



Evaluation of the Human Research Act (HRA)

Executive Summary

On behalf of the Federal Office of Public Health

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Summary

The Human Research Act (HRA) and associated ordinances entered into force on 1 January 2014. The primary purpose of the act is to protect human beings involved in research. It is also intended to create favourable conditions for human research (HR) and help ensure its quality and transparency. Based on the evaluation clause in Article 61 of the HRA, the Federal Office of Public Health (FOPH) has commissioned the Department of Political Science, University of Zurich, and KEK-CDC Consultants to evaluate the HRA. The evaluation focuses on whether the HRA is being executed in an expedient manner and whether it is effective. It considers the different perspectives of those involved in HR and uses a variety of methods and data.

The evaluation concludes that the implementation of the HRA is generally expedient and the authorisation procedures are proving themselves. The risk-based regulatory approach of the HRA allows authorities to treat HR projects for the most part according to their risk. There are certain difficulties, firstly when it comes to coordination between the parties involved in implementation, secondly when applying the legal provisions regarding research with biological material and health-related personal data that have already been collected (research involving further use), and thirdly when monitoring the implementation of approved HR projects.

Based on the collected survey and interview data, the evaluation concludes that the HRA has strengthened the protection of research participants. There are indications that the HRA has led to authorities examining research applications more thoroughly and systematically. Furthermore, the HRA has made researchers more aware of the protection of research participants and has improved the conceptual quality of HR projects. There is, however, a need for optimisation in terms of the comprehensibility of the information provided to research participants. The evaluation also shows that HR transparency is not yet sufficiently ensured.

Based on these results, the evaluation formulates recommendations on institutional questions of the human research regulation, on optimising the regulation of clinical trials and research involving further use, as well as on improving information provided to those concerned and on transparency in human research.

Key words: Human Research Act, risk-adapted regulatory approach, clinical trials, research involving further use, evaluation

1 Introduction

1.1 Background

The human research regulation consisting of the Human Research Act (HRA, SR 810.30) with associated ordinances has been in force since 1 January 2014.¹ The HRA's primary purpose is to protect human dignity, privacy and health of human beings involved in research. The HRA is also intended to create favourable conditions for human research (HR) and help ensure the quality and transparency of HR (Art. 1 HRA). The HRA thus regulates the interplay between the protection of human beings and the interest in human research (freedom of research) which contributes to improving health care.

The human research regulation includes mandatory authorisation for HR projects and defines procedures, duties of researchers and participant rights. HR projects with a high risk for research participants must comply with higher requirements than lower-risk projects, i.e. the human research regulation is based on a risk-adapted approach with three risk categories, A, B and C, with the risk potential increasing from A to C.

Seven cantonal ethics committees (ECs) are responsible for authorising all HR projects. Certain HR projects in the higher-risk categories B and C require *additional* authorisation by a federal authority: While Swissmedic is responsible for clinical trials of medicinal products, medical devices and transplant products (TpPs) as well as clinical trials of gene therapy (GT) and genetically modified or pathogenic organisms (GMOs), the Federal Office of Public Health (FOPH) is responsible for authorising clinical trials of transplantation. In order to harmonise how the ECs implement the HRA, they have formed the joint association swissethics. The FOPH manages the Coordination Office for Human Research (kofam) which ensures an exchange between swissethics, Swissmedic, the FOPH and other federal offices² that prepare opinions for the ECs or Swissmedic as part of the authorisation procedure. kofam also informs the public on the topic of HR. Thus, numerous parties³ need to interact in a coordinated manner in order to implement the HRA.

1.2 Mandate and evaluation questions

The FOPH has commissioned the Department of Political Science of the University of Zurich and KEK-CDC Consultants to evaluate the HRA.

The evaluation aims at assessing the effectiveness of the act and formulating recommendations for optimisation if necessary. The FOPH has chosen the date of the evaluation specifically so that evaluation results are available some five years after the HRA has come into force. The evaluation was carried out in the period between August 2017 and June 2019 and addressed the following four main questions:

- 1) How is the human research regulation being implemented?
- 2) Is the HRA achieving the desired effects as stated in the article defining the purpose of the HRA (Art. 1)? Are there unintended effects (positive, negative, possible interactions)?

¹ The Organisation Ordinance HRA (OrgO-HRA, SR 810.308), the Ordinance on Clinical Trials in Human Research (ClinO, SR 810.305) and the Ordinance on Human Research with the Exception of Clinical Trials (HRO, SR 810.301).

² These are the Federal Office for the Environment (FOEN) and the Swiss Expert Committee for Biosafety (SECB).

³ In the following, we will refer to parties involved in the authorisation procedures as "authorities". These are the ECs, Swissmedic, FOPH, FOEN and SECB.

- 3) Which context factors influence the implementation of the HRA?
- 4) How can the human research regulation and its implementation be improved?

2 Approach and methods

We have chosen a modular approach to address the evaluation questions. This approach is based on the guidelines for evaluation with the federal government⁴ and allows a transparent overview of the individual steps of the analysis. On the one hand, we have used various data collection methods in order to capture the object of the evaluation from different perspectives. On the other hand, when processing the evaluation questions, we also rely substantially on the results of government research projects commissioned by the FOPH.⁵ The data collection period lasted from August 2017 to March 2019. Table 1 presents an overview of the methods used.

Table 1: Summary of methods used

Module: Subject	Survey instruments/data sources
1. Detailed concept and impact model	– 3 informational talks with HR stakeholders – Document analysis
2. Brief description “Stakeholders and processes in HR”	– 8 interviews with HR stakeholders – Document analysis
3. HRA implementation from the perspective of authorities and other stakeholders	– 14 interviews with ECs and federal agencies – Synthesis of government research; document analysis
4. Implementation of the HRA from the perspective of researchers	– 31 telephone interviews with applicants (18 regarding authorised applications; 13 regarding rejected/withdrawn applications) – Synthesis of government research
5. Analysis of research applications	– Secondary data analysis (including government research) – <i>separated</i>: Analysis of the quality of selected research applications⁶
6. Effects “Protection/rights of trial participants”	– Standardised online survey of organisations in the area of protection/rights of trial participants (N=65 respondents from 51 organisations) – Synthesis of government research
7. Effects “HR quality and framework conditions”	– Standardised online survey of research organisations (N=189 respondents from 136 organisations) – Synthesis of government research
8. Context analysis	– Analysis of data on context collected in modules 1 to 7 – Document analysis (including government research)
9. Synthesis	– Two regional-language workshops with HR stakeholders on the need for optimisation – Synthesis of modules 1 to 8, conclusions and recommendations

The commissioner appointed a FOPH in-house steering committee. A broad-based advisory group supported the evaluation, in particular with field expertise on HR. Feedback from the steering committee and the advisory group was incorporated when conducting the evaluation and reporting the results.

⁴ Widmer, Thomas (2005): Leitfaden für Wirksamkeitsüberprüfungen beim Bund. Bern: Federal Office of Justice.

⁵ For the reports on government research projects, cf.: <https://www.bag.admin.ch/bag/en/home/das-bag/ressortforschung-evaluation/forschung-im-bag/forschung-biomedizin/ressortforschungsprojekte-humanforschung.html> [as at 04.01.2019].

⁶ Analysis of selected applications is being carried out separately from the evaluation due to time constraints.

3 Answers to evaluation questions

Evaluation questions 1 to 3 are answered below, based on the data collection and analysis in modules 1 to 8 (see Table 1). The final report of the evaluation describes the specific data sources and methods.⁷ We have not included that information in this executive summary.

1) How is the human research regulation implemented?

Advance services

In order for the authorities to be able to examine research applications in a uniform, coordinated and appropriate manner and also monitor them after approval, advance services are necessary: Authorities and other stakeholders involved in implementation must provide structures, resources and support services and provide overarching coordination services so as to allow reconciliation at the level of authorising individual applications.

The evaluation shows that these advance services are generally expedient: Firstly, the seven ECs, Swissmedic and the FOPH as well as other federal agencies involved (Federal Office for the Environment, Swiss Expert Committee for Biosafety) have the structures and capacities to perform their tasks when it comes to authorising and monitoring HR projects. The support services that swissethics, kofam and the authorities provide for the researchers, such as templates, instructions and information as well as the online portal for submitting applications (BASEC Business Administration System for Ethics Committees) are assessed as useful by the researchers. Secondly, the mergers of thirteen to just seven ECs and the services provided by swissethics have gradually led to a substantial level of harmonisation. However, the evaluation also shows that there is still a need for further harmonisation between ECs in some areas (such as common criteria for demarcating research requiring authorisation).

Even kofam enhanced the coordination between ECs/swissethics and federal authorities, certain coordination difficulties are present in terms, e.g., of reaching consensus on controversial authorisation issues. In addition, the evaluation makes clear that the division of tasks between kofam and the ECs/swissethics is not fully clarified and that there are certain overlaps in the tasks performed as well as gaps in the areas of coordination and exchange.

Authorisation procedure

In 2017, a total of 2,275 applications were submitted to the ECs. Authorisation procedures vary according to type of study and risk category. Table 2 provides an overview of the distribution of applications by type of study and risk category, showing that a total of 233 (10.2%) of these applications required additional authorisation by a federal authority. The share of clinical trials that fall under the Clinical Trials Ordinance (ClinO) is at 23.8%. Consequently, the share of HR regulated by the Ordinance on Human Research with the Exception of Clinical Trials (HRO) is 76.2%.

⁷ Widmer, Thomas/ Frey, Kathrin/ Eberli, Daniela/ Schläpfer, Basil/ Rickenbacher, Julia (2019): Evaluation des Humanforschungsgesetzes (HFG). Schlussbericht. Zürich: Institut für Politikwissenschaft der Universität Zürich und KEK-CDC Consultants.

Table 2: Overview of study types and risk categories according to the HRA

Ordinance	HR projects involving humans		Category		
			A	B	C
ClinO	Clinical trials	of medicinal products*	25 (1.1%)	37 (1.6%)	147 (6.5%)
		of TpPs	1 (0.0%)	0	7 (0.3%)
		of GT or GMOs	0	0	2 (0.1%)
		of medical devices	101 (4.4%)	n.d.	39 (1.7%)
		of transplantation	0	n.d.	1 (0.0%)
		other	151 (6.6%)	30 (1.3%)	n.d.
HRO	Research projects involving measures for sampling biological material or collection of health-related personal data (HRO projects on humans)		802 (35.3%)	24 (1.1%)	n.d.
	Other HR projects				
HRO	Research projects involving biological material or health-related data that has already been collected (further use)				879 (38.6%)
HRO	Research projects involving deceased persons or embryos and fetuses from induced abortions, from spontaneous abortions including stillbirths				29 (1.3%)
Total applications submitted to ECs in 2017 (only lead EC in case of multi-centre applications)					2275 (100%)
* Clinical trials involving medicinal products also include the six combined clinical trials of medicinal products and medical devices (category A: 2, category B: 0; category C: 4).					
Grey highlighting: Types of study requiring authorisation by an EC and a federal authority; in the case of trials of transplantation, by the FOPH; in other cases, by Swissmedic.					
n.d.: Category is not defined in the human research regulation.					
Source: Clinical Trial Unit Basel (2018): BASEC Annual Report 2017. Descriptive statistics on research covered by the Swiss Federal Act on Research Involving Human Beings. January 1, 2017 – December 31, 2017. On behalf of the Federal Office of Public Health and swissethics. Basel: CTU. Page 16.					

The evaluation shows that, after initial difficulties, authorisation procedures are largely proving themselves. Overall, researchers are satisfied with the implementation of the human research regulation. And they consider the decisions of the authorities to be justified, especially regarding ethical aspects.

One area of concern from the researchers' perspective are divergences between the ECs and Swissmedic, which often relate to the risk category. Some researchers are concerned by the fact that the ECs assess scientific aspects despite a (seeming) lack of expertise in the specific field of research. Furthermore, about one in five applicants is of the opinion that ECs assess applications according to different standards. There are also indications that the coordination between ECs during the lead EC procedure is not yet adequate in every instance.

Finally, there are certain difficulties in the area of research involving further use. On the one hand, ECs are reaching the limits of their capacity and competence when it comes to reviewing provisions to ensure secure and correct encryption and storage of samples and data. On the other hand, researchers consider regulation as too complicated and the procedures as (too) laborious.

Monitoring and supervision of project execution

During the conduct of their project, researchers need authorisation for project modifications and are obliged to notify certain events and hand in reports. All these requirements vary depending on the type of study and the risk category. This information enables the authorities to monitor project execution. Swissmedic can also carry out inspections in the case of clinical trials of therapeutic products or TpPs and clinical trials of GT or GMOs. The FOPH can inspect clinical trials of transplantation.

The evaluation shows that the responsible authorities – ECs, Swissmedic and FOPH – monitor and inspect the implementation of approved HR projects to a relatively minor extent. This is partly due to the human research regulation, as it provides for inspections only in a limited scope. Apart from that, the relevant resources of the ECs, Swissmedic and the FOPH are confined. The evaluation shows that ECs incorporate findings from safety and final reports only selectively and unsystematically into implementation practice, and the development of premature study discontinuation is not analysed. The evaluation further determines that the diverging responsibilities in terms of authorisation and monitoring require considerable coordination efforts between Swissmedic and the responsible EC. In addition, there are indications that the insights gained from inspections are not systematically incorporated into research practice and further authorisation practices of the ECs.

2) Is the HRA achieving the desired effects as stated in the article defining the purpose of the HRA (Art. 1)? Are there unintended effects (positive, negative, potential interactions)?

Effect of the HRA on the protection of humans

Since the HRA to a large extent covers HR that carries a risk for humans, and regulates said research according to the level of risk involved, an important prerequisite for protecting humans is met. Certain problematic weaknesses in terms of protecting humans are apparent, on the one hand, in the delimitation between research requiring authorisation and experimental therapy not requiring authorisation, quality assurance, development of medical devices and feasibility analyses. On the other hand, there are difficulties in classifying the HR projects as either ClinO projects or HRO projects and, in specific areas, also in assigning them to a risk category. This applies to the categorisation of clinical trials of medicinal products in particular, which does not do justice to the actual risk of some studies, as regulation refers to the authorisation of the medicinal product in question.

Protection of research participants is also ensured by the liability provision and compensation scheme of the human research regulation, which has generally proved its worth in practice. Existing exemption provisions do, however, limit the protection of participants.

The evaluation also contains indications that the HRA has led the authorities to examine applications more closely and more systematically, and researchers to take better account of the concerns about protection of research participants, and to some overall improvement in other aspects of research quality. However, the evaluation also clearly shows that there is still considerable room for improving the protection of research participants when it comes to the process of providing information, i.e. in terms of the comprehensibility of patient information (informed consent and general consent).

The evaluation also shows a need for further improvement with regard to how the authorities monitor the execution of HR projects. Inspections contribute significantly to the protection of research participants but occur within too limited scope and range which cannot be justified from the perspective of protecting research participants.

Finally, HR transparency cannot yet be considered sufficient. From the research participant perspective, this applies in particular to the transparency of the results of the HR conducted.

Effect of the HRA on the conditions for HR

The impact of the HRA on the conditions for HR varies according to the area of research. Significant improvements were achieved particularly for clinical trials of medicinal products (including mergers of ECs and harmonisation between ECs, timesaving through deadlines and parallel submission options to ECs and Swissmedic). From the perspective of research which has now become subject to national mandatory authorisation, namely for research involving further use, the HRA has led to significant

changes. Article 34 HRA is particularly important here, as it allows further use of biological material and health-related data in exceptional cases even without prior consent of the persons involved. The exemption clause is frequently sought by applicants and tends to be the rule. Researchers appreciate this application practice – which is problematic from more than just the legal-systematic perspective.

Effect of the HRA on the volume of HR

Analysis of the number of applications and authorisations shows that the number of studies involving the collection and further use of biological material and health-related personal data (covered by the HRO) is growing steadily, whereas the number of clinical trials of medicinal products (covered by the ClinO) authorised by Swissmedic was stable for the years 2014–2017. It is difficult to determine to what extent the human research regulation affects this development. Interview and survey data suggest that the HRA has no influence or, if anything, rather an inhibitory influence on the volume of human research in Switzerland.

3) Which context factors influence the implementation of the HRA?

The evaluation shows that two developments are particularly relevant to implementing the HRA, namely scientific and technological progress on the one hand, and international framework conditions on the other.

Scientific and technological progress opens up new possibilities for research, such as through acquired knowledge on the human genome or through new methods of collecting, linking and analysis of large amounts of data. These developments change the risks for persons concerned, for example by allowing sensitive anonymised or encrypted personal data to be de-anonymised or decrypted and the persons concerned to be identified. These developments are also very dynamic, and they give rise to questions concerning data protection and the information provided to research participants. However, digital progress also opens up new options for designing the consent of those concerned (e-consent and dynamic consent) and for how research participants can be involved in research projects.

Given the international orientation of Swiss HR, *international framework conditions* are proving to be key. Consequently, it is important for Swiss human research regulation to be compatible with international regulations. Some of the EU's relevant legal foundations have changed since the HRA came into force, namely EU Regulation 536/2014 on clinical trials on medicinal products for human use and EU Regulations 745/2017 and 746/2017 in the area of medical devices and in vitro diagnostics. While the Federal Assembly has already adopted amendments to the HRA in the area of medical devices in March 2019, no amendments have yet been initiated in the area of clinical trials of medicinal products. There are, however, no fundamental conflicts between the Swiss regulation and the new EU Regulation 536/2014 on clinical trials. What is important is whether the EU considers Swiss regulations to be equivalent.

4 Recommendations

We answer evaluation question 4 by formulating recommendations, which, besides the evaluation results presented in section 3, are based on discussion results from two language-regional workshops to identify and discuss optimisation suggestions.

4) How can the human research regulation and its implementation be improved?

Recommendations are clustered into four groups that deal with institutional questions regarding the human research regulation, clinical trials, research involving further use as well as providing information to those concerned and transparency in HR. When valorising the recommendations, it is important to note that the recommendations and the implementation thereof are partly interdependent. We have also specified whom the recommendations address and whether they require any change in terms of practice and/or law. For changes involving the human research regulation, we have – wherever possible – indicated where a change is expected to occur. However, we have not examined the need for regulation in-depth; this should thus be reviewed, if necessary, when implementing the recommendations.

Recommendations on institutional questions regarding the human research regulation (division of tasks)

Recommendations	Addressees	Amendment	
		Practice	Law
1) The existing institutional structure is generally suitable for ensuring implementation of the human research regulation in the Swiss federal system.	legislative authority, FOPH, ECs, cantons		
2) Harmonisation between ECs is to be continuously strengthened.	swissethics, ECs		
3) The division of tasks between kofam and swissethics is to be clarified and communicated.	FOPH/kofam, swissethics and CMPH		<i>to be clarified</i>
4) Monitoring and supervision of ongoing studies are to be strengthened through suitable measures.	legislative authority, FOPH, Swissmedic, ECs		HRA, ClinO, HRO OrgO-HRA

Recommendations on regulating clinical trials

Recommendations	Addressees	Amendment	
		Practice	Law
5) The definition, categorisation and corresponding requirements for clinical trials are to be aligned to international regulations on clinical trials.	legislative authority, FOPH		ClinO
6) In case of applications for clinical trials of medicinal products, medical devices, TpPs and clinical trials of GT or GMOs, effective coordination between the responsible (lead) EC and Swissmedic is to be ensured by appropriate measures.	legislative authority, FOPH, ECs, Swissmedic		ClinO
7) The HRA's liability and coverage regulations are to be aligned to EU legal developments; existing exemption regimes are to be reviewed critically.	legislative authority, FOPH		ClinO

Recommendations on regulating research involving further use

Recommendations	Addressees	Amendment	
		Practice	Law
8) The exemption provision of Article 34 HRA should be adapted as follows: in the case of older data and samples, regular use of data and samples should be allowed without prior consent of those concerned, subject to certain conditions. In the case of more recent data and samples, the exemption regime should be adhered to.	legislative authority, FOPH		HRA
9) Requirements for research involving further use should be simplified and better communicated; the focus should be on protecting the persons concerned.	legislative authority, FOPH, ECs/ swissethics		HRA, HRO
10) As part of the authorisation procedure, the security of digital data and their protection against unauthorised access and misuse is to be reviewed in a competent manner.	legislative authority, FOPH, ECs, cantons		<i>to be clarified</i>

Recommendations on providing information to those concerned and transparency in human research

Recommendations	Addressees	Amendment	
		Practice	Law
11) ECs should orient any examination of patient information more towards layperson comprehensibility and use appropriate measures to help researchers provide comprehensible information to research participants.	swissethics, ECs		
12) Measures should be developed that allow open science postulates to be taken into account and big data opportunities to be used for research interests, without neglecting the protection of those concerned.	FOPH, swissethics, ECs		<i>to be clarified</i>
13) Registration of HR projects and their results should be promoted as far as international developments will allow.	legislative authority, FOPH		ClinO, HRO