Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

EXPOSURE ASSESSMENT IN THE CONTEXT OF THE SPARE PROJECT:
A MODEL TO SPATIALLY ASSESS EXOTIC DISEASES INCURSIONS
AND SPREAD THROUGHOUT EUROPE

**Crescio Maria Ines[1], Maurella Cristiana[1], Bertolini Silvia[1], Mastrantonio Gianluca[2],
Ingravalle Francesco[1], Bona Maria Cristina[1], Simons Robin[3], De Nardi Marco[4],
Adkin Amie[3], Estrada-Peña Augustin[5]** et **Ru Giuseppe[1]**

ঔঔঔ

ABSTRACT

In this article, we describe a spatially explicit exposure assessment model developed within the SPARE project (www.spare-europe.eu). In particular we show how we estimated the spatial probability that the introduction of one animal infected with a vector borne disease (in our example Bluetongue) will lead to at least one other infected animal, using the Piedmont region of North Western Italy as an example area.

An extensive literature search lead to a systematic and structured inventory of exposure risk factors. This inventory was then used to develop scenario tree pathways, detailing the main exposure pathways, along with the equations and their parametrization. A stochastic model was then implemented and run. Based on the model, we provide maps with a different distribution of the probability of a secondary transmission. This is quite high in the whole region and temperature is the factor most influencing it: districts with smaller temperature peaks around 23°C in the period April-November show the highest risk and the lowest uncertainty. Providing a map of the areas where livestock are more likely to be exposed can be useful to inform national surveillance policies.

Keywords: exposure assessment, vector-borne diseases, Bluetongue.

.../..

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

…/..

RÉSUMÉ

Dans cet article, nous décrivons un modèle d'évaluation de l'exposition, explicité spatialement, développé dans le projet « SPARE » (www.spare-europe.eu). En particulier, nous montrons comment nous avons estimé la probabilité spatiale que l'introduction d'un animal infecté par une maladie vectorielle (la fièvre catarrhale ovine, dans notre exemple) mènera, au moins, à un autre animal infecté, en utilisant la région du Piémont de l'Italie du Nord-Ouest comme zone d'exemple.

Une recherche bibliographique étendue a conduit à la rédaction d'une liste structurée et systématique de facteurs de risque d'exposition. Cette liste a alors été utilisée pour développer des arbres de probabilité, détaillant les principales branches d'exposition, avec les équations et leur paramétrage. Un modèle stochastique a été mis en œuvre et exécuté. Nous fournissons des cartes affichant une distribution différente de la probabilité d'une transmission secondaire fondée sur le modèle. Cette probabilité est très élevée dans toute la région et la température est le facteur principal : les zones avec des petites poussées de température autour de 23°C pendant la période novembre-avril montrent le risque le plus élevé et l'incertitude la plus faible. Fournir une carte des zones où le bétail est le plus susceptible d'être exposé peut être utile pour établir des politiques nationales de surveillance.

Mots-clés : évaluation de l'exposition, maladie vectorielle, fièvre catarrhale ovine.

જ

I - INTRODUCTION

The increasing threat posed by the incursion of exotic animal pathogens such as Lumpy Skin Disease and African Swine Fever to the European Union (EU) has been recently highlighted [Mur *et al.*, 2014, EFSA, 2016]. Moreover, the number of the outbreaks in people, including zoonotic agents, occurring annually throughout the world is increasing [Smith *et al.*, 2014], becoming a great concern at both the global and national level. During the last years, an increasing number of risk assessments have been conducted by international organisations [ECDC, 2016] as well as by individual countries [Roberts, 2016].

One of the main aims of the collaborative European research project SPARE, 'Spatial risk assessment framework for assessing exotic disease incursion and spread through Europe' [SPARE, 2016], is to develop a quantitative risk assessment to describe the spatial introduction and spread of exotic livestock pathogens within Europe, based on the most probable routes of transmission.

The risk assessment was conceived to be modular with the release, exposure and consequence assessments developed independently.

Within SPARE, to focus the work, three case studies pathogens were selected by means of a multi-criteria risk-ranking framework, as described in De Nardi *et al.*, 2016: Bluetongue virus (BTV) (route of transmission: vector borne diseases), classical swine fever (routes of transmission: direct contact and import of animal products) and rabies (routes of transmission: wildlife and people and pet movements). For each case study spatially explicit models concerning either the release or the exposure or the consequences were developed. Aim of this study was to develop a general exposure assessment framework for vector borne diseases. This general model was then validated using BTV as a case study. Here we present the estimation of the spatial probability that introduction of one infected animal affected by BTV will lead to at least one other infected animal, using the Piedmont region of North Western Italy as an example area.

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

II - MATERIAL AND METHODS

To assess the risk of exposure of livestock populations to exotic vector borne diseases we firstly extracted, from the OIE listed diseases, the diseases that can be transmitted by vectors and that are not endemic in Europe (Table 1). For each of these pathogens, an extensive literature search was carried out. The search covered peer reviewed publications and grey literature, using snowball searching and googling [Lecy *et al.*, 2012].

Based on the scientific literature and the expertise available within the research team, the risk factors that may affect the probability of an infectious agent spreading in the susceptible population because of its introduction were identified.

Table 1

List of the OIE listed diseases not endemic in Europe which can be transmitted by vectors

Disease
African Horse Sickness
African Swine Fever
Bluetongue
Crimean Congo Haemorrhagic Fever
Ehrlichia Ruminantium (Heartwater)
Epizootic Haemorrhagic virus
Equine encepahalomyelitis - Eastern and Western
Equine Infectious Anaemia
Japanese Encephalitis
Lumpy Skin Disease
Nairobi sheep disease
Rift Valley Fever
Venezuelan Equine Encephalomyelitis
Vesicular stomatitis
West Nile Fever

The identified risk factors were then characterised in terms of:

- relevance for the exposure assessment model (2 classes: 0='Parameter not necessary (but that can improve the model)'; 1='Parameter necessary');

- potential availability of data sources and quality of data (5 classes: 0='Very good data availability'; 1=' Good data availability'; 2='Acceptable data availability; 3='Poor data availability - Data Gap'; 4='No data - Serious Data gap');

- uncertainty of data sources availability (4 classes: 0='No availability'; 1='Low availability'; 2='Medium availability'; 3='High availability').

The diseases were then ranked on the characterization of the basis of availability of data sources and the quality of data and Bluetongue was select to be modelled for its high ranking.

Focussing on BTV risk assessment, a second extensive literature search on PubMed (http://www.ncbi.nlm.nih.gov/pubmed), was carried out with the following research strings: "Blue Tongue[Text Word]) AND risk

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

assessment[Text Word]" (accessed on 10/03/2016). Moreover, grey literature (*i.e.* national risk assessment reports) was also considered by carrying out a snowball search starting from references of the selected articles and the following string was googled: "Blue Tongue Risk assessment". Scenario trees detailing the main, and most likely, exposure pathways were developed, along with the equations and their most appropriate parametrization based on available data, incorporating variability where relevant.

A stochastic model, based on the developed scenario trees, was then developed in R to provide a spatially explicit quantitative assessment of the BTV risk of exposure to livestock.

Finally an estimate of the spatial probability that introduction of one infected animal affected by BTV will lead to at least one other infected animal was provided at a NUTS 3 level (i.e. districts) in the Piedmont region of North Western Italy, running with 1000 iterations the stochastic model for each district. The model considered cattle and small ruminants as 'animal', and *Culicoides spp* as 'vector'.

III - RESULTS

Seven main categories of risk factors were identified, leading to an overall number of 27 risk factors affecting the exposure to vector-borne diseases. Those factors, along with the results of their characterisation specific to BTV, are reported in Figure 1.

The scenario tree pathway for the exposure to vector-borne diseases leading to the probability of a secondary transmission after the introduction of one infected animal is reported in Figure 2.

Parameters and data sources for the BTV model are reported in Table 2.

The probability of a secondary transmission of BTV after the introduction of one infected animal is quite high in the whole region, with a range from 66% to 92% in cattle and from 48% to 74% in sheep. A sensitivity analysis showed that the factor most influencing the output is temperature: districts with smaller temperature excursions around 23°C (provinces: AT and NO for cattle population; AT, NO and AL for small-ruminants population), showed the highest risk and the lowest uncertainty (Figure 3).

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

Figure 1

Characterisation of the factors affecting the exposure to Bluetongue.

Classes of data availability and uncertainty are expressed as shades of grey: light grey: very good data/no uncertainty; medium grey: good data/low uncertainty; dark grey: sufficient data/medium uncertainty; black: poor data/high uncertainty

BLUETONGUE	Data availability	Uncertainty
INFECTION EPIDEMIOLOGY		
Case definition		
Incubation period (infectious period before the clinical symptoms)		
Average time to end of infectious period		
Differential diagnosis complexity		
* Vaccine availability		
Vaccine efficacy		
DISEASE PREVALENCE IN:		
* Bovine		
* Sheep		
* Goats		
COUNTRY FEATURES		
Vaccine diffusion		
* Existence of a surveillance program		
Surveillance efficiency		
Public health authorities awareness		
Farmer awareness		
Proxy of population awareness		
GEOGRAPHIC RISK		
* Infected areas proximity (geographical borders)		
POPULATION DENSITY		
* Bovine		
* Sheep		
* Goats		
POTENTIAL CONTACTS		
* Bovine movements in Italy		
* Sheep movements in Italy		
* Goats movements in Italy		
Importation of bovine in Italy		
Importation of sheep in Italy		
Importation of goats in Italy		
VECTORS		
Vectors distribution (mosquitoes)		
Presence of wetland		

* Parameters necessary to develop the exposure assessment model.

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

Figure 2

A fishbone diagram showing the scenario tree pathway for the exposure to vector-borne pathogens after the introduction of an infected animal (Bluetongue). P.= Probability
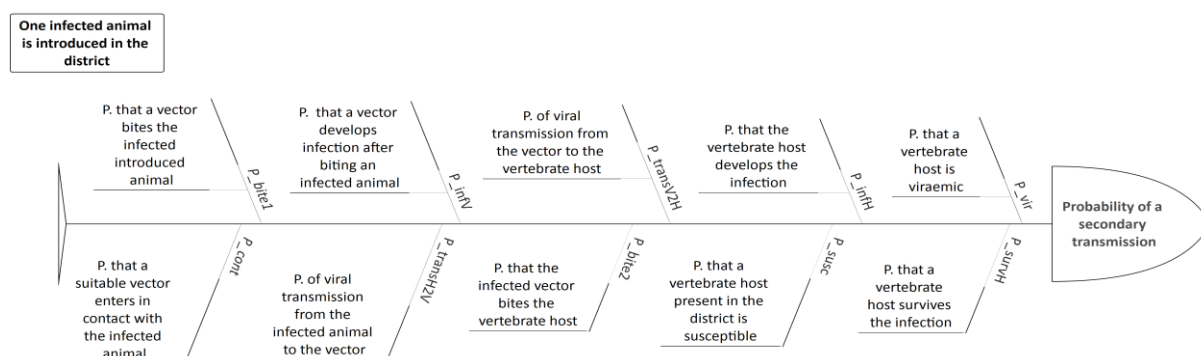

Table 2

Parameters and data sources for the stochastic model for Bluetongue virus exposure assessment.

Notation	Variable	Distribution	Parameter	Data source
T	Temperature °C (T)	Normal (μ, σ)	μ=mean σ=standard deviation	Global Climate data (http://www.worldclim.org/)
H	Number of hosts Host density			National Cattle Registry (www.vetinfo.it)
F	Number of farms Farm density			National Cattle Registry (www.vetinfo.sanita.it)
d	Days of life for a vector		111.84*exp(-0.1547*T)	Mullens *et al.*, 2004; Gerry *et al.*, 2000
V	Vector density	Uniform(a,b)	a=min number of Culicoides, b=max number of Culicoides	Entomologic Bluetongue surveillance data Piedmont
S	Spread of vector (Km)	Uniform(a,b)	a=51, b=152.5	Roberts *et al.*, 2016; Kluiters *et al.*, 2015
P_cont	Probability that a suitable vector enters in contact with the infected animal		=1-(((1-((1-P(H))*(1-P(F)))^S)^*d*)	
b	Vector probability of biting a host		=1-exp(-0,000171*T*(T-3,6966)*(41,8699-T)^(1/2,7056))	Mullens *et al.*, 2004; Gerry *et al.*, 2000
P_bite	Probability that a vector bites the introduced infected animal		=(1-B(V/(H*F),1/H))*b*P_cont	
t	Probability of transmission from host to vector	Uniform(a,b)	a=0.8, b=1	Hartemink *et al.*, 2009
P_transH2V	Probability of viral transmission from the infected animal to the		=P_bite*t	

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

	vector			
y	Probability for a vector to become infectious		=1-EXP(-0,0003*T*(T-10,4))	Hartemink *et al.*, 2009
P_infV	Probability that a vector develops the infection after biting the infected animal		P_transH2V*y	
P_bite2	Probability that the infected vector bites the vertebrate host		1-(((1-(1-P(F))*(1-P(H/F)))^S)^d)	
m	Probability of transmission from vector to host	Uniform(a,b)	a=0.001, b=0.15	Guis *et al.*, 2011
P_transV2H	Probability of viral transmission from the vector to the vertebrate host		m*P_bite2*P_cont	
C	Vaccine coverage	Uniform(a,b)	Cattle: a=0.01, b=0.3 Small ruminants: a=0.3, b=0.6	Anonymous, 2002
E	Vaccine efficacy	Uniform(a,b)	a=0.98, b=1Cattle: a=0.01, b=0.3 Small ruminants: a=0.3, b=0.6	EFSA, 2007, Anonymous, 2002
P_susc	Probability that a vertebrate host present in the district is susceptible	Uniform(a,b)	a=0.98, b=1 1-(C*E)	EFSA, 2007
i	Probability for a susceptible host to develop infection	Uniform(a,b)	a=0.97, b=1	http://www.discontools.eu/
P_infH	Probability that the vertebrate host develops the infection		P_susc*i*P_transV2H	
k	Probability of dying	Uniform(a,b)	Cattle: a=0.000010, b=0 0.00001 Small ruminants: a=0.01, b=0.001	http://www.discontools.eu/
P_surv	Probability that a vertebrate host survives the infection		1-k	
D	Duration of infection	Uniform(a,b)	Cattle: a=18, b=25 Small ruminants: a=14, b=20	Guis *et al.*, 2011
P_vir	Probability that the vertebrate host is viraemic		=1-EXP(-0,0003*T*(T-10,4))(1-(1-(P_surv*P_infH))^D)	

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

Figure 3

Output of the stochastic quantitative assessment of the probability of exposure to vector-borne diseases after the introduction of one infected animal in Piedmont in the period of *Culicoides spp* presence (April-November).

The map combines two types of information: the probability that a domestic animal is infected after the introduction of one Bluetongue infected animal (shown from bottom to top in the legend) and how certain it is (shown from left to right in the legend).

Cattle

Small ruminants
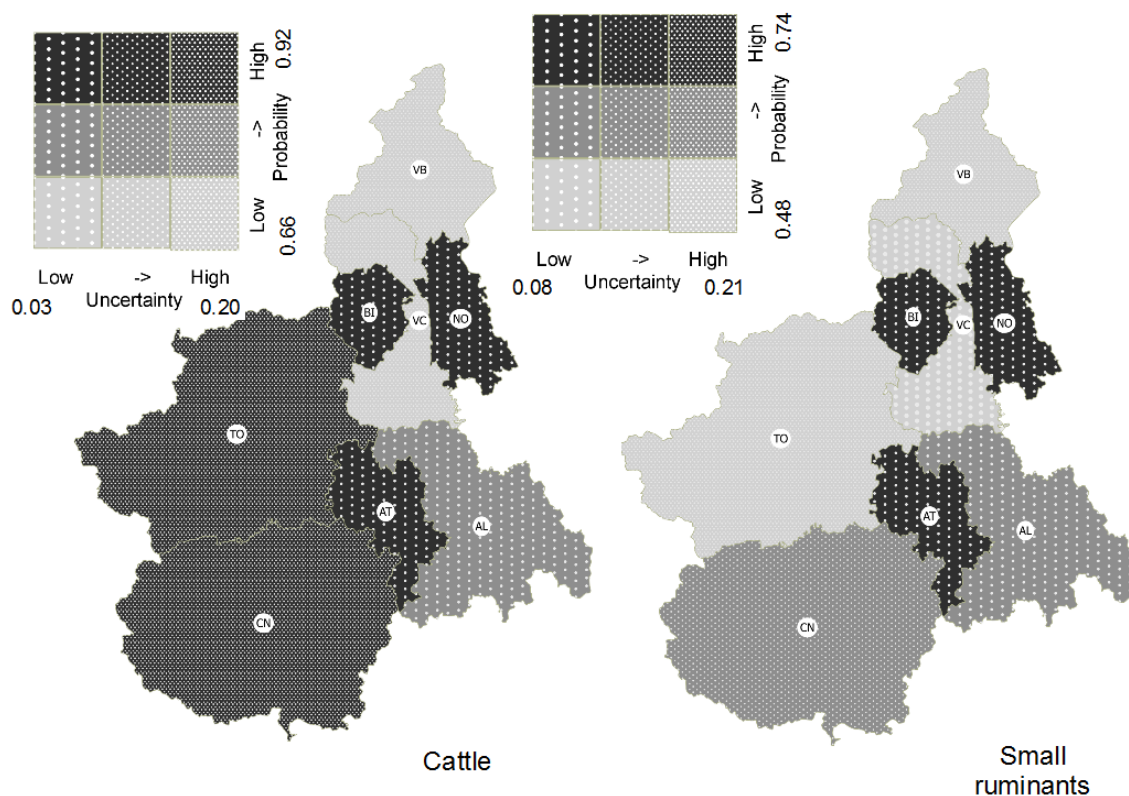
IV - DISCUSSION AND CONCLUSION

In this paper, we present a generic exposure model framework for secondary transmission of an exotic vector-borne disease, after the introduction of one infected animal to a specific geographical area. Exposure to bluetongue virus in the Piedmont region of Italy was used as case study, and modelling was carried out based on the parameterisation of the relevant factors. Results from the stochastic model suggest varying levels of risk between the different districts of Piedmont, with temperature being identified as the most influential parameter in the model. Differences between species reflects not only the different population densities, but also the disease related

variables (e.g.: duration of disease, severity of disease, probability of dying).

Our choice of modelling Bluetongue, a disease far to be exotic in Europe, was driven by its selection as case study pathogen for the SPARE project. This was in part due to data availability and uncertainty: when dealing with Italian livestock like cattle and small ruminants, data of good quality are available and the needed input parameters (e.g. population densities) may be quantified with little uncertainty.

Moreover modelling Bluetongue allows us to integrate our model with the outputs of an ongoing network analysis on livestock movements

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

(recorded in Italy only for cattle and, with some limitation, for sheep).

The generic framework presented here is designed to be adaptable to other vector-borne diseases, such as West Nile or African Horse Sickness and also to other geographical regions. However, data availability is likely to be an issue in some cases. For example, in Italy Equidae registration, even if mandatory, may be still poor and good data about population density are lacking, which would be a problem for modelling African Horse Sickness.

In our model, we took advantage of observed data on *Culicoides* abundance, coming from entomological surveillance; however this could have led to a certain degree of overestimation of vector abundance in some part of the region, as traps were not evenly distributed over districts.

The role of temperature on vector activity and its impact on spread of infection is well reported in the literature [Racloz *et al.*, 2008; Elbers *et al.*, 2015], but the knowledge of the relationship between vector biology and climatic factors is limited to studies conducted on *Culicoides sonorensis*, and could be different for *Culicoides imicola* (widespread in Southern Europe) and *Culicoides obsoletus complex* (present in Northern Europe).

In conclusion, taking into account the uncertainties, the outputs of this assessment can help to inform national surveillance policies, by providing evidence for geographical areas where livestock are more likely to be effectively exposed.

BIBLIOGRAPHY

Anonymous - Risk analysis on the introduction into free territories of vaccinated animals from restricted zones. 2002. (https://bluetongue.izs.it/j6_bluetongue/resources/pdf/docTecnici/analisiRischio/dicembre_2002.pdf)

De Nardi M., Adkin A., Simons R., Bertolini S., Crescio M. I., Estrada-Peña A., Horigan V., Léger A., Maurella C., Ru G., Schuppers M., Stärk K.D.C. - A multi-criteria risk-ranking framework to prioritize pathogens: a case study for transboundary animal diseases in Europe. At: Swedish Agricultural University, Uppsala, Sweden. 2016. Conference: Annual Scientific Conference of the European College of Veterinary Public Health (ECVPH)

ECDC - European Centre for Disease Prevention and Control. Rapid Risk Assessment. Zika virus disease epidemic: Sixth update. 20 May 2016. Stockholm.

EFSA - AHAW Panel (EFSA Panel on Animal Health and Welfare) Scientific Opinion on request from the European Commission on bluetongue vectors and vaccines. *The EFSA Journal,* 2007, **479**, 1-29.

EFSA - AHAW Panel (EFSA Panel on Animal Health and Welfare), Statement: Urgent advice on lumpy skin disease. *EFSA Journal,* 2016, **14**(8), 4573.

Elbers A.R., Koenraadt C.J., Meiswinkel R. - Mosquitoes and Culicoides biting midges: vector range and the influence of climate change. *Rev. Sci. Tech.,* 2015, **34,** 123-137.

Gerry A.C., Mullens B.A. - Seasonal abundance and survivorship of *Culicoides sonorensis* (Diptera: Ceratopogonidae) at a southern California dairy, with reference to potential bluetongue virus transmission and persistence. *J. Med. Entomol.,* 2000, **37,** 675-688.

Guis H., Caminade C., Calvete C., Morse A.P., Tran A., Baylis M. - Modelling the effects of past and future climate on the risk of bluetongue emergence in Europe. *J. R. Soc. Interface.,* 2011. Published online. DOI: 10.1098/rsif.2011.0255.

Hartemink N.A., Purse B.V., Meiswinkeld R., Brownc H.E., de Koeijer A., Elbers A.R.W., Boender G.J., Rogers D.J., Heesterbeek J.A.P. - Mapping the basic reproduction number (R0) for vector-borne diseases: A case study on bluetongue virus. *Epidemics*, 2009, **1,** 153-161.

Kluiters G, Swales H, Baylis M. - Local dispersal of palaearctic *Culicoides* biting midges estimated by mark-release-recapture. *Parasites & Vectors*, 2015, **8**, 86.

Lecy J.D., Beatty K.E. - Representative Literature Reviews Using Constrained Snowball Sampling and Citation Network Analysis. 2012. Available

Épidémiol. et santé anim., 2017, **71**, 139-148

Exposure Assessment in the context of the SPARE project:
A model to spatially assess exotic diseases incursions and
spread throughout Europe

at SSRN: https://ssrn.com/abstract=1992601 or http://dx.doi.org/10.2139/ssrn.1992601.

Mullens B.A., Gerry A.C., Lysyk T.J., Schmidtmann E.T. - Environmental effects on vector competence and virogenesis of bluetongue virus in Culicoides: interpreting laboratory data in a field context. *Vet. Ital.,* 2004, **40**,160-106.

Mur L., Martinez-Lopez B., Costard S., de la Torre A., Jones B.A., Martinez M., Sanchez-Vizcaino F., Munoz M.J., Pfeiffer D.U., Sanchez-Vizcaino J.M., Wieland, B. - Modular framework to assess the risk of African swine fever virus entry into the European Union. *BMC Veterinary Research,* 2014, **10**, 145.

Racloz V., Venter G., Griot C., Stärk K.D.C. - Estimating the temporal and spatial risk of bluetongue related to the incursion of infected

vectors into Switzerland. *BMC Vet. Research*. 2008, **4**, 42.

Roberts H., Moir R., Matt C., Spray M., Boden L., Bessell P. - Risk assessment for Bluetongue Virus (BTV-8): risk assessment of entry into the United Kingdom. 2016 (https://www.gov.uk/government/publications /qualitative-risk-assessment-bluetongue-virus-btv-8-entry-into-the-uk)

Smith K.F., Goldberg M., Rosenthal S., Carlson L., Chen J., Chen C.C., Ramachandran S. - Global rise in human infectious disease outbreaks. *Journal of the Royal Society Interface,* 2014, **11**(101), DOI: 10.1098/rsif.2014.0950

SPARE. - Spatial Assessment of Risk for Europe for evaluating the incursion and spread of exotic animal disease through Europe, 2016. http://www.spare-europe.eu/.

❧