (but limited) data indicate that the present mean human dietary PCDD/F and dl-PCB exposure has not substantially changed compared to estimates based on food samples collected between 2008 and 2010 (EFSA, 2018, page 192, 4th para). The SCAHT therefore uses the more comprehensive 2008-2010 dietary exposure database as outlined in tables 9 and 10 for its HHRA.**

8.2.4 Switzerland dietary exposure estimates

BAFU states that the dioxin burden of the Swiss population is comparable to that in neighboring countries (BAG 2008, page 10, table 3). Summary data are shown in **table 11**. A direct comparison of the exposure data shown in table 11 with data in **tables 8, 9 and 10** is not possible because they make reference to different baselines. While **table 11** lists average total exposure of the general population in pg/kg bw per day as WHO_{1997} TEQ, **table 8, 9 and 10** give exposure data for different age classes as WHO_{2005} TEQ.

⇒ **However, SCAHT assumes that the dioxin burden of the Swiss population is comparable to that in neighboring countries, which justifies the use of EFSA dioxin and dl-PBC exposure data in toddlers for its HHRA**.

Table 11: PCDD, PCDF and dl-PCB burden across countries

Land	PCDD/DF*	cPCB*	PCDD/DF + cPCB*
Schweiz	0.6	1.4	2.0
Belgien	1.00	1.04	2.04
Deutschland	0.7	1.3	2.0
Frankreich	0.5	1.2	1.8
Italien	0.96	1.3	2.28
Niederlande	0.6	0.5	1.1
Schweden	1.12	0.79	1.92

* Angaben in pg/kg Körpergewicht und Tag als WHO_{97}-TEQ

(Source: BAG, 2008)

8.2.5 Contribution of the congeners and congener families to the total dietary exposure

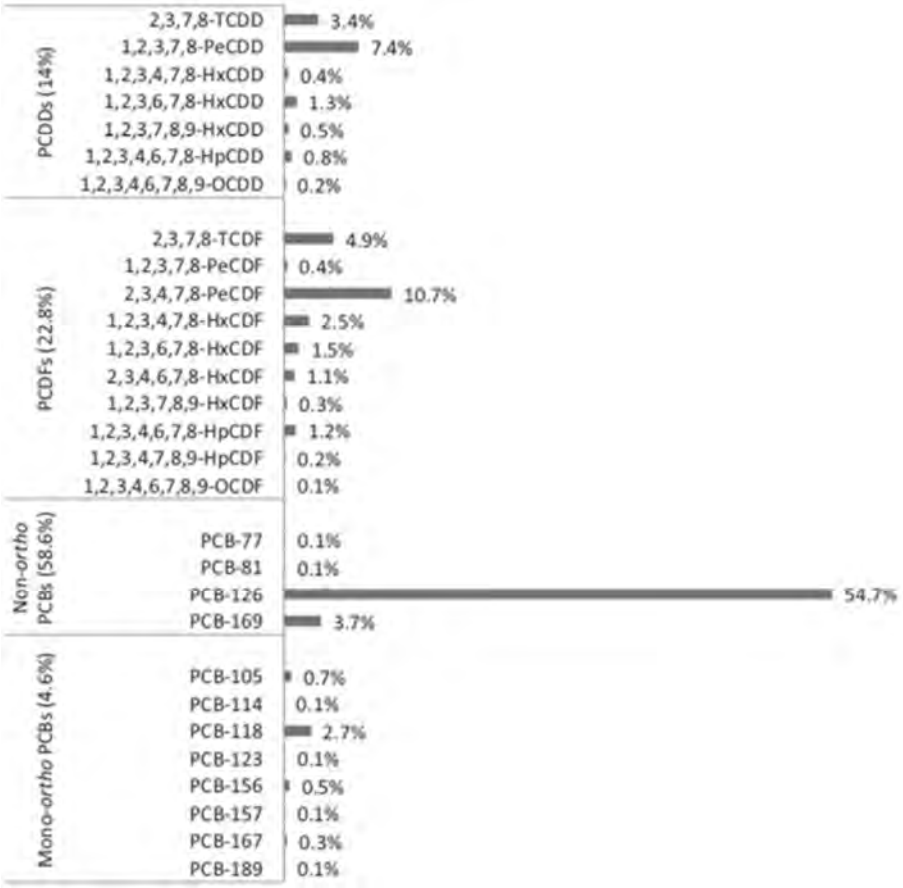
Average contribution of individual congeners and congener families to the exposure was investigated, e.g. in EFSA (2018).

The percentages of contribution to the mean LB TEQ exposure of the 29 PCDD/Fs and dl-PCBs and their corresponding families (in Assessment group A) are shown in **table 12**, and contributions to the mean LB TEQ exposure of the 17 PCDD/Fs and their corresponding families (in Assessment group B) are presented on **table 13**. Further details for contributions to the corresponding UB exposures are presented in EFSA 2018, Annex B, table 7).

The figures show that with the current WHO_{2005}-TEFs, **PCB-126 (3,3',4,4',5-Pentachlorobiphenyl) contributes most to the exposure,** followed by 2,3,4,7,8-PeCDF, PeCDD, TCDF, PCB-169 and TCDD. The HxCDDs and HxCDFs contribute, respectively, 2.2% and 5.4% to the exposure, whereas the heptas and octas contribute very little, similar to most other dl-PCBs. Consequently, considering the congener families, PCDD/Fs constituted 37% and dl-PCBs 63% of the mean total intake. The non-ortho PCBs had the biggest contribution (58.6%) to the overall LB exposure, followed by the PCDFs with a contribution of 22.8%.

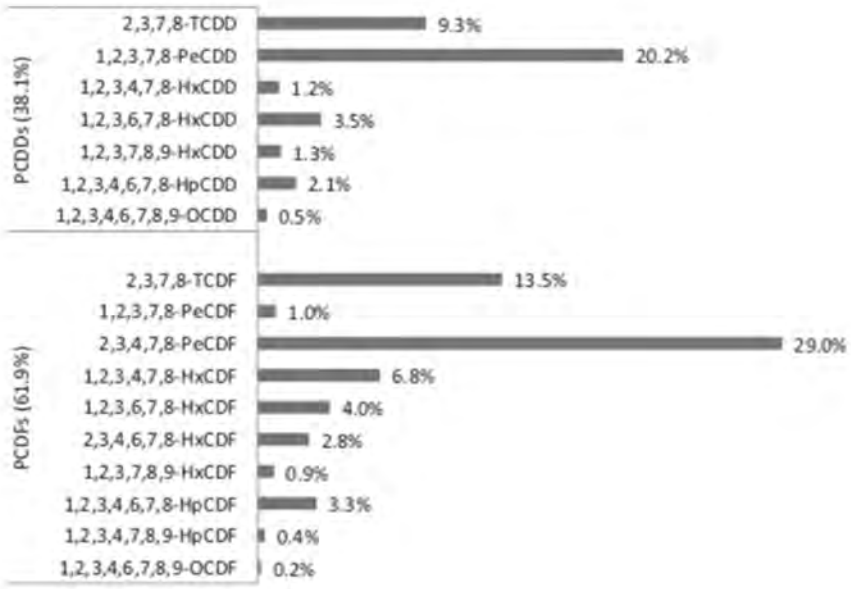
Taking into consideration only the families of the 17 congeners of PCDDs and PCDFs (Assessment group B), in the LB exposure scenario, 61.9% of the exposure is coming from the PCDFs (EFSA 2018, chapter 3.3.1, pages 186, last paragraph).

Table 12: Congener contribution to the overall LB mean exposure of the 29 PCDD/Fs and dl-PCBs



Source: EFSA 2018, chapter 3.3.1, page 187, figure 19

Table 13: Congener contribution to the overall LB mean exposure of the 17 PCDD/Fs



Source: EFSA 2018, chapter 3.3.1, page 187, figure 20

9 SCAHT risk assessment

SCAHT assumes that soils contaminated with a maximum of 14 ng WHO_{2005} TEQ PCDD/DFs and dl-PCBs/kg do, per se, not present a health risk for toddlers, who ingest 250 mg contaminated soil per day, 365 days per year. This assumption does not consider exposure from sources other than soil (see also 9.2).

In November 2018, the EFSA CONTAM panel set a new HBGV in the form of a TWI for PCDDs, PCDFs and dl-PCBs in food of 2 pg WHO_{2005} TEQ/kg bw per week which is protective for the general population. This TWI translates into a TDI of 0.286 pg WHO_{2005} TEQ/kg bw per day, which is 7-times lower that the HBGV previously derived by the EU SCF in 2001 of 2 pg WHO_{2005} TEQ/kg bw per day (table 4).

As shown in table 14, when considering exclusively exposure via soil ingestion (and disregarding any other sources of exposure), the TDI of 0.286 pg WHO_{2005} TEQ/kg bw per day is reached, but not exceeded, when the combined PCDDs, PCDFs and dl-PCBs content in soil is 14 ng WHO_{2005} TEQ /kg soil.

Table 14: Exposure at 100% of the TDI via soil ingestion only

The TWI of 2 pg WHO_{2005} TEQ/kg bw per week translates into a TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day. The non-rounded figure for the TDI is used in the calculation. Max. allowable PCDD/DFs and dl-PCBs exposure on a daily basis: 0.286 pg WHO_{2005} TEQ/kg bw per day Max. allowable PCDD/DFs and dl-PCBs daily exposure for a 12,5 kg child: 0.286 * 12,5 = 3.57 pg WHO_{2005} TEQ per day Max. allowable PCDDs/DFs and dl-PCBs content in 250 mg soil (daily amount of soil ingested, assuming an oral bioavailability of 100%): 3.57 pg WHO_{2005} TEQ /250 mg soil **Max. allowable PCDD/DFs and dl-PCBs content in 1 kg soil, considering soil exposure only: 3.57 * 4000 = 14'286 pg WHO_{2005} TEQ/kg soil = 14 ng WHO_{2005} TEQ/kg soil**

SCAHT recommends to introduce a single concentration value for the sum of the 29 PCDDs, PCDFs and dl-PCBs which are considered toxicologically relevant.

This is justified by the following reasons:

(i) in the environment PCDDs, PCDFs and dl-PCBs are always present as chemical mixtures, albeit in varying compositions;

(ii) PCDDs, PCDFs and dl-PCBs exert similar toxic effects; and

(iii) binding to the aryl hydrocarbon receptor (AhR) is the common key initiating event and the combined effect of complex PCDDs, PCDFs and dl-PCBs mixtures are considered additive.

Although the toxic potency of the individual PCDDs, PCDFs and dl-PCBs varies greatly Toxic Equivalency Factors (TEFs) have been developed to compare the toxicity of the various chemicals and to allow the combined effect of PCDDs, PCDFs and dl-PCBs to be assessed. TEFs express the concentrations of other PCDDs, PCDFs and dl-PCBs as a concentration equivalent to the most toxic

dioxin 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD)**.** For individual PCDDs, PCDFs or dl-PCBs, the 2,3,7,8-TCDD toxic equivalent quotient (2,3,7,8-TCDD TEQ) is the product of its concentration in an environmental mixture and its corresponding TEF. For a mixture of PCDDs, PCDFs and dl-PCBs the total TEQ is the sum of the individual 2,3,7,8-TCDD TEQs. This TEF/TEQ-approach provides a means for determining the toxicity of a mixture of PCDDs, PCDFs and dl-PCBs, in the absence of individual toxicity data. The method also supports the regulation of PCDDs, PCDFs and dl-PCBs as a group, instead of regulating each compound individually.

SCAHT also recommends to identify the fraction of the total TEQ attributable to 2,3,7,8-TCDD (for which uncertainty is relatively low) and the fraction attributable to the sum of 29 PCDDs, PCDFs and dl-PCBs (for which uncertainty is relatively higher).

This is justified by the following reasons:

(i) 2,3,7,8-TCDD is used as the index substance in the TEF-approach;

(ii) it is one of the most toxic dioxins; and

(iii) the toxicological database on 2,3,7,8-TCDD is most advanced.

SCAHT also recommends to identify the fraction of the total TEQ attributable to the sum of the 12 dl-PCBs, **although their toxicological potency is well below PCDDs and PCDFs.**

The driver for this would be practical risk management considerations. Unlike PCDDs and PCDFs which often represent diffuse sources of contamination because they are naturally occurring by-products of combustion and of various industrial processes that can travel long distances in the air, PCBs are not natural substances. They were manufactured in the past (with PCDFs as by-products), but today PCB manufacture is prohibited under the Stockholm Convention on Persistent Organic Pollutants. However, PCB release into the environment still occurs. The large-scale disposal of electrical equipment and waste can be regarded as a point source of PCB contamination.

9.1 SCAHT risk management considerations

SCAHT considers an additional exposure from incidental ingestion of contaminated soil accounting for 10% of the TWI/TDI to be most likely not associated with a significant additional health risk (see table 15).

As shown in table 15, under these assumptions, a soil concentration value of 1.4 ng WHO_{2005} TEQ/kg soil would most not pose a significant additional health risk under the SCAHT exposure scenario.

Table 15: Exposure at 10% of the TDI via soil ingestion only

The TWI of 2 pg WHO_{2005} TEQ/kg bw per week translates into a TDI of 0.286 pg WHO_{2005} TEQ/kg bw per day. The non-rounded figure for the TDI is used in the calculation.
Max. allowable PCDDs, PCDFs and dl-PCBs exposure at 10% of the TDI: 0.0286 pg WHO_{2005} TEQ/kg bw per day
Max. allowable PCDDs, PCDFs and dl-PCBs daily exposure for a 12,5 kg child: 0.0286 * 12,5 = 0.357 pg WHO_{2005} TEQ per day
Max. allowable PCDDs, PCDFs and dl-PCBs content in 250 mg soil (daily amount of soil ingested):

0.357 pg WHO_{2005} TEQ /250 mg soil

Max. allowable PCDD/DFs and dl-PCBs content in 1 kg soil, considering additional exposure accounting for 10% of TWI is without any significant additional risk: 0.357 * 4000 = 1429 pg WHO_{2005} TEQ /kg soil = 1.4 ng/WHO_{2005} TEQ /kg soil

9.2 Uncertainties related to the SCAHT risk assessment

9.2.1 Exposure from all sources

SCAHT assumes that soils contaminated with a maximum of 14 ng WHO_{2005} TEQ PCDD/DFs and dl-PCBs/kg do, per se, not present a health risk for toddlers, without considering exposure from other sources. However, using an integrated approach to risk assessment and risk management that encompasses other routes and other sources of exposure would suggest that the soil-based concentration value for PCDDs, PCDFs and dl-PCBs should be kept as low as reasonably or technically feasible (ALARA principle) because dietary exposure is already exceeding the TWI.

Most human exposure is through ingestion of contaminated food and estimated unavoidable dietary background exposure for toddlers is already exceeding the TWI for PCDDs, PCDFs and dl-PCBs in food of 2 pg WHO_{2005} TEQ/kg bw per week. Therefore, there is no more room for additional exposure from accidental ingestion of contaminated soil and the soil-based concentration value for PCDDs, PCDFs and dl-PCBs should follow the ALARA principle. The EFSA CONTAM panel used 2008-2010 dietary exposure estimates to assess the exposure of the general population. Based on these data toddlers were (in most cases) the age groups with the highest exposure (table 9 and table 10). For toddlers the sum of 29 PCDD/Fs and dl-PCBs mean chronic dietary exposure estimates range from min 0.68 to max 5.94 pg WHO_{2005} TEQ/kg bw per day[5], indicating that all toddlers are exposed above the EFSA CONTAM panel derived TWI of 2 pg WHO_{2005} TEQ/kg bw per week or the TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day. In toddlers, dietary exposure is exceeding the TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day by a factor of 2.3 (min LB of the mean = 0.68, divided by 0.3) to 19.8 (max UB of P95 = 5.94, divided by 0.3).

9.2.2 Focus on non-cancer toxicological endpoints

The common feature of the HHRA by EU SCF, JECFA, US EPA and EFSA CONTAM is that all the values are very low although they were derived only from non-carcinogenic endpoints. Although several PCDDs, PCDFs and dl-PCBs are considered to be carcinogenic in humans (**table 2**) these carcinogenic effects were not considered to be critical in the derivation of health-based guidance values (HBGVs) (WHO, 2010). Nevertheless, the proposed existence of dose-response thresholds for non-genotoxic carcinogens has led to a major controversy in the risk extrapolation process and some people would

[5] The lowest estimated chronic dietary exposure for toddlers accounts for 0.68 pg WHO_{2005} TEQ/kg bw per day, which represents the mean, minimum lower bound. The mean maximum upper bound is 2.57 pg WHO_{2005} TEQ/kg bw per day (table 9).

The highest estimated exposure for toddler accounts for 5.94 pg WHO_{2005} TEQ/kg bw per day, which represents the 95th percentile (P95) maximum upper bound. UB. The P95, minimum lower bound is 2.02 pg WHO_{2005} TEQ/kg bw per day (table 9).

argue that a risk assessment based on carcinogenic endpoints would result in even lower tolerable intake values.

The most recent EFSA CONTAM evaluation considered decreased sperm concentrations as the most critical effect (EFSA 2018, abstract). PCDDs, PCDFs and dl-PCBs are not genotoxic carcinogens and it is assumed that the mechanism of carcinogenesis, involving the aryl hydrocarbon receptor, means that there is a threshold for carcinogenicity. WHO 2010 argues that the tolerable intake guidance value based on the most sensitive non-cancer end-points (developmental effects, reprotoxicity) is protective for dioxin carcinogenicity (WHO, 2010) because it is already very low. SCAHT shares this opinion.

9.2.3 Selecting compound-specific toxicological endpoints

Impaired semen quality in humans, following pre- and postnatal exposure was considered to be the most critical/sensitive toxicological endpoint and was the key driver for setting the TWI for the sum of the PCDDs, PCDFs and dl-PCBs. The critical study was the Russian Children's Study, a longitudinal, prospective children's cohort study, which showed a NOAEL of 7.0 pg WHO_{2005} TEQ/g fat in blood sampled of boys at age 9 years, based on PCDD/F-TEQs. Impaired semen quality in the Russian Children's study was not associated with dl-PCB-TEQs.

Therefore, setting a soil concentration value for the sum of PCDDs, PCDFs and dl-PCBs based on a TWI that was primarily driven by a toxicological endpoint related to PCDDs and PCDFs would be seen to be conservative.

9.2.4 Using WHO_{2005}-TEQs for dl-PCB-126

The CONTAM Panel noted that in the Russian Children's Study, no association was observed for dl-PCB- TEQ or the sum-TEQ of PCDD/Fs and dl-PCBs. This might be explained by observations from in vitro studies with human cells, showing that PCB-126 is much less potent in humans than suggested by the WHO_{2005}-TEF of 0.1.

As PCB-126 is the dl-PCB contributing most to the current intake of PCDD/Fs and dl-PCBs and therefore dominates the TEQ level, the CONTAM Panel considered that the impact of the uncertainties on the risk assessment of PCDD/Fs and dl-PCBs, due to the uncertainty in the relative potency of PCB-126 in humans, is high. Overall, the assessment is likely to be conservative.

The current WHO_{2005}-TEFs should be re-evaluated in order to take into account new in vivo and in vitro data. In particular, more insight into the relative potency of PCB-126 in humans is required.

9.2.5 Assuming 100% bioavailability

In the SCAHT risk assessment, bioavailability of soil contaminants or relative bioavailability of soil contaminants compared to the bioavailability of the same contaminants in food is another key driver for exposure to environmental contaminants. Whether or not ingestion of contaminated soil presents a health risk largely depends on the bioavailability of PCBs, PCDDs and PCDFs in soil. Assuming a 100% bioavailability for PCDD/Fs and dl-PCBs seems conservative.

In 2010 US EPA published a report titled "Bioavailability of Dioxins in Soil and Soil-Like Materials" which presents a summary of the published literature and analysis of the available data regarding the relative bioavailability (RBA) of PCDDs and PCDFs in soil (US EPA, 2011). In 2011, this report was peer reviewed by three subject matter experts (US EPA, 2011). There was consensus among the three reviewers that the relative bioavailability of PCDDs and PCDFs in soil is less than 100%. There was also agreement that congener chlorine content will influence the RBA of the congeners. Two of the three reviewers agreed that there were too few studies data to support a nationally-applicable value for RBA for use in risk assessments and therefore no RBA-value < 100% could be recommended. The

third reviewer recommended assigning a national RBA value of 75% as a compromise, arguing that the few studies which have been carried out have consistently shown RBA of around 50% (US EPA, 2011).

9.2.6 Continuous exposure to contaminated soil

The SCAHT assumption of daily exposure to contaminated soil for 365 days a year, for 3 years in a row, from incidental ingestion of contaminated soil presents a worse-case scenario, which would only reflect the exposure pattern of a small fraction of the toddlers. This may lead to over-conservatism. The actual number of days children are playing outside in private gardens might actually be lower, but this can vary considerably, based on the specific family environment. For example, children might spend more time in private gardens if a parent doesn't work or if there is no public playground close-by.

Even if we assume a daily ingestion of contaminated soil over 3 years this rather represents a sub-chronic than a chronic exposure scenario. However, SCAHT uses chronic HBGVs in its assessment. Acute and chronic HBGVs are typically derived for most chemicals and the chronic HBGV is more relevant in the SCAHT risk assessment scenario.

9.2.7 Incidental soil ingestion rates

In the SCAHT risk assessment, ingestion of soil by young children is a key driver for exposure to environmental contaminants. Estimates of soil ingestion have been made by several studies but differ substantially (Stanek et al, 2012; Wilson, 2013; see also discussion in Aicher and Roth, 2017). For example, a meta-analysis (4 studies) by Stanek et al (2012) on 216 children based on aluminum and silicon as tracer elements suggests that the mean (median) soil ingestion could be as low as 26 mg/day (33 mg/day), with the 95th percentile estimated as 79 mg/day.

In its risk assessment SCAHT assumes a much higher incidental ingestion of 250 mg soil from hand-to-mouth activities. This assumption was based on personal discussions with US EPA representatives (US EPA, 2014), when SCAHT ran the first risk assessment of this kind for FOEN (Aicher and Roth, 2017). The SCAHT soil ingestion parameter considers the sum of soil and outdoor dust ingestion and indoor settled dust, assuming that indoor dust contamination in private homes is closely correlated to outdoor soil contamination in private gardens. The assumption is still valid today and supported by the latest revision of the US EPA exposure factor handbook on soil and dust ingestion (US EPA, 2017) as outlined in the **table 16** below.

Table 16: Values for daily soil and dust ingestion (mg/kg)

Table 5-1. Recommended Values for Daily Soil, Dust, and Soil + Dust Ingestion (mg/day)[a]

	Soil + Dust		Soil[b]				Dust[c]	
Age Group	General Population Central Tendency[d]	General Population Upper Percentile[e]	General Population Central Tendency[f]	General Population Upper Percentile[f]	Soil Pica[g]	Geophagy[h]	General Population Central Tendency[f]	General Population Upper Percentile[f]
<6 months	40	100	20	50	—	—	20	60
6 months to <1 year	70 (60–80)	200	30	90	—	—	40	100
1 to <2 years	90	200	40	90	1,000	50,000	50	100
2 to <6 years	60	200	30	90	1,000	50,000	30	100
1 to <6 years	80 (60–100)	200	40	90	1,000	50,000	40	100
6 to <12 years	60 (60–60)[i]	200	30	90	1,000	50,000	30	100
12 years through adult	30 (4–50)[j]	100[j]	10	50	—	50,000	20	60

[a] Ranges are provided in parentheses, when applicable, and represent the range of means from the various studies. Ranges are not provided for age groups for which the recommendations are based on a single study.
[b] Includes soil and outdoor settled dust.
[c] Includes indoor settled dust only.
[d] Based on the average of the central tendency values from the various studies for each of the three methodologies (tracer, biokinetic modeling, activity pattern), averaged over the three methods. Recommendation for <6 months of age based on Wilson et al. (2013) (note that data for 0 to <7 months in Wilson et al. [2013] were used to represent the 0 to <6 months age group). Recommendations for children 6 months to <1 year based on the average of values from Hogan et al. (1998) and von Lindern et al. (2016). Recommendations for 1- to 2 year-olds and 2- to <6-year-olds based on von Lindern et al. (2016). Recommendations for children ages 1 to <6 years based on the average of values from Calabrese et al. (1989) as reanalyzed in Stanek and Calabrese 1995a (mean of the median values for the best 4 tracers for each child); Calabrese et al. (1997a) (average of the best tracer for each child); Calabrese et al. (1997b) (average of aluminum and silicon); Davis et al. (1990) as reanalyzed by Stanek and Calabrese, 1995a (mean of the median values for 3 tracers for each child); Hogan et al. (1998); Özkaynak et al. (2011); von Lindern et al. (2016); and Wilson et al. (2013). The recommendations for ages 12 years to adults are based on the average of data for teens (ages 12 to <20 years), adults, and seniors from Wilson et al. (2013) and on adults from Davis and Mirick (2006). All recommended values were rounded to one significant figure. See Table 5-34 for additional details.
[e] Based on the average of the 95th percentile values from the various studies for each of the three methodologies (tracer, biokinetic modeling, activity pattern), averaged over the three methods. Based on the 95th percentile values for the same studies as used for the central tendency estimates except for age 12 years through adults. Upper percentile recommendation for 12 years of age through adults based on the assumption that the ratio of the 95th percentile to the mean value for adults is the same as the average of the ratios of 95th percentiles to means for all other age groups (i.e., average ratio of the 95th percentile to mean recommendations = 3.2). See Table 5-34 for additional details.
[f] Estimates of soil and dust were derived from the soil + dust values assuming 45% soil and 55% dust, rounded to one significant figure.
[g] Professional judgement based on: ATSDR (2001); Barnes (1990); Calabrese et al. (1997b, 1991, 1989); Stanek et al. (1998).
[h] Vermeer and Frate (1979).
[i] Range based on two studies with estimates of 55 and 56 mg/day; both of these estimates round to 60 mg/day.
[j] Soil + dust ingestion rates may be higher for adults following a traditional rural or wilderness lifestyle. Based on Doyle et al. (2012) and Irvine et al. (2014) the central tendency adult soil + dust ingestion rates is 50 mg/day (20 mg/day soil and 30 mg/day dust) and the upper percentile rate is 200 mg/day (90 mg/day soil and 100 mg/day dust).
— = No data.

(Source: USEPA Exposure Factors Handbook, Chapter 5, Soil and Dust ingestion, rev. September 2017)

9.3 Interpretation of the results in the Swiss context (NABO data, EMPA)

In a Swiss study conducted by the Swiss soil monitoring network (NABO) soil dioxin and PCB values were measured across Switzerland (Schmid et al., 2005; EMPA 2009). Concentrations of 6 out of 7 toxicologically relevant polychlorinated dibenzo-p-dioxins and 9 out of 10 toxicologically relevant dibenzofurans (PCDD/F) and 7 polychlorinated biphenyls (6 ndl-PCB: 28, 52, 101, 138, 153, 180 and 1 dl-PCB:118) were measured in 23 soil samples collected at reference sites of the Swiss national soil monitoring network (NABO).

The total levels for the sum of 15 PCDD/Fs were between 72 and 703 ng/kg soil corresponding to 1.1-11 ng I-TEQ/kg. Despite the fact that one out of 7 PCDDs (1,2,3,4,6,7,8,9-OCDD) and 1 out of 10 PCDFs (1,2,3,4,6,7,8,9-OCDF) which are considered toxicologically relevant were not measured in the NABO study, the levels for the sum of 15 PCDD/Fs measured by NABO are a good representation for the sum of 17 PCDD/F considered toxicologically relevant, because 1,2,3,4,6,7,8,9-OCDD which was not measured in the NABO study contributes only 0.2% and 1,2,3,4,6,7,8,9-OCDF which was also not measured contributes only 0.1% to the overall exposure to the 29 toxicologically most relevant PCDD/Fs and dl-PCBs (see **table 12**).

Unfortunately, the toxicologically relevant dl-PCB 126, which is most abundant in PCDD/Fs and dl-PCB mixtures and contributes 55% to the overall exposure to the 29 toxicologically most relevant PCDD/Fs and dl-PCBs has also not been captured in the NABO study.

- ⇒ However, if we assume that the 1.1-11 ng I-TEQ/kg measured for the sum of 15 PCDD/Fs represents only 45% of the 29 toxicologically most relevant PCDD/Fs and dl-PCBs, the total level can roughly be estimated to be 2.45-24.4 ng TEQ/kg (disregarding any differences between I-TEQ and WHO_{2005} TEQ).
- ⇒ At the lower level of soil contamination measured by NABO, a toddler with a time-weighted average body weight of 12.5 kg, who incidentally ingests 250 mg contaminated soil per day would be exposed to 0.05 pg/kg bw per day (2.45/4000*12.5=0.049) which is 6-times below the TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day. At the higher soil ingestion level exposure would be ca. 0.5 pg/kg bw per day (24.4/4000*12.5= 0.488) which is above the TDI of ca. 0.3 pg WHO_{2005} TEQ/kg bw per day.
- ⇒ **Therefore, contribution from soil ingestion would be a relevant exposure pathway**.

10 A comparison of international soil clean-up values

A summary guidance on soil screening levels (SSLs) (GAHP, 2013; Appendix 1) which addresses the selection and use of “screening levels” in prioritizing contaminated sites for remediation efforts has been published by the Global Alliance on Health and Pollution (GAHP). The GAHP document is based on a detailed comparison of values for the most common chemical contaminants. The systems included in the review were the US EPA, Canada, Australia, the Netherlands and UK.

The GAHP guidance is principally based on US EPA SSLs, but in order to derive a system that is more widely applicable, some adjustments were made to the EPA values, particularly in relation to a number of substances categorized as possible carcinogens, where the high-risk factors applied in the USA result in stringent levels that may not be as appropriate in other countries. For agricultural use of land, where US EPA SSLs are not available, relevant values from Canadian and UK systems have been used.

Generally, there is a very wide variation in the values adopted in different systems and the spread of SSL values does not allow “consensus” values to be identified. When interpreting the data, it must be

taken into account that the US, Canadian and UK data were developed in the specific context of their national systems and regulations and that the GAHP guidance represents the views of individual GAHP specialists and of invited outside experts and do not necessarily represent the views of any specific government or agency. Care must be taken in adapting the GAHP values for use in other systems. However, they are based on careful science and rigorous analysis and therefore provide a very good basis from which to work.

For 2,3,7,8-TCDD, **table 17** lists a soil clean up value for residential soils of $4{,}5*10^{-6}$ mg/kg soil (4.5 ng/kg soil). For dioxin mixtures, the soil clean-up value for residential soils is 20 times higher, namely $9{,}4*10^{-5}$ mg/kg soil (94 ng/kg soil). For PCBs of "high risk" the soil clean-up value is 0.22 mg/kg soil (roughly 50'000 times higher than for TCDD and 2500 times higher than for dioxin mixtures.

Table 17: List of soil clean-up values

Pollutant	Residential	Industrial	Agric.
METALS			
Arsenic	0.61	2.4	12
Cadmium	70	800	1.4
Chromium - Total	64	87	64
Chromium - Hex	0.29	5.6	0.4
Lead	400	800	70
Mercury - Elemental	10	43	26
Mercury - Inorganic	23	310	6.6
Mercury - Methyl	7.8	100	
Uranium (soluble salts)	230	3,100	23
NON-METALS			
Asbestos	1% in soil	1 % in soil	1% in soil
Cyanide	22	140	0.9
Dioxin - mixed	9.4x10-5	3.9x10-4	4x10-6
Dioxin - 2,3,7,8-TCDD	4.5x10-6	1.8x10-5	
Fluoride	3,100	41,000	200
PCBs - "high risk"	0.22	0.74	0.50
Phenol	18,000	180,000	3.8
Vinyl Chloride	0.06	1.7	

Soil clean-up values (ppm): 1 part per million = 1 milligram/kilogram
PCBs – "high risk" is not further specified. Unclear whether "high risk" refers to dl-PCBs.

(Source: GAHP, 2013, Annex 2, page 7)

10.1 Swiss legislation on soil contamination (VBBo, CSO)

The Contaminated Site Ordinance (CSO, AltV) Annex 3, chapter 2 lists no concentration values (Konzentrationswert, K-Wert) for 2,3,7,8-TCCD alone, or the mixture of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) with or without dioxin-like polychlorinated biphenyls (dl-PCBs) or for dl-PCBs alone. It only lists a soil clean up value for the sum of six ndl-PCBs (Nr. 28, 52, 101, 138, 153, 180) (**table 18**).

The Swiss Regulation on soil contamination (VBBO) lists only soil clean-up values for the mixture of PCDDs and PCDFs without dl-PCBs of 100 ng I-TEQ/kg soil but does not further specify the PCDD and PCDF congeners included in the mixture (**table 19 and table 20**).

The VBBo lists no adequate soil clean-up value for dl-PCBs. The soil clean-up value for playgrounds and private gardens of 1 mg I-TEQ/kg soil (**table 18**) refers to a PCB mixture of six ndl-PCBs and one dl-PCB. The one dl-PCB (Nr 118) is a mono-ortho dl-PCB-congener with a low TEF (WHO_{2005} TEFs: 0.00003). The six ndl-PCBs are the same as the six ndl-PCBs listed in the AltV.

Table 18: Swiss standards for PCDDs, PCDFs and dl-PCBs in contaminated soil

	CSO, 26. August 1998 (updated 1. Mai 2017) **Konzentrationswert**	**VBBo,** 1. Juli 1998 (updated 12. April 2016) Prüf-, Richt- und **Sanierungswerte**
2,3,7,8-TCDD alone (2,3,7,8-tetrachloro-dibenzo-p-dioxin	No value	No value
PCDDs + PCDFs with dl-PCBs	No value	No value
PCDDs + PCDFs without dl-PCBs	No value	100 ng I-TEQ/kg soil[6] Congeners not specified
dl-PCBs alone	No value	No value
ndl-PCBs alone	1 mg/kg soil **Σ6 ndl-PCBs x 4.3** Congeners: 6 ndl-PCBs: Nr. 28, 52, 101, 138, 153, 180	1 mg I-TEQ/kg soil for Σ6 ndl-PCBs + dl-PCB Nr 118 Congeners: 6 ndl-PCBs: Nr. 28, 52, 101, 138, 153, 180. 1 mono-ortho dl-PCB: 118 with WHO_{2005} TEF: 0.00003

AltV: https://www.admin.ch/opc/de/classified-compilation/19983151/index.html

VBBo: https://www.admin.ch/opc/de/classified-compilation/19981783/201604120000/814.12.pdf

[6] Soil clean-up values for playgrounds and private gardens. For agricultural land the soil clean-up value is 1000 ng I-TEQ/kg soil

Table 19: PCDDs, PCDFs: Verordnung über die Belastung des Bodens, Anhang 2, Abschnitt 11

– 11 Werte für Dioxine (PCDD) und Furane (PCDF)

Werte	PCDD/F-Gehalte[1] (ng I-TEQ/kg TS für Böden bis 15 % Humus, ng I-TEQ/dm^3 für Böden über 15 % Humus)	Probenahme-tiefe (in cm)
Richtwert	5	0-20
Prüfwerte		
Nutzungen mit möglicher direkter[2] Bodenaufnahme	20	0-5
Nahrungspflanzenanbau	20	0-20
Futterpflanzenanbau	20	0-20
Sanierungswerte		
Kinderspielplätze	100	0-5
Haus- und Familiengärten	100	0-20
Landwirtschaft und Gartenbau	1000	0-20
I-TEQ= Internationale Toxizitätsäquivalente	TS= Trockensubstanz	
[1] PCDD/F = Summe der polychlorierten Dibenzo-*p*-dioxine und polychlorierten Dibenzofurane [2] oral, inhalativ, dermal		

The I-TEQs used in the Swiss legislation have been update twice by WHO in 1997 and 2005 as new data became available. SCAHT recommends using the most recent WHO_{2005} TEFs for any upcoming revisions.

Table 20: PCBs: Verordnung über die Belastung des Bodens, Anhang 2, Abschnitt 13

– 13 Werte für polychlorierte Biphenyle (PCB)

Werte	PCB-Gehalte[1] (mg/kg TS für Böden bis 15 % Humus, mg/dm^3 für Böden über 15 % Humus)	Probenahmetiefe (in cm)
Prüfwerte		
Nutzungen mit möglicher direkter[2] Bodenaufnahme	0,1	0-5
Nahrungspflanzenanbau	0,2	0-20
Futterpflanzenanbau	0,2	0-20
Sanierungswerte		
Kinderspielplätze	1	0-5
Haus- und Familiengärten	1	0-20
Landwirtschaft und Gartenbau	3	0-20
TS= Trockensubstanz		

[1] Summe der 7 Kongeneren gemäss IRMM (Institute for Reference Materials and Measurements), IUPAC-Nr. 28, 52, 101, 118, 138, 153, 180

[2] oral, inhalativ, dermal

Please note that the PCB-mixture addressed contains 6 ndl-PCBs but only one dl-PCB, and is therefore of limited relevance for a comparison of soil clean up values for dl-PCB.

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