REVIEW

Survey of Systems for Comparative Ranking of Agents that Pose a Bioterroristic Threat

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Impacts

- Survey about existing open-source risk ranking systems for biological agents and comparison of these prioritization schemes by revealing differences in methods and focus.
- Presentation and structuring of criteria that were used for the evaluation of risk of specific biological agents deriving from the surveyed prioritization schemes.
- Thus, identification of need for generic comparative ranking of zoonotic agents that pose a bioterroristic threat.

Keywords:
Risk assessment; prioritization; categorization; zoonoses; bioterrorism; high-risk biological agents

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Received for publication December 12, 2012

doi: 10.1111/zph.12065

Summary

Strong efforts are made to improve preparedness for the prevention and counteraction of possible deliberate release of highly pathogenic biological agents at national and international level. An objective risk assessment for highly pathogenic biological agents is urgently needed for the purpose of prioritizing measures, evaluating the vulnerabilities and supporting rapid decisions on a scientific base in case of an emergency. Hitherto, several differing ranking schemes were developed. In general, the purpose of such ranking schemes is a comparative classification of agents under consideration of different transmission paths as well as agents threatening human and/or animal health. The analysed prioritization methods differ from qualitative to (semi-)quantitative with each its benefits and disadvantages in preciseness of the result, complexity and duration of the assessment but also in comprehensibility. Mainly, risk was defined as the product of probability and impact. In this survey, factors frequently used for the assessment of the probability and impact of a deliberate agent release were identified. Main criteria for the probability of an application were the history of use, the accessibility of the agent and possible paths of introduction and contamination as well as the feasibility of agent production. For the estimation of the impact, mainly the agent's effects on human and/or veterinary public health, depending on the target population, were examined. This includes the morbidity and mortality rates as well as the severity of induced illness, possible measures for diagnosis, and treatment and prevention. Furthermore, the economic and socioeconomic consequences were considered. In this review, the authors give an overview on open-source publications dealing with risk ranking of biological agents by outlining the criteria that were applied for risk ranking.

Introduction

Highly pathogenic biological agents comprise bacteria and viruses as well as biological toxins. They are, besides explosives and toxic chemicals, considered as potential means of terrorists that could cause illness or death in people, animals and/or plants. It is furthermore conceivable that biological agents could be used with the main intention of causing direct and indirect economic losses by disrupting the food supply chains, undermining social stability or impairing the public or veterinary health sector. Such an intentional release of one or more biological agents would be called a bioterroristic incident. To support the development of appropriate national and international security

policies and standards, it is therefore important to create a science-based ranking scheme to categorize highly pathogenic biological agents regarding their potential use for bioterroristic application. This ranking scheme should be based on an assessment of the probability and impact of a deliberate release of these agents. The term 'probability' in this sense is not meant in a strict statistical sense but should indicate the likeliness that an agent would be chosen with criminal intent because of its technical and methodological suitability for bioterroristic purposes. In relation to the currently ongoing chemical, biological, radiological and nuclear (CBRN) harmonization process within the EU (e.g. CBRN Action Plan (Anon, 2009), a ranking scheme could also support the work of determining appropriate biosafety and biosecurity measures. This could include for example restricted access to highly hazardous agents or specific protection measures against theft or loss. Other application areas of agent ranking are the support in

1. decision-making on regulations affecting laboratories dealing with certain agents,
2. identifying suspicious actions like loss or theft,
3. highlighting insufficiencies in crisis management capabilities,
4. revealing needs to develop treatments or prevention measures,
5. quick situation analysis and risk assessments.

Several ranking lists on highly pathogenic biological agents already exist. However, there is an ongoing debate concerning the applied methodology for the creation of underlying ranking schemes and their applicability for specific issues. Currently, there are lists available classifying the most dangerous biological agents in respect to their impact on human health, animal health, international trade or the food supply chain (Anon, 2012; Cardoen et al., 2009; Federal Office of Public Health/Switzerland, 2004; Franz et al., 1997; Havelaar et al., 2010; Tegnell et al., 2006; World Health Organization (WHO), 2006; World Organization for Animal Health (OIE), 2004; World Organization of Animal Health (OIE), 2009. Due to these different fields of application, the rankings vary. For example, ranking lists with focus on possible food associated bioterroristic incidents identify agents as 'hazardous', which are usually out of other lists scope, such as *Listeria monocytogenes* or *Campylobacter* spp. because of their particular occurrence in and adaptation to the medium 'food' (Federal Office of Public Health/Switzerland, 2004; Federal Ministry of Food Agriculture and Consumer Protection/Germany, 2008).

Additionally, several approaches were described for the risk ranking of biological agents: a qualitative approach, assembled the relevant agents into a list without internal ranking according to expert opinions (Valenciano, 2001). In contrast, some authors used a quantitative method to enhance preciseness of risk assessment (Kemmeren et al., 2006; Fosse et al., 2008). This was accomplished by a time-consuming collection of detailed data regarding specific characteristics of agents that resulted in a very accurate assessment of the biological agents of concern. An approach in between these two mentioned procedures is the risk evaluation in a semiquantitative manner. This comprises the establishment of several graduated scores to estimate the probability and impact of utilization of specific biological agents. By means of this method, it is possible to bypass imprecise knowledge so that it is also feasible to assess the risk of pathogens with low data availability.

Methods

A literature research for existing publications regarding risk ranking of biological agents was conducted. As a starting point, a search in ISI Web of Knowledge was performed using several combinations of the terms 'risk assessment', 'risk analysis', 'bioterror*', 'methodology', 'risk ranking', 'pathogen' and 'biological agent'. Additionally, published lists of pathogens and open-source risk ranking schemes of biosecurity-related authorities and institutes in several countries as well as of international institutions were checked resulting in 34 documents. An analysis of these publications was executed regarding the applied methodology for the risk assessment (qualitative, semiquantitative or quantitative), the definition of risk and the criteria used for risk ranking.

In the majority of the examined publications, most of the criteria necessary for the ranking are mentioned inside a discourse in different designations and are not presented clearly in the form of a table or something comparable. Thus, the authors conducted the collection of criteria and their classification to probability or impact at least by four-eye but mostly by six-eye principle to cover all aspects. To generate a comprehensive list of agent properties, these aspects were structured hierarchically into 'categories' containing 'criteria' that are described by 'measures' because these should be preferably based on measurable information. As a key requirement for the resulting catalogue, we postulated that criteria have to be mutually exclusive and exhaustive at the level of the categories. As a consequence, each of the measures used for the description of the criteria has to be defined in terms of its precise meaning. However, not only the definition of the categories, criteria and measures is an important step in the development of a risk ranking scheme but also a universal definition of risk is essential as varying definitions of this term are existent and were revealed in the literature survey. Subsequently, an analysis of methodologies and a consideration of advantages and disadvantages of the different methodologies were performed in expert discussions keeping in mind the focus

of the risk ranking system as a support for decision-makers and for quick situation analysis.

Overview

The analysis of existing publications in the field of comparative risk ranking revealed numerous differences regarding the focus areas, the applied methodology for risk assessment, the applied criteria and the definition of risk. Focus areas, risk assessment method as well as the structure of the risk ranking and the generated list of biological agents are presented in Table 1.

Not only the perspectives and applied methodologies differ, but also the ranking list structure itself: some of them are organized with respect to specific agent properties; some are lists with agents in hierarchical order regarding their threat potential, whereas others just provide an enumeration of agents without any ordering.

Furthermore, some of these documents only propose methods for risk ranking of biological agents and are not applied to obtain a list of ranked biological agents, they are called 'theoretical' in Table 1. Others contain catalogues of criteria that are used to generate unranked and sometimes also ranked lists of pathogens without objective explanations for this graduation ('qualitative'). A survey of existing publications concerning risk ranking of high-risk pathogenic biological agents and an evaluation of the used categorization criteria revealed many relevant properties. Due to the different foci of used publications out of the feed, farm, food and human health perspectives as well as the production of plants that were considered (literature see Table 1), a broad range of criteria was specified.

Important systems for risk ranking and lists of agents with bioterroristic potential are as follows:

1. the tiered bioterrorism agents list of the Centers for Disease Control and Prevention (CDC), evaluating the agents by the threat they pose to the national U.S. security (Centers for Disease Control and Prevention (CDC), 2007),
2. the tiered HHS and USDA Select Agents and Toxins list amended by the Federal Experts Security Advisory Panel of the USA (Anon, 2012; Select Agent Program, 2012),
3. the list of the European Commission in their interim document 'Technical guidance on generic preparedness planning for public health emergencies' (European Commission: DG SANCO, 2005),
4. the Australia Group list – the Australia Group is an informal forum of different countries such as all EU Member States and some candidate countries, Switzerland, USA, Canada and Australia. It was founded to minimize the risk of chemical and biological weapon proliferation (Australia Group, 2011a,b),
5. the German categorization of biological agents with respect to bioterroristic threats mediated through food or water – published by the Federal Ministry of Food, Agriculture and Consumer Protection in Germany (Federal Ministry of Food Agriculture and Consumer Protection/Germany, 2008),
6. the list of the Swiss Federal Office of Public Health considering the deliberate distribution of the biological agents by food or water (Federal Office of Public Health/Switzerland, 2004),
7. the former and the present OIE prioritization lists on animal diseases (World Organization for Animal Health (OIE), 2004; World Organization of Animal Health (OIE), 2009).

Supplemental to these lists, several scientists presented additional relevant criteria: for example in 2004, Davis mentioned several criteria with respect to animal diseases (Davis, 2004). Additionally, also in other fields, such as for biomedical and bioscience laboratories, relevant criteria for the prioritization of high-risk biological agents were evaluated by experts of Sandia National Laboratories (USA) in 2003 (Salerno et al., 2003).

Pappas et al. provocatively raised some questions regarding the selection of biological agents for which awareness is needed (Pappas et al., 2009). They argued that it is laborious to unfeasible to apply selected criteria of a risk ranking stringently and objectively in all cases as the graduations of the biological agents for different criteria are often contradictory and complicate the generation of a clear ranking. This shows that for the generation of a reliable risk analysis, it is crucial to look from a broad perspective, considering all aspects of probability and impact of the respective biological agent.

It is essential to define the term 'risk', which is the basis of each prioritization scheme. The definition of ISO/IEC Guide 73 could be considered as a general definition. In this document, risk is determined as product of probability and impact (International Organization for Standardization, 2009). This definition also represents the most common definition in literature about risk ranking of biological agents and was also used in the surveyed literature, if a classification of criteria was conducted (Ackermann and Moran, 2004; Ezell et al., 2010; Danish Centre for Biosecurity and Biopreparedness, 2012).

As already mentioned before, the prioritization of agents could be conducted in different ways: qualitative risk ranking sets are based on expert opinions, whereby reproducibility of the results is sometimes low. As no data collection but a survey among experts is necessary, this method is easily conductible and time-saving but is only based on the opinions of an expert panel (Anon, 2012; Australia Group, 2011a,b; Federal Ministry of Food Agriculture and Consumer Protection/Germany, 2008; Irlenkäuser, 2007; World

Table 1. Surveyed literature, listed in alphabetical order of sources

Reference	Focus	Risk Assessment Method[a]	Structure of Agent List[b]
Ackermann and Moran (2004)	General	Qualitative (theoretical)	–
Animal and Plant Health Inspection Service, USDA (Anon, 2012)	Animal	Qualitative (probably; based on expert panel)	2 tiers
Anonymous (2001)	Human	Unknown (probably qualitative)	Unranked
Australia Group (2011a)	Animal	Qualitative (expert opinion)	Unranked
Australia Group (2011b)	Human	Qualitative (expert opinion)	Unranked
Capek (2010)	General	Semiquantitative	3 tiers
Cardoen et al. (2009)	Human	Semiquantitative (based on expert, opinion, experts were equipped with fact sheets), weighting factors	Quantitative (integer scores between 0 and 20 possible)
Centers for Disease Control and Prevention (CDC) (2007); Rotz et al. (2002)	Human	Semiquantitative	3 tiers
Codex Alimentarius Commission (1999)	Food	Theoretical	–
Davis (2004)	Animal	Qualitative	Unranked
Department for Environment Food and Rural Affairs (DEFRA/UK) (2007)	Animal	Semiquantitative (theoretical)	–
Doherty et al. (2000)	Human	Semiquantitative	Unranked
Elad (2005)	Food	Theoretical	–
European Commission: DG SANCO (2005)	Human	Unknown (probably qualitative)	2 tiers
European Technology Platform for Global Animal Health (2010)	Animal	Semiquantitative (theoretical)	–
Federal Ministry of Food Agriculture and Consumer Protection/Germany (2008)	Food	Qualitative	3 tiers
Federal Office of Public Health/Switzerland (2004)	Food	Semiquantitative	5 tiers
Franz et al. (1997)	Human	Qualitative	Unranked
Havelaar et al. (2010)	Human	Semiquantitative	Quantitative (scores between 0 and 1 possible)
Irlenkäuser (2007)	Animal	Qualitative	Unranked
Krause (2008)	Human	Semiquantitative by experts	–
Lele (2010)	Human	Theoretical	–
MacIntyre et al. (2006)	Human	Semiquantitative	Quantitative (all integer scores between 0 and 20 possible)
NATO -Departments of the Army, the Navy and the Air Force/USA (Anon, 1996)	Human	Qualitative (theoretical)	–
Okelo and Food and Drug Administration/USA (FDA) (2008)	Feed	Quantitative (with exponential range; theoretical)	–
Panel on Biological Hazards (BIOHAZ) (2008)	Feed	Qualitative/unknown	–
Pappas et al. (2009)	Human	Semiquantitative	Quantitative (all integer scores between 0 and 30 possible)
Radosavljevic and Belojevic (2009)	Human	Semiquantitative (theoretical)	–
Salerno et al. (2003)	Human	Theoretical	–
Tegnell et al. (2006)	Human	Semiquantitative	5 tiers
Wheelis (2000)	Animal	Theoretical	–
World Health Organization (WHO) (2006)	Human	Semiquantitative (by experts)	Quantitative
World Organization of Animal Health (OIE) (2009)	Animal	Qualitative	2 tiers
World Organization for Animal Health (OIE) (2004)	Animal	Qualitative	Unranked

[a]Theoretical: criteria were listed without the generation of a list of relevant pathogens. Qualitative: criteria were considered (by the authors or other experts) and are the basis of a list of relevant agents (subjective). Semiquantitative: used criteria take values that are ordinal-scaled integer numbers. These numbers are, summed or multiplied and in parts also weighted, the basis for a list of relevant biological agents. Quantitative: used criteria take all metric positive values. These numbers are, summed or multiplied and in parts also weighted, the basis for a list of relevant biological agents.
[b]Quantitative: all metric positive values are possible for the selected biological agents (sometimes the number of values is somewhat restricted). Unranked: formation of a list of threatening agents without comparative graduation within the list.

Organization for Animal Health (OIE), 2004; World Organization of Animal Health (OIE), 2009). A risk assessment in a semiquantitative way is a compromise between preciseness of the result and complexity and duration of the assessment (Cardoen et al., 2009; Centers for Disease Control and Prevention (CDC), 2007; Department for

Environment Food and Rural Affairs (DEFRA/UK), 2007; Rotz et al., 2002; Tegnell et al., 2006; World Health Organization (WHO), 2006). For a quick situation analysis in emergency situations, the time-saving advantage of a semi-quantitative approach is crucial. Additionally, it is more intuitively understood by the target group, like decision-makers and stakeholders, and is an easily applicable compromise in comparison with a stringent and full quantitative risk assessment approach. The most precise method, a quantitative risk assessment, requires detailed data with good data quality including information on the variability and uncertainty about all considered criteria to get reliable results (Okelo and Food and Drug Administration/USA (FDA), 2008). Unfortunately, for several biological agents with potential for bioterroristic application, these data are not or are only available with low preciseness with the resulting consequences for the predictive value of the risk ranking.

According to the most frequent definition of risk (risk = probability × impact), the authors categorized all criteria found in the literature research for simplification purposes in categories according to their contribution to the sections 'probability' and 'impact'. For a detailed overview of all aspects considered for each category and criterion in the sections 'probability' and 'impact', please refer to Table 2.

All aspects that are related to the likelihood of applying a specified biological agent in a bioterroristic incident are covered by the section 'probability'. One relevant category identified in the literature survey concerning probability is the 'history of use', which includes not only former attacks and attempts of attack with the specific agent but also former bioweapon programs that could have resulted in abounding stocks of the agents stored in more or less safeguarded facilities. In contrast, the category 'accessibility of the agent' considers the availability of the agent for bioterroristic purposes in terms of natural or laboratory existence. Referring to this, diverse aspects were considered: the possibility of a perpetrator to get access to the desired biological agent is influenced by the number of laboratories possessing the agent (access by theft), the numbers of human or animal cases per year (access e.g. through patient samples), the biosafety level of the biological agent (assuming that a low BSL results in higher accessibility due to low safeguard and more laboratories possessing the agent) and the prevalence of the agent in the environment (direct access to the agent possible). The category 'feasibility of production' includes the production efforts as well as the feasibility to manufacture and store larger amounts of the biological agent by individuals or terroristic organizations. This considers not only the necessary technical equipment but also the skilled personnel, which are needed for the production of the desired quantity of the agent. Furthermore, by evaluating all possible ways of an agent introduction into the target population, the possibility of agent-'dissemination' was found as an important category. Several introduction paths for biological agents are known: some bacteria, viruses and toxins can be transmitted as aerosols or can be used for the contamination of water or food. Another possibility to generate mainly economic damage and social disruption displays the introduction of biological agents via animal feed or farm animals into the food chain because it is closely linked to the consumer. These distinct paths of insertion differ clearly with regard to the applicable agents, the difficulties of preparation and introduction of the agents, and the impact of the consequential incident. Moreover, the release of a pathogen by aerosol requires more effort in preparation and weaponization of the pathogen combined with augmented knowledge of the personnel needed. Thus, the contamination of food or water is appraised as one of the easy realizable ways (Federal Office of Public Health/Switzerland, 2004).

To the section 'impact', all consequences connected with the release of a specific agent were assigned. These consequences include the adverse effects on 'human and veterinary public health', that is lethality and morbidity rates as well as the severity of the disease and the possible consequential need for hospitalization in case of human illness. Another important category for the estimation of the impact is the availability of 'countermeasures' comprising of direct treatment and preventive measures like vaccination. Furthermore, the availability of established 'diagnostics' is a major issue because it is crucial for an efficient surveillance system but also for the rapid detection of biological agents in patient and matrix samples. The rapid and reliable detection of the agent in samples also contributes to response efforts to contain the outbreak, hamper secondary cases and reduce further spread of the disease. Many authors consider the potential of transmission within or between populations as a very relevant aspect for risk ranking (Centers for Disease Control and Prevention (CDC), 2007; Doherty et al., 2000; Havelaar et al., 2010; World Health Organization (WHO), 2006). For zoonotic or animal diseases, the effects on human public health as well as on veterinary public health have to be taken into account. A biological agent that possesses a high potential for transmission from individual to individual (e.g. determined by a high morbidity rate) could easily induce an extensive impact as it was seen in the human population for influenza pandemics, such as in 1918, and among livestock for foot-and-mouth disease during the 2001 outbreak in the United Kingdom. These epidemics also revealed another consequence of outbreaks, regardless whether natural or deliberate: each outbreak with large amounts of infected individuals leads to an enormous economic impact. Therefore, 'economic and socioeconomic losses'

Table 2. Aspects considered for risk assessment of biological agents in literature of Table 1

	Category	• Criterion ○ Measure
Probability	History of use (MacIntyre et al., 2006; Lele, 2010)	• Former attacks in example function
Probability	Availability/Accessibility of the agent (Anon, 2012; Ackermann and Moran, 2004; Capek, 2010; Cardoen et al., 2009; Davis, 2004; Department for Environment Food and Rural Affairs (DEFRA/UK), 2007; DISCONTOOLS initiative, 2011; Doherty et al., 2000; Elad, 2005; European Technology Platform for Global Animal Health, 2010; Federal Office of Public Health/Switzerland, 2004; Fosse et al., 2008; Havelaar et al., 2010; Irlenkäuser, 2007; Krause, 2008; Lele, 2010; MacIntyre et al., 2006; Pappas et al., 2009; Radosavljevic and Belojevic, 2009; Salerno et al., 2003; World Health Organization (WHO), 2006; World Organization of Animal Health (OIE), 2009)	• Number of laboratories possessing the agent • Prevalence in humans per year • BSL level • Prevalence of the agent in the environment
Probability	Feasibility of reproduction (Anon, 1996, 2012; Ackermann and Moran, 2004; Davis, 2004; Department for Environment Food and Rural Affairs (DEFRA/UK), 2007; Elad, 2005; Federal Ministry of Food Agriculture and Consumer Protection/Germany, 2008; Federal Office of Public Health/Switzerland, 2004; Rotz et al., 2002; Salerno et al., 2003; Tegnell et al., 2006)	• Production efforts (organizational, financial) • Large-scale production possibility • Storage life (duration of toxicity/infectivity under optimal circumstances)
Probability	Agent dispersion (Anon, 1996, 2012; Ackermann and Moran, 2004; Capek, 2010; Department for Environment Food and Rural Affairs (DEFRA/UK), 2007; DISCONTOOLS initiative, 2011; Doherty et al., 2000; Elad, 2005; Irlenkäuser, 2007; MacIntyre et al., 2006; Pappas et al., 2009; Radosavljevic and Belojevic, 2009; Rotz et al., 2002; Salerno et al., 2003; Tegnell et al., 2006; World Organization of Animal Health (OIE), 2009)	• Paths for dispersion of the agent (food, feeding stuff, aerosol, water, animated and inanimated vectors) • Survival in the environment • Weaponizability
Impact	Human and Veterinary Public Health (Anon, 1996, 2012; Ackermann and Moran, 2004; Capek, 2010; Cardoen et al., 2009; Centers for Disease Control and Prevention (CDC) (2007); Davis, 2004; Department for Environment Food and Rural Affairs (DEFRA/UK) (2007); DISCONTOOLS initiative, 2011; Doherty et al., 2000; European Technology Platform for Global Animal Health, 2010; Federal Ministry of Food Agriculture and Consumer Protection/Germany, 2008; Federal Office of Public Health/Switzerland, 2004; Fosse et al., 2008; Havelaar et al., 2010; Irlenkäuser, 2007; Krause, 2008; MacIntyre et al., 2006; Okelo and Food and Drug Administration/USA (FDA), 2008; Pappas et al., 2009; Rotz et al., 2002; Salerno et al., 2003; Tegnell et al., 2006; World Health Organization (WHO) (2006); World Organization of Animal Health (OIE) (2009)	• Case-fatality rate • Morbidity rate • Severity of disease ○ Course of disease ○ Main affected organ system ○ Infectious dose/LD_{50} • Time of incubation • Duration of illness • Risk rate for complications • Individuals susceptible in the EU (existence of YOPI) • Capacity in medical facilities (human) ○ Type of treatment needed • Transmission paths ○ Type of transmission ○ Zoonotic disease (human) ○ Potential for inter-species transmission (animals)
Impact	Countermeasures (Anon, 2012; Ackermann and Moran, 2004; Capek, 2010; Doherty et al., 2000; Federal Office of Public Health/Switzerland, 2004; Krause, 2008; MacIntyre et al., 2006; Pappas et al., 2009; Salerno et al., 2003; Tegnell et al., 2006; World Health Organization (WHO) (2006)	• Treatment in humans (availability of medicine) • Containment in humans (availability of vaccines) • Containment of the outbreak [necessary disaster management efforts (e.g.: disinfection)]

Table 2. (Continued)

	Category	• Criterion ○ Measure
Impact	Diagnostics (Anon, 2012; Ackermann and Moran, 2004; Capek, 2010; Department for Environment Food and Rural Affairs (DEFRA/UK) (2007); DISCONTOOLS initiative, 2011; Elad, 2005; European Technology Platform for Global Animal Health, 2010; Federal Office of Public Health/Switzerland, 2004; Okelo and Food and Drug Administration/USA (FDA), 2008; Pappas et al., 2009; Radosavljevic and Belojevic, 2009; World Organization of Animal Health (OIE) (2009)	• Detection of agent in the matrix ○ Perception by senses ○ Prescribed surveillance in food ○ Prescribed surveillance in feed ○ Detection systems for food of animal origin ○ Detection systems for feeds • Diagnostic detection in the population ○ Communicability of disease ○ Detection system for patient samples ○ Commercial kits available
Impact	Economic and socioeconomic losses (Anon, 2012; Ackermann and Moran, 2004; Anonymous, 2001; Capek, 2010; Cardoen et al., 2009; Davis, 2004; Department for Environment Food and Rural Affairs (DEFRA/UK) (2007); DISCONTOOLS initiative, 2011; Doherty et al., 2000; European Technology Platform for Global Animal Health, 2010; Fosse et al., 2008; Havelaar et al., 2010; Irlenkäuser, 2007; Wheelis, 2000; World Health Organization (WHO) (2006); World Organization of Animal Health (OIE) (2009)	• Containment of the outbreak in animals (availability of vaccines) • Economic loss (costs of treatment if available) ○ Loss of productivity through animal diseases ○ Culling of animals ○ Trade restrictions • Socioeconomic losses ○ Calculation by DALY (disability-adjusted life years) • Ecological damage
Impact	Public perception (Ackermann and Moran, 2004; Centers for Disease Control and Prevention (CDC) (2007); Doherty et al., 2000; Irlenkäuser, 2007; Pappas et al., 2009; Radosavljevic and Belojevic, 2009; Rotz et al., 2002; World Health Organization (WHO) (2006); World Organization of Animal Health (OIE) (2009)	• Public panic potential

are considered as another relevant category for 'impact'. This economic impact could be caused either by direct economic losses in terms of trade restrictions, culling of animals and/or the refusal of the consumer to buy the potentially contaminated product or by indirect, socioeconomic damage originating in the costs of medical treatment and the loss of manpower. Besides the economical damage, bioterroristic incidents could also aim at disturbing the social system or provoking public panic by the release of an infectious agent. The harm caused by public panic should not be underestimated. The 'public perception' of biological agents as a further category is mainly influenced by frequency and manner of mass media coverage regarding potential consequences of the incident and the government's approach concerning crisis management and communication. The real or fictive threat posed by biological agents could aggravate the situation by social disrupting behaviour, panic buying and rush to physicians and hospitals, for example to gain preventive measures that should be dedicated to affected individuals. Frightening scenarios of such bioterroristic incidents were sketched in a special issue of Emerging Infectious Diseases in 1999 by O'Toole focussing on smallpox and Inglesby dealing with anthrax (Inglesby, 1999; O'Toole, 1999).

Discussion

Numerous ranking schemes for risk ranking of biological agents with potential bioterroristic application originating from several fields of expertise have been published in the past. However, most of these ranking schemes only focus on food, human or veterinary public health separately and merely estimate the impact for the particular perspective. For the generation of a comprehensive risk assessment regarding potential bioterroristic agents, it is crucial to consider all perspectives because they are closely associated with each other.

In fact, the limited view resulting from individual fields of expertise does not correspond to the real complex situation in the case of a bioterroristic incident where

especially zoonotic agents have a broad impact on human and veterinary public health as well as on economy. This is the reason why the development of a universal generic risk ranking system considering all these aspects is very desirable. For the assessment of agents from different points of view, a weighting system could be used. Filling in all critical parameters of these generic criteria set and a subsequent weighting of these parameters would allow the objective assessment of each considered biological agent and consequently a ranking of all agents from 'low risk' to 'high risk' with regard to the specific (emergency) situation.

It is a very challenging task to generate criteria set for the prioritization of biological agents that finally sums up and assigns weights to different properties. However, a ranking scheme is often the basis for management decisions that are necessary for the establishment of different security levels in the legislation, for graduated preventive measures or for responding to a bioterroristic attack. Therefore, the effort to develop a scientific-based and transparent ranking scheme is highly reasonable.

It has to be kept in mind that the results of the agent ranking performed with the criteria set only reveal the hypothetical risk of application for each agent. On the one hand, the thoughts and intentions of a perpetrator do not necessarily have to be rational and are therefore not predictable. On the other hand, the categorization of an agent as 'high risk' could lead to adjustments of regulations for this agent with consequences for accessibility and security aspects. As the threshold between 'high' and 'medium' risk is artificial while in reality the transition is fluent, agents categorized as 'medium risk' could be attractive to terrorists due to their less strict regulations or easier access and production. This highlights the fact that risk ranking is a dynamic process: it strongly influences subsequent security efforts and vice versa.

Conclusion

The survey illustrates that a lot of work was done in risk assessment of biological agents in general and potential bioterroristic biological agents in particular, but hitherto, no universally accepted and generic approach applicable to all fields of impact was developed. The demonstration of such a need is the first step in the development of a generic risk ranking scheme for high pathogenic agents.

Eventually, such a risk ranking system for high-risk pathogenic biological agents with potential for bioterroristic application could support decision-makers and stakeholders in many (emergency) situations. In combination with data sheets for the most important biological agents and selected tools for adapting the ranking scheme to different perspectives, a generic risk ranking system could contribute to strategic decisions and an effective response in emergency situations with regard to biological contaminations whether natural or deliberate.

Acknowledgements

This research was executed in the framework of the EU-project AniBioThreat (Grant Agreement: Home/2009/ISEC/AG/191) with the financial support from the Prevention of and Fight against Crime Programme of the European Union, European Commission – Directorate General Home Affairs. This publication reflects the views only of the authors, and the European Commission cannot be held responsible for any use, which may be made of the information contained therein.

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