U.PORTO
INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

Internship Report

Master Degree in Veterinary Medicine

BIOLOGICAL AGENTS AS POTENTIAL THREAT RESOURCES – A REVIEW

Mariana Martins Marrana

Tutor

Professor Doutor João Niza Ribeiro

Co-tutor

Tianna Brand

Porto 2016

U.PORTO
INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

Internship Report

Master Degree in Veterinary Medicine

BIOLOGICAL AGENTS AS POTENTIAL THREAT RESOURCES – A REVIEW

Mariana Martins Marrana

Tutor

Professor Doutor João Niza Ribeiro

Co-tutor

Tianna Brand

Porto 2016

Foreword

This report concerns the curricular internship from the Master's Degree in Veterinary Medicine, subordinated to the Public Health field. The internship took place between 22nd February and 24th June 2016 at the World Organisation for Animal Health (OIE) headquarters, in Paris, France.

During this training period, I was under the supervision of Tianna Brand, who is the Chargée de Mission for Biological Threat Reduction. I integrated the Scientific and Technical Department and I was assigned some projects besides writing the present report.

During the first month, I updated the technical disease cards available at OIE website. I made changes and updates based on *OIE Terrestrial Animal Health Code*, *OIE Manual for Diagnostic Tests and Vaccines* and also on relevant scientific publications, such as those from the Iowa State University's Center for Food Security and Public Health (CFSPH).

Besides, I built a database for organising information regarding Laboratory Twinning projects. This assignment allowed me to exponentially develop my Microsoft Access skills, since the data output concerning project reports delivery dates is complex.

From the beginning of April onwards, I started to create another database, this one for cross referencing potential biological threat agents between the CFSPH publications, Center for Disease Control and Prevention (CDC) and OIE listed diseases.

The latter assignment sparked my interest for the biological threat reduction field, so I decided to further develop the subject and embrace it as my report's theme.

I also had the opportunity of writing an article for OIE Bulletin. I wrote about the *IVSA Animal Welfare Conference*, which I attended from the 22nd to the 24th April in Utrecht, The Netherlands.

Afterwards, I was assigned to update the information available on "Rinderpest – Post-eradication" website, which allowed me to deepen my notions on international cooperation and policy making. Also regarding biological threat reduction, I was asked to help in the preparation of *the 2017 OIE Biological Threat Reduction Conference*. My tasks were to investigate was had been done regarding previous conference recommendations (2015) and to explore what activities, partnerships, and publications relevant organizations had been developing in meantime. I also created an internal newsletter – "Biothreat watch", which is going to be sent periodically to the Scientific and Technical Department colleagues.

Furthermore, from the 21st to the 27th of May, I attended *OIE 84rd General Session*, in Paris. This was a great chance to be at the centre of all decisions concerning animal health in the world, to have contact with the 180 delegates and their commissions, and my colleagues at OIE.

My next project was the creation of a web portal about peste des petits ruminants (PPR) and the Global Strategy for its control and eradication. I also updated Rinderpest's web portal, which now focuses on post-eradication activities. I took that opportunity to update the PPR and rinderpest Disease Information Summaries. Finally, I restructured the Biothreat Reduction portal, including the strategy document, factsheet and PowerPoint presentations available there.

My last assignment was a cooperative project with Tongan farmers, for whom I provided information on how to assemble a duck raising farm.

In the final analysis, this internship has exceeded every expectation I might have had, even though they were quite high. I had the chance to collaborate with almost every department, to attend many meetings and had hoc group reunions and to be a part of several OIE events.

Summary

The use of biologic agents as means of causing distress is as ancient as human conflict. However, biologic agents can pose a threat even without a mischievous perpetrator planning their release. The evolution of scientific and technological resources allows for the creation of new agents, new pathways of introduction and new threats to arise. These emerging threats, in combination with climate change and growth in international trade and human migration pose increasing challenges upon surveillance systems and response mechanisms.

This report comprises a review of possible ways of introduction of biological threats, agents of concern and the role International Organizations play on the prevention of natural and deliberate outbreaks, as well as their response mechanisms and cooperation agreements. It has been made a reflexion on the likeliness of the occurrence of a deliberate biological attack comparing it to the occurrence of accidental or natural episodes and how to differentiate both.

The purpose of this report is to make a revision of the current situation regarding biological agents which have potential to pose a significant threat to humans, animals and the environment, both on health and economic perspectives.

Sumário

O recurso a agentes biológicos como meio de causar vicissitudes é tão antigo como o conflito humano. De todo o modo, estes podem representar uma ameaça, mesmo sem um prevaricador que planeie a sua introdução no meio. A evolução dos recursos científicos e técnicos permitiu a criação de novos agentes, novas vias de introdução e novas ameaças. Estas ameaças emergentes, em combinação com as alterações climáticas e o crescimento do comércio global e dos movimentos migratórios humanos, representam um desafio crescente para os sistemas de vigilância e mecanismos de resposta.

Este relatório inclui uma revisão das possíveis vias de introdução de ameaças biológicas, dos agentes de interesse e do papel que as Organizações Internacionais desempenham na prevenção de surtos quer naturais, quer intencionais, assim como os seus acordos de cooperação. Além disso, foi feita uma reflexão acerca da probabilidade e impacto da ocorrência de um ataque biológico, em relação à ocorrência de episódios acidentais ou naturais e de como os distinguir.

O objetivo deste relatório é a realização de uma revisão dos potenciais agentes de ameaça biológica e as suas vias de introdução, ou fatores que predispõem a sua ocorrência, com especial enfoque nos agentes que possam causar especial prejuízo à saúde humana, animal e ambiental, para além de trazer consequências económicas significativas.

Acknowledgements

Aos meus pais, por todas as oportunidades que me proporcionaram e pela confiança que sempre depositaram em mim e nas minhas escolhas.

Aos amigos, por me ouvirem, aconselharem e estarem sempre disponíveis.

Aos Professores, especialmente ao Professor Niza Ribeiro, pelos conselhos, orientação e contactos.

To Tianna Brand and all the OIE staff, who could not be more welcoming, inclusive, and committed to provide me the best learning experience possible.

"What is surprising is not the magnitude of our forecast errors, but our absence of awareness of it. This is all the more worrisome when we engage in deadly conflicts: wars are fundamentally unpredictable (and we do not know it). Owing to this misunderstanding of the causal chains between policy and actions, we can easily trigger Black Swans thanks to aggressive ignorance-like a child playing with a chemistry kit."

Nassim Nicholas Taleb, *The Black Swan: The Impact of the Highly Improbable*

Abbreviations

ASF	– African Swine Fever
BSE	– Bovine Spongiform Encephalopathy
BTWC	– Biological and Toxin Weapons Convention
CCHF	– Crimean-Congo haemorrhagic fever
CDC	– Centres for Disease Control and Prevention
DNA	– Deoxyribonucleic Acid
EU	– European Union
EVD	– Ebola virus disease
FAO	– Food and Agriculture Organization
FMD	– Foot-and-mouth disease
GHSA	– Global Health Security Agenda
IHR	– International Health Regulations
OIE	– World Organisation for Animal Health
PVS	– Performance of Veterinary Services
SARS	– Severe Acute Respiratory Syndrome
STEC	– Shiga toxin E. Coli
UN	– United Nations
UNISDR	– United Nations Office for Disaster Risk Reduction
UNODA	– United Nations Office for Disarmament Affairs
UNSGM	– United Nations Secretary General Mechanism
US	– United States of America
VEE	– Venezuelan Equine Encephalomyelitis
WHO	– World Health Organization
WTO	– World Trade Organisation
WWI	– First World War
WWII	– Second World War

Index

Foreword i
Summary iii
Sumário iv
Acknowledgements v
Abbreviations vi
Index vii
1. Biological Warfare 1
Historical context 1
Definitions 2
Synthetic agents 2
Current situation 3
2. Natural and Intentional Spread of Disease 5
Wildlife and Invasive Species 5
Emerging infectious diseases 6
Steps in the emergence of pandemic zoonosis 8
Deliberate usage 9
Accidental releases 9
How to differentiate? 10
3. Biological Resources 13
Concerning agents and diseases 13
Agents/diseases overview 13
Anthrax (Category A) 14
Plague (Category A) 14
Smallpox (Category A) 14
Tularemia (Category A) 15
Botulism (Category A) 15
Viral Haemorrhagic Fevers 15
Food safety threats (Category B) 16
Water safety threats (Category B) 17
Alphaviruses (Category B) 18
Glanders (Category B) 19
Hantavirus (Category C) 19
Nipah (Category C) 19

Other agents and diseases 19
Rinderpest 19
Rift Valley Fever 20
Vector-borne diseases 20
Highly Pathogenic Avian Influenza 21
Foot-and-mouth disease virus 21
Classical and African Swine Fever 21
4. Role of International Organisations and its mechanisms for coordinating efforts 22
United Nations 22
WHO 22
FAO 23
OIE 23
Funds, Programmes, Solidarity 24
Global Health Security Agenda 24
Surveillance, Monitoring and Early Response 25
Laboratory safety 26
5. Reality check 28
Concerning issues 28
Myth busters 29
6. Conclusions 31
References 32
Annexes 36
Biological Risk Analysis Process 36
Laboratory Biosafety Levels 37
Internship projects 38
Technical disease cards updated 38
“Biothreat Watch” newsletter 39
OIE Bulletin article 42
Other projects 46

1. Biological Warfare

Historical context

The use of disease agents as military weaponries is as old as human conflict. There are records of poisons being used as a means to neutralize enemy troops from as early as the VI century BC. In antiquity, disease affected animal and human cadavers were thrown over opponents' walls as a way of spreading disease – the catapulting of bubonic plague (*Yersinia pestis*) victims onto the besieged city of Kaffa, in 1346, and the subsequent flee of Genovese merchants, changed the course of history, as it represented the spread to the Mediterranean basin of the world pandemics, which ended up killing around 50% of European and Asian populations.[18, 56] There are many more historical examples which have had milder consequences than the previous one – wine contaminated with leprosy patients' secretions, saliva from rabid dogs shoot over enemy troops, plague infected clothing, etc. Napoleon even built a swamp around the Italian city of Mantua, hoping to favour the spread of malaria among the British army. Perhaps, the most well-known episode is the delivery of smallpox drenched clothing to the Native Americans by English and French colonial armies. [56]

In the past century, the 1st World War (WWI) saw the rising of the first livestock-oriented biological threats – the German anti-livestock programme deserves special mention, as it was the first of its kind organised at a national level, with scientific foundations and one of the couple that happened during war period. The other programme belonged to Japan and killed hundreds of people in the attempt of developing bioweapons and understanding the effects of pathogens on human origin systems.[60]

The WWI culminated with the signature of Geneva Protocol by the League of Nations, in 1925. This document prohibits the use of 'asphyxiating, poisonous or other gases, and of all analogous liquids, materials or devices' and 'bacteriological methods of warfare'. This is now understood as a general prohibition on chemical and biological weapons, but does not impose limits on production, storage or transfer of these instruments.[30] However, this agreement was not respected by nations such as United States of America, United Kingdom, Japan and Soviet Union.[18]

Both the 2nd World War (WWII) and the Cold War brought innovation in bioweapon investigation field. Not only animal diseases were more deeply studied than ever before, but also vaccines (such as rinderpest's) were developed. Besides, new disease transmission vehicles were created.[60]

In 1972, resulting from efforts of the international community to create a treaty that would supplement the Geneva Protocol, the Biological and Toxin Weapons Convention (BTWC) was

created and signed by more than 100 countries at the time. It commits the parties to prohibit the development, production and stockpiling of such weapons. However, the absence of any formal verification regime to monitor compliance has limited the effectiveness of the Convention, as it is essentially based on trust.[31] Nevertheless, prior to the Gulf War, it was documented the use of chemical weapons in Iraq. Also, in 1992, Russia admitted that the former Soviet Union, despite being a co-depository of the BTWC, had continued a massive offensive biological weapons programme for years.[60]

Therefore, in 1985, an informal group of countries, known as the Australia Group, gathered efforts to help member countries identify the exported commodities which need to be controlled so as not to contribute to the spread of chemical and biological agents. The scope of the export controls discussed by the Group in its annual meetings has evolved to address emerging threats and challenges.[20]

Definitions

'Biological warfare' (biowarfare) and 'bioterrorism' are defined as 'the intentional use of microorganisms or toxins derived from living organisms as an act of war or political violence with the intent to cause death or disease in humans, animals or plants'.[12] 80% of pathogens that could potentially be used for bioterrorism are of animal origin.[37] Biowarfare programs seek to inflict sufficient severe disease to paralyse a city and perhaps a nation. They happen at large scale, as between governments or from populations against its government. To be effective, bioterrorism does not need to achieve the level of impact sought by biowarfare programs – it impacts humans through fear, as well as through disease and death, thereby exploiting pathogens as weapons for mass destruction; the initiative departs from individuals, cults or extremist groups. The greatest difference is that bioterrorism can have a major impact with only a few cases of disease.[17]

'Biorisk' refers to the risk associated with a particular biological event (in the present context: naturally occurring diseases, accidents, unexpected discovery, or deliberate misuse of biological agents and toxins), which may affect adversely the health of populations and the environment.

Animal pathogens may be used as biological weapons, in biocrimes or in bioterror because they have a high impact, are cheap, easy to acquire and propagate, and can be readily smuggled through border checks undetected.[36]

Synthetic agents

Synthetic biology is an interdisciplinary area, comprising contributions from biologists, engineers, physicists, computer scientists, etc. It relies on the findings from the genetic

investigation field, concerning recombinant DNA and genome sequencing. The ultimate goal of synthetic biologists is not further from building a biological system from scratch.[21] The biotechnology revolution means that options for engineering animal pathogens are increasing all the time (and becoming more widely available), whilst the cost of doing so is decreasing. Most pathogens that have been used to develop bioweapons have been animal pathogens.[36]
In the last decades, not only scientists were able to recreate extinct viruses, such as the Spanish flu virus, but also to increase the virulence of already existing viruses, although not always intentionally.[42] Perhaps, the most concerning point might be the availability of genetic information/material to the general public – as illustrated in 2002, when a team of virologists at the State University of New York synthesized the poliovirus using genetic information obtained off the internet.[42]

Since the beginning of the XXI century, and especially after the 'Anthrax letters' episode[41] in the US, governments have expressed concern about the misuse of biotechnology. This anxiety finds its roots in the belief that globalization and the rapid development of biotechnology facilitate access to specialized knowledge, making it easier for terrorists to apply scientific advances to wicked purposes. On December 20th 2011, the press announced that the US government had requested *Science* and *Nature* to refrain from publishing a full account of an experiment that increased the transmissibility of bird flu virus H5N1, aiming to avoid the replication of the process by rogue actors.[42]

However, from a non-sensationalist perspective, these concerns seem to underestimate the painstaking planning and bench-work that such scientific endeavours require. It took decades of failed attempts until the achievement of the above mentioned results. Scientific publications typically do not stipulate the difficulties, mistakes, and failures that scientists endure, nor do they clearly specify how problems have been solved. They only present the successful results in a sanitized way. The truth is that, in spite of technological progress, scientific work remains the result of the cumulative and cooperative work of teams of scientists whose skills derive from years of experimentation and testing. [42] Saying that biology is as much an art as a science, might not be an over-statement. However, this would be an art that requires a certain organizational environment to express itself fully.

Current situation

The domestic and international spread of infectious animal disease may occur through natural, accidental, or intentional means. 60% of human infectious diseases evolve from animal pathogens and 75% of emerging human infectious diseases have an animal disease origin.[37] Transnational spread of disease may result from movement of animals, animal products or cultures from infectious organisms.[8] Nowadays, a single case of a high profile disease (as

Bovine Spongiform Encephalopathy (BSE), Foot-and-Mouth Disease (FMD) or Peste des Petits Ruminants(PPR)), or a small number of cases of more common diseases (as Newcastle disease or Bovine Tuberculosis) may result in international sanctions that cause major economic losses for agriculture and related industries.[17] In a global panorama where countries seek to improve their external image as a means of favouring trade and international relations, such episodes can be devastating. Since 1998, the OIE has the mandate from the World Trade Organization (WTO) to officially recognise disease-free areas of countries for trade purposes. The procedure for the official recognition of disease status by the OIE is voluntary and applies currently to 5 diseases – BSE, PPR, FMD, Contagious Bovine Pleuropneumonia, African Horse Sickness and Classical Swine Fever (CSF). However, OIE member-countries have the possibility to self-declare their country or a region within their territory free from certain OIE-listed diseases other than those for which the OIE has put in place a specific procedure for official recognition of freedom from disease- status. Self-declaration of a compartment, as is the case for a country or zone, is made under the full responsibility of the Member Country concerned. [39]

Good examples of the above mentioned situation are the inadvertent introductions of FMD and CSF viruses in the UK in 2001. The resulting CSF epidemic caused great economic hardship, since pig farmers in the area were obliged to slaughter their pigs a preventive measure and the export of pig products from the UK was suspended. News reports in March 2001 indicated that at least one of the relict endemic sheep breeds of England (Herdwick sheep) was severely threatened through sanitary slaughter as a consequence of the FMD outbreak.[12] Modern high-density industrial livestock facilities, centralised feed supply systems, and transportation methods increase the susceptibility of livestock populations to disease outbreaks, and the vulnerability of economies to disruption as a result of disease epidemic in livestock.[12]

Regarding eradicated diseases – Rinderpest and Smallpox – and diseases that are already restricted to small parts of the globe, as well as to laboratory repositories, biosafety is especially important. The greatest threats to biodiversity and international trade may well come from accidental, or intentional, releases of virulent broad-spectrum disease agents, as the result of inadequate containment within production, transport or storage facilities, or inadvertent releases resulting from offensive strikes against production or storage facilities.[12] Transmission of biological agents through the air is likely to impact the greatest number of individuals, but transmission by other means, such as water, food, insect and arthropod vectors, etc.--may also be routes of exposure of individuals to biological agents.[46] Although the probability of a deliberate or accidental release may be relatively low, the impact may be catastrophic from a national to a global level.[36]

2. Natural and Intentional Spread of Disease

Wildlife and Invasive Species

Invasive species of animals or their accompanying microorganisms may pose a threat to environment and to the natural balance of ecosystems, whether their introduction is intentional or not. Invasive species are defined as 'alien species (not native, introduced through human activity) that reach the final stage of the invasion process and have the capacity to spread'.[29] Alien species can thrive and scatter in their new environment, particularly in the absence of natural enemies. They can also prey upon or out-compete native species for food and for habitat. Moreover, alien species sometimes carry pathogens which threaten native species. The International Union for Conservation of Nature has reported that 51% of all known endangered species are threatened because of invasive ones.[47]

It may come as an unusual perspective for some, but actually human species has invaded the largest surface area of the planet, occupying almost every land mass. We spread out from our native Africa, throughout all earth's habitats and ecosystems – never doing it alone, but rather accompanied by parasites, commensals, food, ornamental crops and domesticated animals.[29] And, to this day, we keep on doing it, not only as a part of our careers and leisure activities, but also to escape conflict situations, such as the current one in the Middle-East, or natural disasters and extreme climate events.

The introduction of species into new areas, if not accidental, may have purposes as different as acclimatisation (creating variety), pest control, recreational, etc. These movements have been done frequently without any structured intent or pre-established strategy, generating consequences as damaging as if the intentions of the perpetrator were mischievous.[29] A good example is the introduction of myxomatosis virus in Australian (1937) and French (1952) rabbit populations, as an attempt of reducing their overgrowing populations. This initiative was a complete failure, as in Australia several attempts were needed to achieve a result, whereas in France a single introduction was sufficient to spread the virus throughout Europe. In the end, neither the host nor the virus died out in either of the countries.[29] From the beginning of the XXI century, the accidental introduction of Asian *Vespa velutina* in Europe is contributing to the loss of honeybees (*Apis mellifera*) colonies and decrease in pollinators. This biological invasion has led to several serious problems because *V.velutina* preys on the domestic honeybees, disrupts the ecological role of the honeybees, potentially alters biodiversity, harms commercial beekeeping activities and is potentially deadly to people who are allergic. This species was identified for the first time in France in 2004. Currently it has spread across Spain, Portugal, Belgium, and Italy.[27]

More recently, in May 2016, Australian authorities announced that, after conducting extensive research on the possible impacts of such measures, they are going to release *Cyprinid Herpesvirus-3* over the European Carp population that has invaded the Murray-Darling basin area. These fish account for more than 90% of the local biomass and are nearly useless as a fishing product.[10]

The risk of dispersing invasive species through acts of bioterrorism, especially human pathogens, cannot be neglected. However, that risk appears quite low in comparison to the risk of intentionally releasing animal pathogens that could disrupt the livestock producing industries of countries which rely on them economically.[29]

Although it is not directly related to bioterrorism, the intentional release of unwanted exotic companion animals (such as Burmese python and prairie dogs) also has a major environmental and economic impact and, possibly, animal and human health impact, in case of accidental release of zoonotic agents. Taking prairie dogs as an example – tularaemia and plague are two zoonotic diseases that have occurred in animals intended for companion animal trade. Keeping prairie dogs as pets in the US is no longer possible, after a monkeypox outbreak in 2003.[7]

Emerging infectious diseases

According to current literature, the frequency with which new pathogens emerge is increasing, even if the increased global surveillance is taken into account. Also, the global distribution of all the major groups of emerging diseases strongly correlates with human population density, supporting the theory that disease emergence is driven by largely anthropogenic changes – namely the expansion of agriculture, travel routes, trade, and land use.[28] Zoonotic disease risks are predicted to further increase as environmental changes continue and population continues to grow exponentially.[55] Despite their substantial repercussion on global public health and our growing understanding of the process by which they emerge, no pandemic has so far been predicted before infecting human beings. However, patterns in the origin and spread of new pathogens can be noted and are an intrinsic, although necessarily tailored, as part of a surveillance strategy.[28]

Emerging infectious diseases, including those which are evolving to evade currently available control options (vaccines and antimicrobials), pose an increasing risk to health. The mechanisms for disease emergence are complex and often incompletely understood, but it is likely that the trend for new diseases to emerge will only continue as global movements of people and animals increases and as human behaviours change the environment around us.[36]

Emergence in new regions is caused primarily by pathogen movement, due to trade and travel, whereas local emergence is driven by a combination of environmental changes, that affect vectors and wildlife hosts, and social changes (e.g., poverty and conflict), that affect human exposure to vectors.[25]

Endemic animal diseases are a daily burden for health and agriculture in some of the world's poorest countries, obstructing economic and social development and limiting food availability.[36] Increasing demand for food due to an expanding global population has led to a substantial susceptibility of our populations to food-borne zoonosis. Pathogens in the livestock production chain are a particular risk, with repeated outbreaks from meat, eggs, milk, and cheese, or meat by-products incorporated into foods as flavouring, oils, or stock. Globally, most types of domesticated and wild vertebrates and many invertebrates are food for people – thus capable of harbouring zoonotic bacteria, viruses, or parasites.[24]

The same diseases, whether they are or not foodborne, when introduced to developed countries, which may have already eliminated them, spread rapidly through naïve animal populations and represent severe consequences for livestock production, for business, and for the availability/y and price of food on domestic and international markets.[36]

Figure 1 – Global aviation network. In Kilpatrick *et al*, 2012

Transmission rates are usually higher in dense than in sparse populations, due to higher frequency of contacts and feebler immune systems, and spread is often greatly enhanced by air travel or human migration.[28] The ease associated with air travel, enabling global transit in a single day (Figure 1), has accelerated introductions since it has allowed many pathogens that cause acute infections to reach other continents within the few days that hosts are infectious (e.g., Chikungunya and West Nile viruses), and even during the latent period for some diseases. Several of these pathogens were also favoured by the climate changes of the XX century, which resulted in the introduction of another key vector - *Aedes spp.* in areas previously free from its presence.[45] This mosquito can carry many viral pathogens, including the Yellow Fever virus, Zika virus, Dengue and Chikungunya, as well as several filarial nematodes. Thus, the most recent wave of pathogen introductions, and those likely to occur in the near future, are strikingly abrupt when is taken in consideration the smooth establishment of vectors in the last centuries.[25]

Steps in the emergence of pandemic zoonosis

Among the several described processes for the emergence of zoonotic diseases, Daszak's model (Figure 2) is the most adequate for the purposes of this report, as it focus on the dynamics of infection, rather than pathogen proprieties. It comprises three stages:

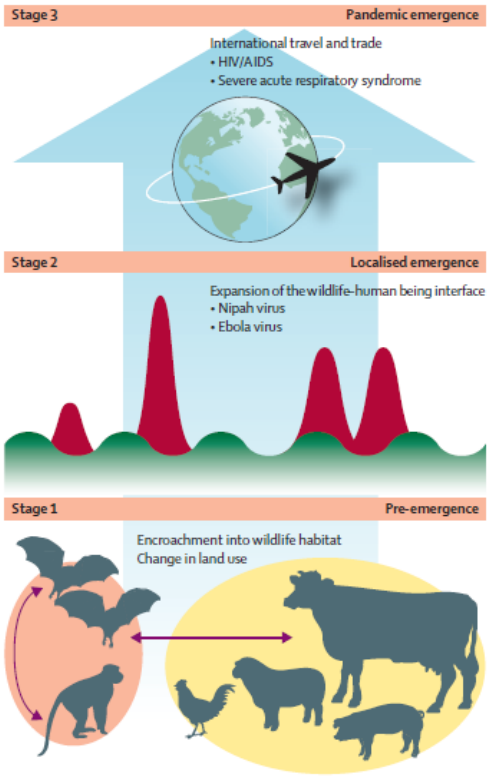


Figure 2 – Emergence of zoonotic disease. In Morse *et al*, 2012

- The first stage - disease emergence, takes place within the reservoir host species. Ecological, social, or socioeconomic changes alter the dynamics of pathogen transmission within the host or between hosts and allow the pathogen to expand within its host population, spread to a new region, or to be transmitted to another non-human host population or species. Each of these changes increases the likelihood of the pathogen making contact with and spilling over into human beings (and thus progressing to stage 2).The drivers that cause stage 1 emergence tend to be large-scale environmental, agricultural, or demographic shifts.
- The second stage - localised emergence, represents the initial spill-over of a wildlife or livestock pathogen to people. Causes vary widely, from handling of carcasses, to exposure to fomites in markets, or in the wild.
- The final stage - full pandemic emergence, is rarely achieved. It represents sustained person-to-person transmission and large scale spread.

Alternatively, some pathogens can spread among human beings without evolutionary change from the genotypes present in the wildlife host (e.g., Ebola virus) and thus can enter human population at stage 2. The ultimate goal of successful pandemic prevention is to move the control point to the first stage.

Spill over infections, just below the threshold for self-sustainment in people (R_0<1), have been suggested as prime epidemics in waiting. Also, pathogens can transfer from human beings to animals and between animal species before being transferred back to people, allowing remixing and evolution with spillback and potentially enhanced pathogenicity.[28] Understanding the complex population biology and transmission ecology of multi-host parasites has been declared as one of the highest priorities for biomedical sciences during the XXI century.[55]

Deliberate usage

To use biological agents as weapons is not as easy as it might seem. Besides the presence of the agent, it is required a delivery system, either to convey the agent, or to facilitate its dispersion.

However, almost any disease-causing organism (such as bacteria, viruses, fungi, prions or rickettsiae) or toxins (natural or synthetically produced) can be used in biological weapons. The agents can be enhanced from their natural state, to make them more suitable for mass production, storage, and dissemination as weapons.[32] Regarding delivery mechanisms, there is a variety of methods. Past programmes have constructed missiles, bombs, hand grenades and rockets to deliver biological weapons. A number of programmes also designed spray-tanks to be fitted to aircraft, cars, trucks, and boats.

On a less sophisticated side, and on a smaller- scale, delivery mechanisms can be as simple as a pen or a stick contaminated with the agent and brushed on susceptible animals. There have also been documented efforts to develop delivery devices for assassinations or sabotage operations, including a variety of sprays, brushes, and injection systems as well as means for contaminating food and clothing.[32]

Accidental releases

Working with highly virulent or highly pathogenic strains of virus or bacteria is a double edged sword. On the one hand, the development of vaccines and antimicrobials is essential for human and animal health, and the preparedness for the emergence of pandemic strains can spare many lives. But on the other hand, the risk of laboratory escape of these high-consequence pathogens far outweighs any potential advance. Accidental laboratory releases are a recurrent scenario.

The risk of a manmade pandemic sparked by a laboratory escape is not hypothetical: one occurred in 1977 in China, with H1N1 Influenza. It occurred because of concerns that a natural pandemic might be imminent, due to reports of large outbreak of swine Influenza in the US .[19]

From 1938 to 1972, the Venezuelan Equine Encephalitis vaccine caused most of the very outbreaks that it was called upon to prevent, due to poor inactivation of vaccine strains - a clear self-fulfilling prophecy.[19]

The first fully acknowledged laboratory escape occurred in 1972, with the infection of a laboratory assistant at the London School of Hygiene and Tropical Medicine, who was working with live smallpox virus. The assistant got sick and infected healthcare workers, other patients, and their visitors.[19]

The 2003 Severe Acute Respiratory Syndrome (SARS) outbreak spread to 29 countries. Since 21% of all cases involved hospital workers, it had the potential to shutdown health care services wherever it struck. This pathogen is particularly dangerous to handle in the laboratory because

there is no vaccine, and it can be easily transmitted via aerosols. SARS has not re-emerged naturally, but there have been six escapes from virology labs: one in Singapore (August 2003) and one in Taiwan (December 2003), and four different escapes at the same laboratory in Beijing (2004).[19]

Regarding FMD, the disease reappeared in Britain in 2007, 4 kilometres away from a biosafety level 4 laboratory (see chapter 4). The identified strain was the same that had caused an outbreak in 1967 in the United Kingdom, but was not then circulating in animals anymore. It was, however, used in vaccine manufacture at the nearby Pirbright facility. Investigations concluded that construction vehicles had carried mud contaminated with FMD from a defective wastewater line at Pirbright to the first farm. The resulting major outbreak disrupted UK agricultural production and exports, and cost an estimated 200 million pounds.[19]

In 2010, WHO released a guidance document named *Responsible life sciences research for global health security* with the purpose of informing Member States about the risks posed by accidents or the deliberate misuse of life sciences research and to propose measures to minimize them within the context of promoting and harnessing the power of the life sciences to improve health for all people. This guide also focuses on one measure of biorisk reduction, namely the biorisk management framework for responsible life sciences research (Figure 3). The framework emphases a vision of promoting excellent, high-quality, responsible, safe and secure research, where the results of the research promote advancements in health, economic development, global health security, evidence-informed policy-making and public trust in science.[58]

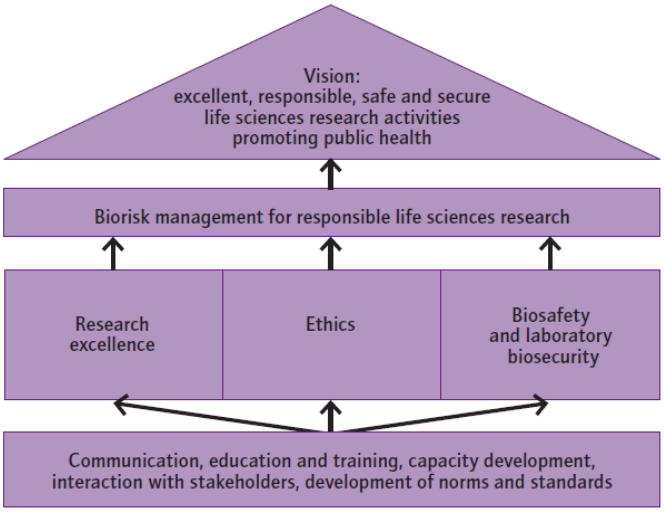


Figure 3 – Biorisk management framework for responsible life sciences research. Source: WHO: Responsible life sciences research for global health security; 2010.

How to differentiate?

It is possible to differentiate between deliberate and natural occurrences of disease through current genome sequencing technologies. The field of studies designated to such investigations is called microbial forensics – its ultimate goal is to identify and criminally prosecute the responsible parties for a deliberate outbreak of disease. It is an important part of a strengthened capability to respond to biocrime and bioterrorism, and works in parallel with an epidemiological investigation. The latter aims to find the source of the outbreak and to clarify its

routes of transmission, in order to hinder its further spread, and reduce the risk of future outbreaks, through effective preventive measures. The epidemiologic investigation might begin before or after the microbial forensics intervention, depending on the nature of the outbreak – in deliberate overt outbreaks, when the perpetrator informs authorities of his intentions, both investigations take place at the same time.[50]

Gene sequencing technologies allow the differentiation between closely related isolates. While in human DNA the chances of finding two samples with coincidental profiles are minimal, the same does not happen with asexually reproducing organisms. Regarding bacterial populations, the genetic variation inducing mechanisms make it possible for a cell to differ from its ancestor and can also cause unrelated organisms to contain shared sequences.[50] Therefore, when comparing individual strains of a microbial species, a complete or near-complete match between individual strains does not necessarily reflect identity. Similarly, minor genetic differences between strains do not necessarily exclude the possibility that they might originate from the same source. However, the assumption when using genome-sequencing systems is that individual isolates that share marker profiles are related. Most bacterial genetic comparisons that have been reported to date rely on genetic marker systems, in which each marker reflects a specific part of the microbial genome.[50] Collections of reference strains have been created and can be used to compare new isolates, in order to analyse population structures and the relationships between the species' individual strains.

Sequencing and analysis of the entire genome of an organism can reveal subtle genetic differences that would not be detected by older methodologies. Until recently, the process of whole-genome sequencing and analysis was meticulous, expensive, and time-consuming. However, the recent development of the so called "next-generation sequencing technologies" has revolutionized biology by greatly reducing the time and expenses required. The development of whole-genome sequence databases will be extremely valuable in successfully tracing pathogens in the future.[50]

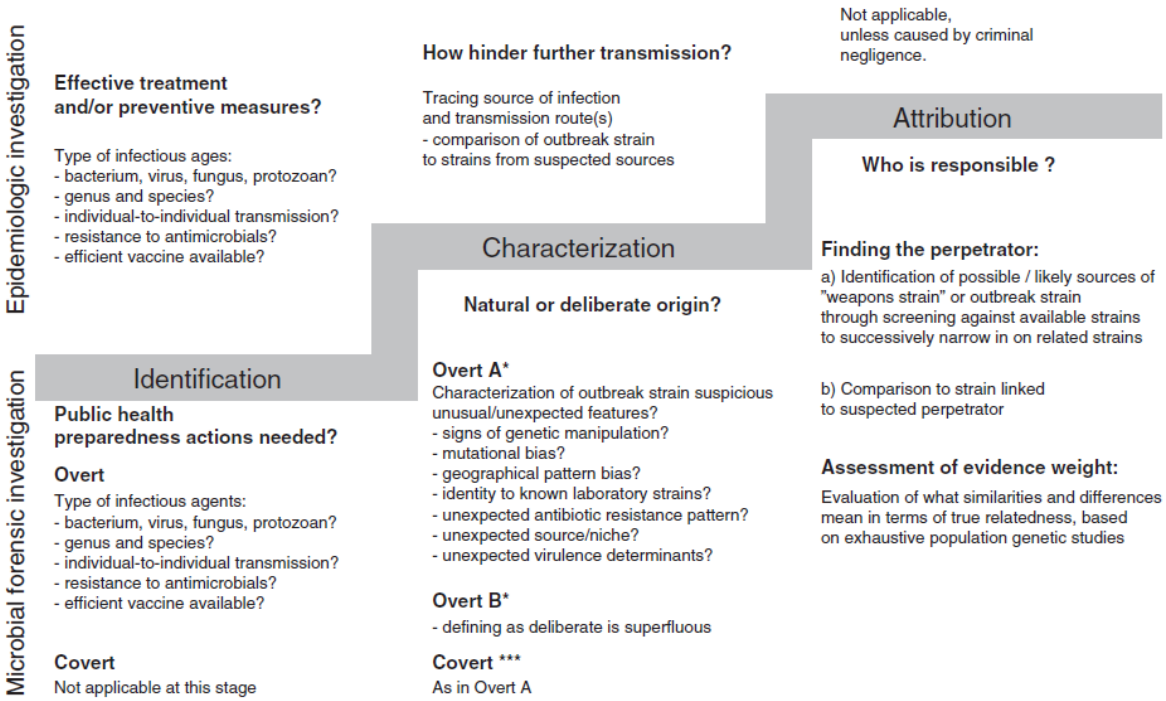


Figure 4 – Characterization of a suspect occurrence investigation stages. Source: Sjodin A *et al*: The need for high-quality whole-genome sequence databases in microbial forensics. *Biosecur Bioterror* 2013 [50]

Microbial forensic investigations have been described as consisting of three interrelated stages described in detail on Figure 4:

- identification of the biological agent(s) responsible for the event;
- characterization of the event as either intentional or unintentional;
- if the event is deemed illegitimate, attribution of use to a specific perpetrator.

Many of the questions asked during the first two stages of a microbial forensics investigation are identical to those examined in an epidemiologic investigation, and the same methods and technologies are generally used to answer them. However, the third stage is unique to microbial forensics. At this stage, in addition to the usual forensic analyses of recovered materials from the crime scene, detailed analyses are conducted of the attack strain. Epidemiologic and microbial forensic investigations are generally conducted in parallel, and over time they may converge and diverge. The course of the investigation, will be influenced by whether the attack is overt or covert and especially by whether investigators are in possession of the utilized strain.

3. Biological Resources

Concerning agents and diseases

Different health-related organizations have distinct lists of pathogens of concern regarding biological threat agents. While there is an extensive list of pathogens identified as agents of interest, there are a few which are considered to have a higher risk of being used as biological or agricultural weapons. The criteria for such classification[8] are:

- highly pathogenic or highly infective;
- broad dispersion or availability;
- low levels of immunity to the agent in the target population;
- overall negative effects of their release, regarding biologic and economic sectors;
- not posing a threat to the perpetrator;
- predictable clinical course;
- passible of being attributed to a natural outbreak.[60]

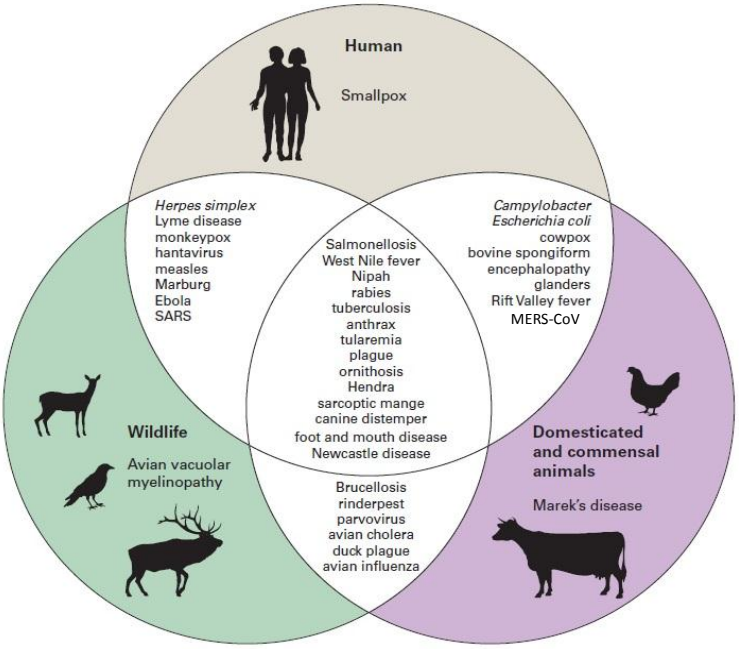


Figure 5 – Examples of linkages between important diseases of wildlife, domestic animals and humans. Source: Friend M; Biowarfare, Bioterrorism, and Animal Diseases as Bioweapons. In: *Disease Emergence and Resurgence: The Wildlife-Human Connection. Circular 1285 (*2006) - Modified

The agents of interest change, according to our focus on human or animal threat potential (Figure 5). Domestic animal pathogens are primarily considered from the perspective of economic trade impacts and/or ease of transmissibility. Whereas human pathogens are considered mainly from the perspective of potential mortality rates and/or public fear of the disease.[17]

Agents/diseases overview

According to the list of critical biological agents for public health preparedness created by the American Centres for Disease Control (CDC), on the next section follows an overview of the most relevant ones, concerning the purposes of this report. CDC's list classifies agents in three categories (A, B, C) according to:

- their ease of transmission;
- associated morbidity and mortality;
- likelihood of use.

Anthrax (Category A)

Anthrax is the disease caused *Bacillus anthracis*, a bacterial zoonotic agent, which can be transmitted through inhalation or ingestion.[14] Despite being endemic in some areas of the world, it usually causes a limited number of animal cases and, quite rarely, human cases. Its prevalence has decreased consistently in the last few years.[40]

In the past, anthrax has been used as a biowarfare resource. Namely, during WWI when Germany targeted horses, reindeers, mules and cattle in the US, Spain, Norway, and France with unknown, although possibly successful, results.[60] Also, in 1978-80 in Rhodesia (now Zimbabwe), anthrax was introduced by the Rhodesian security forces as an attempt to undermine the moral of those seeking freedom, through the destruction of cattle populations.[60] In 2001, an unknown perpetrator sent "anthrax letters" to strategic targets in the US, killing five people and infecting 17 others.[41] More recently, in May 2016, Kenyan Intelligence Services foiled an attack by an ISIS group which intended to release Anthrax spores on civilians, through a "large-scale" attack.[22]

Plague (Category A)

Plague is caused by *Yersinia pestis*, which is a zoonotic, vector-transmitted bacteria, that can also be transmitted through inhalation.[14] The plague pandemic that swept through Eurasia and North Africa in the mid-XIV century was probably the greatest public health disaster in recorded history. Given the explosive nature and history of disease spread over wide areas, plague could be a dangerously effective biological weapon. In fact, during WWII, Japan successfully initiated a plague epidemic in China through the release of 15 million laboratory-infected fleas per attack from aircraft over Chinese cities[17]. Plague continues to be a life-threatening disease unless detected and treated early. Following the reappearance of the disease during the 1990s in several countries, plague was categorized as a re-emerging disease, and remains of great significance under the International Health Regulations (2005), as a plague outbreak may constitute a public health emergency of international concern.[2]

Smallpox (Category A)

Smallpox, also known as *Variola*, is caused a poxvirus and is exclusively a human disease.[14] It was the first disease to be declared eradicated, in 1980. This was achieved through focused surveillance and ring-vaccination. The guidance and support provided by Pan-American Health Organization and WHO were decisive. After its official certification as eradicated, an agreement was reached under which all remaining stocks of the virus would either be destroyed or passed to one of two secure laboratories – one in the US and another one in the Russian Federation.[59]

Tularemia (Category A)

Tularemia is the disease caused by *Francisella tularensis* bacteria. It is a zoonotic, vector-borne disease, that can also be transmitted through direct contact, inhalation and contaminated food and water.[14] It is one of the most infectious pathogenic bacteria known, requiring inoculation or inhalation of as few as 10 organisms to initiate human infection. It occurs widely in nature and can be isolated and grown in quantity in a laboratory, although manufacturing an effective aerosol weapon would require considerable sophistication. However, person-to-person transmission is uncommon and the dispersion of *F. tularensis* as a weapon would be unlikely to generate secondary human cases or persist within targeted human population.[7] There are reports from the beginning of the XXI century which describe the release of tularemia-infected squirrels in order to initiate epizootics and reduce small rodents populations.[17]

Botulism (Category A)

This disease is caused by *Clostridium botulinum*'s toxin and affects both humans and livestock. It can be present in contaminated food and water or be inhaled.[14] Botulism seems to be increasing in cattle, possibly due to the increase in use of plastic-packaged grass silage - these outbreaks can cause significant economic losses.[51] Human botulism is a serious but relatively rare paralytic disease. There are seven recognized types of the toxin that cause botulism, four of which (types A, B, E and rarely F) cause human botulism. Types C, D and E also cause illness in mammals, birds and fish.[2] *Clostridium botulinum* neurotoxin, especially A type, is one of the most lethal natural substances known.[34]

Viral Haemorrhagic Fevers

This name is a general term for severe illness, sometimes associated with bleeding, that may be caused by a number of viruses. These agents fall into different categories, according to CDC classification. The term is usually applied to disease caused by *Arenaviridae* (Lassa fever, Junin and Machupo), *Bunyaviridae* (Crimean-Congo haemorrhagic fever (CCHF), Rift Valley Fever, Hantaan haemorrhagic fevers), *Filoviridae* (Ebola and Marburg) and *Flaviviridae* (yellow fever, dengue, Omsk haemorrhagic fever, Kyasanur forest disease)[59].–Some of these are zoonotic diseases, most of them vector-borne (mosquitos, ticks, rats and bats), which also can be transmitted through direct contact between infected humans. and affect non-human primates and guinea pigs.[14] Surprisingly, most of these diseases do not cause significant clinical signs on their animal hosts, but can be fatal to humans.[3] The following paragraphs will cover the most relevant ones for the purposes of this report.

CCHF (Category C)

CCHF is an expanding tick-borne disease with increasing human and animal health impact. It can cause severe outbreaks in humans, with high mortality rates, but is asymptomatic in cattle and ruminants, which act as amplifying hosts and reservoirs for human infection.[2] It is endemic

in Africa, the Balkans, the Middle East and Asia, in countries south of the 50th parallel north.[59] Due to its high pathogenicity and the lack of approved vaccines, for either people or livestock, and specific intervention strategies, CCHF virus must be handled under biosafety level 4 containment (see chapter 4). The recent emergence of CCHF, causing either sporadic human infections (Greece, 2008 and Uganda, 2013) or epidemics in previously unaffected areas (Turkey, 2003) has raised animal and public health concerns.[44]

Ebola virus disease (EVD) (Category A)

EVD has been present for a long time in African countries; it is a severe, often fatal illness in humans. EVD outbreaks have a case fatality rate of up to 90%.[2] However, over the span of a few weeks during July and August 2014, events in West Africa changed perceptions of Ebola virus disease from an exotic tropical disease to a priority for global health security. The epidemic was recognized as the largest in history, since more cases were reported than in all previous Ebola outbreaks combined. Recent investigations support the idea that bats were the source of the current epidemic in West Africa and enlarge the list of plausible reservoirs to include insectivorous bats, besides fruit bats, which may not be the ultimate source of past outbreaks.[26]

Marburg virus disease (Category A)

The virus was first identified in 1967, during epidemics in Marburg and Frankfurt, in Germany, and in Belgrade, in the former Yugoslavia, having originated from importation of infected monkeys from Uganda. It is a severe and highly fatal disease caused by a virus from the same family as the one that causes Ebola. These viruses are among the most virulent pathogens known to infect humans. Both diseases are rare, but have a capacity to cause dramatic outbreaks with high fatality.[59]

Lassa fever (Category A)

The disease typically occurs in humans in West Africa. It can be transmitted mainly through handling rats, food or house-hold items contaminated by rats' urine and faeces. The virus can spread between people through direct contact with the body fluids of a person infected with Lassa fever, as well as contaminated bedding and clothing. Lassa fever has killed more than 160 people in West Africa, most of them in Nigeria, since November 2015.[59]

Food safety threats (Category B)

Salmonellosis

Outbreaks of salmonellosis have been reported for decades. In fact, it is one of the most common and wide distributed foodborne diseases. However, it is considered an emerging disease because its incidence has recently increased in many continents. [59] Since the

beginning of the 1990s, strains of salmonella that are resistant to a range of antimicrobials have emerged and threaten to become a serious public health problem.[59] Salmonella has been used in the past for terrorist purposes – in 1984, during an election in Oregon, USA, the Rajneesh cult introduced Salmonella in local salad bars, in order to keep voters away from the polls.[23]

E. coli O157:H7

This strain of E.coli (STEC) produces a highly hazardous substance called *Shigatoxin*. Around 5–10% of those who are diagnosed with STEC infection develop a potentially life-threatening complication known as haemolytic uremic syndrome. STEC lives in the intestines of ruminants, including cattle, goats, sheep, deer and elk. STEC that cause human illness generally do not cause clinical disease in animals. Other kinds of animals, including pigs and birds, sometimes pick up STEC from the environment and may spread it. The transmission is faecal-oral, and people usually get sick through the consumption of faeces-contaminated foods, raw milk or by working in close proximity with animals.[6]

Shigella

Shigella is a very contagious bacteria, highly adapted to humans and some non-human primates; a small inoculum (10 to 200 organisms) is sufficient to cause infection. There are several species of *Shigella,* but the most concerning are those producing *Shigatoxin*, such as *Shigella dysenteriae.* Transmission occurs via faecal-oral route, and the pathogen may be present in contaminated foods or water. Post infection complications, such as arthritis, septicaemia, seizures or haemolytic uremic syndrome can occur.[6]

Water safety threats (Category B)

Vibrio cholerae

Cholera is a major cause of epidemic diarrhoea throughout the developing world; it is caused by infection with toxigenic *Vibrio cholerae* serogroups O1 or O139. Large epidemics are often related to faecal contamination of water supplies or street vended foods. The disease is occasionally spread through eating raw or undercooked shellfish that might be naturally contaminated. There are no known animal hosts for *Vibrio cholerae.* Natural infection and currently available vaccines offer incomplete protection of relatively short duration and no multivalent vaccines are available for O139 infections. People with severe cholera can develop acute renal failure, severe electrolyte imbalances and coma. If untreated, severe dehydration can rapidly lead to shock and death in hours.[6]

Cryptosporidium parvum

There are many species of *Cryptosporidium* that infect animals, some of which also infect humans. While this parasite can be spread in several different ways, water (drinking water and

recreational water) is the most common way to spread the parasite. *Cryptosporidium* may also be found in soil, food, or surfaces that have been contaminated with faeces from infected humans or animals. Symptoms of cryptosporidiosis generally begin 2 to 10 days after becoming infected with the parasite, the most common being watery diarrhoea, which lasts for 1 or 2 weeks.[6]

Legionnaires' disease

The term given to severe pneumonia and systemic infection caused by *Legionella sp.* bacteria is Legionnaires' disease. Water is the major natural reservoir for Legionella, and the pathogen is found in many different natural and artificial aquatic environments such as cooling towers or water systems in buildings, including hospitals. Bacteria of the genus Legionella are recognised as a common cause of community-acquired pneumonia and a rare cause of hospital-acquired pneumonia.[11] Although there is antimicrobial treatment available, which allows for full recovery, the disease was included in this category due to the high consequences that a deliberate introduction of this bacteria in a water retention system can have. For example, in October to November 2014, a contaminated wet cooling system triggered the largest outbreak to date of Legionnaires' disease in Portugal, among the largest ever reported in Europe.[48] According to experts, 'the concordance between the independent analysis of meteorological conditions and temporal modelling supports the theory that the prevailing weather conditions created a unique setting for *Legionella* multiplication and may explain the large scale of the outbreak'.[48] However, modern disinfection through chlorination and the dilution of the agent in great amounts of waters should be enough to render it ineffective. Also, usually municipal water centres have security in place, which may deter potential perpetrators of deliberate introduction.[54]

Alphaviruses (Category B)

This category comprises Venezuelan (VEE), Western and Eastern Encephalitis viruses. VEE virus is more likely as a biowarfare candidate than other equine encephalitis viruses, because of its lower human infectious dose.[7] These are zoonotic mosquito-borne diseases, that affect horses, causing encephalitic disease on both human and equine species.[14] Aerosol transmission may also occur, and it is the ability of these viruses to remain highly infectious in aerosol state which particularly leads to their consideration as biological weapons. In addition, these alphaviruses can be produced in large quantity, in inexpensive and simplified systems and are relatively stable when stored or manipulated. In the 1960s, US military weaponized and stockpiled VEE virus to be used as an incapacitating agent; the stored viruses were later destroyed.[49]

Glanders (Category B)

Glanders is a zoonotic disease of equids and other animals caused by *Burkholderia mallei* bacteria. It is transmissible via direct contact or through inhalation. During WWI, Germany used Glanders agent targeting horse, cattle and mules in locations as different as the US, Romania, Spain, Argentina and France. The results of the most of the attacks are unknown, although possibly successful.[60]

Hantavirus (Category C)

This zoonotic virus is carried asymptomatically by rodents, but causes severe haemorrhagic fever with renal syndrome in human hosts.[2, 14] Hantaviruses represent the most widely distributed rodent-borne zoonotic viruses, and are transmitted through inhalation of the virus from infected rodent faeces. Thus, certain occupational groups – such as farmers, sweepers and labourers who are likely to have high exposure to infected dust – and people living in rural areas are at higher risk of infection.[2]

Nipah (Category C)

Nipah virus was first recognized in 1999 during an outbreak among pig farmers in Malaysia.[2] It is a zoonotic disease agent, which affects pigs and other domestic animals, with less severe clinical signs, and causes severe encephalitis in humans.[14] Since its initial identification, there have been nipah outbreaks almost every year in Southern Asia, causing severe disease and death in people and thus making it an emerging disease of serious public health concern. The virus has caused severe disease outbreaks in pigs, resulting in significant economic losses for farmers in Malaysia, India and Bangladesh.[2, 40]

Other agents and diseases

Although the following agents and diseases are not part of CDC's list, they deserve a special mention as they are relevant, concerning the purposes of this report. They were selected because they either have a high economic impact, since they disseminate quickly through livestock, or because they severely affect human populations. Also, they might lack control strategies applicable to them, such as vaccines and antimicrobials. Agents that have a long incubation period, that are preventable through easily achievable vaccination strategies, or that only cause mild zoonosis, were not included here.

Rinderpest

Rinderpest is an exclusively animal disease, caused by a virus which affects ruminants and swine.[14] The world was declared to be officially free from rinderpest infection at the 79th OIE General Session, in May 2011.[39] Historically, the disease occurred in Europe, Africa and Asia and had major epizootic potential. In fact, the OIE was created, in 1924, in order to assemble an appropriate response to the occurrence of a rinderpest epizootic in Europe, after the

introduction of infected zebu cattle, via the Belgian port of Antwerp.[29] Rinderpest virus stocks are still present at several facilities around the world. It is a OIE-FAO priority to destroy or relocate the all remaining vaccine and virus stocks to one of the 5 approved facilities[1] until 2018. These laboratories follow strict regulations regarding biosafety and are subject to OIE re-evaluation every 3 years.[17]

Rift Valley Fever

Rift Valley Fever is a mosquito-borne viral zoonotic disease of ruminants and other animals.[14] The virus also has the ability to infect humans; the vast majority of human infections result from direct or indirect contact with the blood or organs of infected animals, but can also be consequence of bites of infected mosquitoes.[59] It can also be transmitted as an aerosol – a number of laboratory workers has already been infected through this route. This virus was included by the Working Group on Civilian Biodefense (convened by the John Hopkins University) among those considered to be likely used as a biological weapon.[7]

Vector-borne diseases

This category comprises diseases transmitted by arthropod vectors such as Chikungunya, Dengue, Zika, Malaria and Leishmania. The WHO estimates that one-sixth of the illnesses and disabilities suffered worldwide are related to vector-borne diseases, with more than half of the world's population being currently at risk.[59] The ongoing climate change affects positively the lifecycles of arthropod vectors, such as *Aedes*, *Anopheles* and *Culex* mosquitos, and *Phlebotomine* sand flies.[33] The burden of climate-sensitive diseases is greatest for the poorest populations. For example, the *per capita* mortality rate from vector-borne diseases is almost 300 times greater in developing than in developed regions, where vector-borne diseases constitute an important cause of death, disease burden and health inequity, a brake on socioeconomic development, and a strain on health services.[4] A key challenge arises from the non-specificity and similarity of symptoms caused by many of mosquito-borne viruses, especially Zika virus, Dengue, and Chikungunya virus, that present acute fever similar to many diseases endemic in the tropics, such as Malaria.[25] A recent WHO report, summarizing the importance of vector-borne diseases, states that previously relatively stable geographical distributions are now changing owing to a range of factors, 'including climate change, intensive farming, dams, irrigation, deforestation, population movements, rapid unplanned urbanization, and phenomenal increases in international travel and trade'.[4, 59]

Altogether, climate has an important influence on vector-borne disease transmission, and there is evidence that ongoing climate change is affecting and will continue to affect the distributions and burdens of these infections. The interactions are complex, and to move beyond broad

[1] OIE has established two types of holding facilities. Type A can store any kind of Rinderpest containing material, except for vaccines, while type B is allowed to store vaccines and material for their production.

generalizations in order to build health policies, an assessment of individual diseases with respect to specific disease control decisions is required.[4]

Highly Pathogenic Avian Influenza

The infection causes a wide spectrum of symptoms in birds but does not normally infect humans. However, certain strains have managed to cross the species barrier and infect people. Since humans have little or no immunity to such strains, they cause severe respiratory disease (e.g. pneumonia) or death. It has been learnt that the past three world pandemics have been due to influenza of avian origin. Today, avian influenza is entrenched in poultry in some countries, resulting in millions of affected and culled chickens, several hundred human cases, and many human deaths. Outbreaks in poultry have seriously impacted livelihoods, food security, the economy and international trade in affected countries.[2]

Foot-and-mouth disease virus

FMD is a highly contagious viral disease of livestock with significant economic impact; it is not readily transmissible to humans. The disease affects cattle and swine as well as sheep, goats, and other cloven-hoofed ruminants. In a susceptible population, morbidity approaches 100%. Intensively reared animals are more susceptible to the disease than traditional breeds. FMD is the first disease among the OIE listed ones for which the OIE established an official status of freedom referring to countries and zones.[39]

Classical and African Swine Fever

These swine diseases are not related. Nevertheless, they share some common characteristics – they are absent from the majority of developed countries, their most virulent strains have 100% morbidity and high mortality rates, and their occurrence represents a heavy burden for the swine production industry. While there is no vaccine for ASF, CSF can be prevented through vaccination protocols. However, most of “disease free” countries apply a “no vaccination” policy, and have control systems that provide emergency vaccination capacity.

4. Role of International Organisations and its mechanisms for coordinating efforts

United Nations

United Nations Organization has specific bodies assigned to deal with biological threats and disaster prevention and relief. The United Nations Office for Disarmament Affairs (UNODA) works on the promotion of disarmament as a means to achieve global peace. It supports the implementation of BTWC through a specific unit and raises awareness to the importance of disarmament issues. The UNODA works at a very high level, creating opportunities for governments to reach diplomatic agreements, and also at the field in specific missions. Besides, the UN Secretary General Mechanism for Investigation of Alleged use of Chemical and Biological Weapons conducts field operations to ensure that BTWC dispositions are fulfilled. The BTWC is revised periodically and the 8th Review Conference will take place in Geneva, in August 2016.[32]

UNISDR is the UN Office for Disaster Risk Reduction. It promotes the coordination of efforts to ensure that natural disasters and deliberate attacks have the least possible consequences, through the improvement of preparedness, establishment of frameworks and avocation of cooperation between governments and organizations. Currently, the UNISDR is campaigning very actively in the application of Sendai Framework 2015 – 2030. This is a disaster risk reduction programme, which emerged from a voluntary agreement between nations, supported by the UNISDR. It is based on seven pillars, and its main goal is '*The substantial reduction of disaster risk and losses in lives, livelihoods and health and in the economic, physical, social, cultural and environmental assets of persons, businesses, communities and countries*'[52].

WHO

The WHO is an organisation which falls under UN institutions. International Health Regulations (IHR), which entered into force on 15th June 2007, are WHO's legal instrument for safeguarding public health - they require countries to report certain disease outbreaks and public health events to WHO.[35] Also, the OIE and FAO work closely with the WHO to improve the ability of National animal and public health systems to respond to current and emerging animal health risks with public health consequences.[9] Together, these organizations form a Tripartite Alliance which essentially addresses high priority transversal issues, such as rabies, zoonotic influenza and antimicrobial resistance. All the previously mentioned activities fall under the One Health framework.

FAO

The FAO is the UN body responsible for the achievement of food security, eradication of hunger and malnutrition, and driving forward of economic and social progress, mainly in developing countries. FAO's activities address many overlapping animal health issues, since animal products do not only represent a source of high-quality food, but are also a source of income for many small farmers and animal holders in developing countries. FAO supports countries' capacity development to achieve their own goals in food security, nutrition and agricultural development. [16]

OIE

The OIE was created in 1924, before the United Nations, to assemble an appropriate response to the Rinderpest pandemics ravaging throughout Europe. The organisation plays an important role in minimising animal and public health risks attributable to zoonosis and other animal diseases, which can have severe consequences for global food safety and security.[9] Also, the OIE promotes animal welfare, while creating standards for safe trade of animals and their by-products.[39]

In 1995, the standards developed by the OIE were recognised by the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) of the WTO. SPS Agreement's goal is to minimise the risk of importing pathogens and to remove unjustifiable sanitary restrictions to international trade. Hence, an importing country can only apply sanitary measures to imports if a similar level of protection is applied internally and to all imports. Member countries may introduce standards providing a higher level of protection than that provided by OIE standards if they have a scientific justification and had performed science-based risk analysis.[53] The National Veterinary Services which implement OIE animal and welfare standards and other measures, are the first line of defence against zoonotic and other animal diseases, and must meet the core requirements for its diagnostic and control. The OIE provides assistance to its member countries through 'PVS Pathway' initiative, which shifts the emphasis from short-term, emergency-type approaches, to improving veterinary services towards a more sustainable, long term strengthening of capabilities and resources.[9]

Regarding disaster risk reduction and preparedness, OIE summoned a roster of experts on the theme to assemble an *ad hoc* group, whose purpose was to a set of guidelines to be applied in disaster management. These guidelines provide a framework that veterinary professionals can use to develop processes and procedures for managing the veterinary sector's actions to reduce the adverse consequences of disasters as they outline guiding principles and the roles that Veterinary Services play in reducing the impact of disasters in all phases of the Disaster Management Cycle.[39]

Funds, Programmes, Solidarity

The UN System comprises several institutions devoted to promoting international financial stability and to supporting capacity building in developing countries, such as the International Monetary Fund and the World Bank Group. These institutions are financed by Member Countries and external donors. Besides, some countries have their own programmes oriented to disaster reduction and relief. Some of these programmes work well over borders to help struggling countries and to donate to specific UN bodies, such as UNDC, UNDP, FAO, etc.

The OIE has its own solidarity fund - The OIE World Animal Health and Welfare Fund. It was created on 2004 by the OIE World Assembly of Delegates and has been established 'for the purpose of projects of international public utility relating to the control of animal diseases, including those affecting humans, and the promotion of animal welfare and animal production food safety'.[39]

The OIE World Fund's goals are: to improve governance of animal health systems, to modernise existing national veterinary legislation, to develop veterinary education and to develop tools which empower Members to deal with urgent situations regarding the prevention and control of animal diseases (e.g. vaccine banks, communication programs). Also, it aims to improve the animal health scientific community worldwide through laboratory twinning projects, twinning projects on veterinary education, and twinning projects between veterinary statutory bodies. Lastly, it offers the PVS Evaluation Missions to improve compliance of Member Countries with OIE standards. [39]

Global Health Security Agenda

GHSA is a programme, launched in February 2014, endorsed by 50 nations and several organizations. It acknowledges the essential need for a multilateral and multi-sectoral approach to strengthen both the global capacity and nations' capacity to prevent, detect, and respond to infectious diseases threats whether naturally occurring, deliberate, or accidental. GHSA is facilitating collaborative, capacity-building efforts to achieve specific and measurable targets in biological threat reduction area, while accelerating achievement of the core capacities required by the WHO's IHR, the OIE's Performance of Veterinary Services Pathway, and other relevant global health security frameworks. It is comprised of Action Packages, subscribed by countries, which are sets of goals related to a pressing issue, to be achieved in a 5 year timeframe. Also, it offers an Assessment Tool, to measure countries' status and progress in building capacity. This partnership is led and supported by a GHSA Steering Group composed of 10 member nations. In addition to individual countries, advisory partners include the WHO, the FAO and the OIE, Interpol, the Economic Community of West African States, the UNISDR, and the European Union.

Surveillance, Monitoring and Early Response

Animals play an important role as biosensors for accidental or deliberate releases of infectious agents and toxins, and for emerging diseases. The same disease surveillance and intelligence systems that are in place to detect day-to-day occurrences of natural outbreaks in animals within countries and at national borders, will also detect deliberate and accidental releases.[36]

The OIE Animal Health and Information System gathers daily data from around the world. The information is predestined at decision makers and other stakeholders, to enable them to take the necessary preventive measures. Under this system, the occurrence of a disease must be reported as soon as possible (within 24 hours) to the OIE Headquarters, which then redirects the information through appropriate channels.[53] The response to disease is the same whether it is directed against natural infection and deliberate or accidental release. In the case of zoonotic diseases, coordination of the animal health and public health response is essential, and control is often more successful if focused on eliminating or controlling the pathogen at the animal source.[36]

Warning systems provide a worldwide surveillance network for the early detection and rapid reporting of any suspicious disease occurrence that is natural or could have its origin in an act of bio/agroterrorism. Currently, the 'Global Early Warning System for major disease including zoonosis' (GLEWS) is one of the mechanisms used together by the OIE, FAO, and WHO for monitoring health data from existing event-based surveillance systems and to track and verify relevant animal and zoonotic events.[15] However, GLEWS is not the only existing system for input of diseases epidemiological knowledge. Some other unofficial platforms, such as 'ProMed' (by the International Society for Infectious Diseases) and 'Epicore' (a newer tool by the same institution) use networks of professionals spread all over the world to communicate disease occurrence suspicions and to do rumour tracking. The early detection of high-risk diseases is, in most of the cases, done by suspicious field clinicians. That type of surveillance should be encouraged through regular educational sessions aimed at field players. The sensitiveness of surveillance networks may be greatly increased through analysis and modelling efforts, in order to guide and concentrate the surveillance activities.[13]

When there is suspicion of malicious release, collaboration with law enforcement agencies becomes an important part of the response. Recent events (e.g. Ebola outbreaks in West Africa) have shown that in the absence of strong well governed health systems, infectious disease can rapidly spread and get out of control with devastating consequences and heightened risk for the whole world. It is much smarter and more economically viable to provide sustainable funding for animal and public health services than to deal with a large outbreak which has got out of hand because a national detection and response was insufficient. [36]

Unfortunately, pockets of civil instability continue to emerge in different parts of the world. This may exacerbate the risk of infectious disease threats since civil instability often leads to health systems falling apart. Infectious disease may also lead to instability because it may damage micro and macro economies or it may lead to reduction in food supply, both of which can motivate people to take unprecedented and unpredictable actions.[36]

In order to respond promptly to crisis situations, the FAO and OIE launched jointly in 2006 the 'Crisis Management Centre – Animal Health'. It works closely with the GLEWS and the 'Emergency Prevention System' to continuously track and analyse the animal disease situation worldwide missions to countries to help assess epidemiologic situations, diagnose outbreaks of animal diseases, and set up immediate measures to prevent or stop disease spread.[35]

On what concerns human health, WHO has developed a comprehensive 'event management system' to verify critical information about outbreaks and ensure accurate and timely communications between key international public health professionals, including WHO Regional Offices, National Services, collaborating centres and partners in the Global Outbreak Alert and Response Network.[59]

Laboratory safety

Expert investigations carried out by health authorities are needed to establish the cause of a disease outbreak and veterinary laboratories are often the first to discover its source.[36] A veterinary laboratory is held accountable for a range of issues apart from the delivery of basic diagnostic services. These may include health and safety, biosecurity, animal welfare and ethics, environmental contamination, genetic manipulations and quality assurance. In addition to general health and safety issues, veterinary laboratories have the responsibility of containing pathogens and preventing their accidental release. Laboratory biological risk management practices should specifically recognise the potential for bioterrorist threats including the concept of the insider threat (e.g. the bioterrorist threat posed by a staff member).[38]

Veterinary laboratories and other animal related facilities routinely handle biological materials that may constitute or contain infectious agents and toxins, which may cause adverse animal or public health and economic effects, due to uncontrolled release inside or outside the laboratory.

Laboratory and animal facilities managers are responsible for providing a management system that ensures safe and secure handling, storage, and transport of these biological materials (a biological risk management system).[38] The laboratory is expected to perform a risk analysis process, as shown in Flowchart 1 (Annexes).

Laboratory facilities are categorized as basic – Biosafety Level (BSL) 1; basic – BSL 2; containment – BSL 3; and maximum containment – BSL 4. BSL designations are based on a

combination of the design features, construction, containment facilities, equipment, practices and operational procedures required for working with agents from the various risk groups. It is available in Annexes section a table (Table 1) where laboratories and agents characteristics regarding BSL classification are described in further detail. There is a correspondence, although not direct, between agents' CDC risk group (A, B and C) and the required BSL of laboratories working with them. Thus, the assignment of a BSL takes into consideration the pathogenic agent, the facilities available, and the equipment practices and procedures required to conduct work safely in the laboratory.[57]

5. Reality check

Concerning issues

Globalisation has made it far more difficult to keep animal diseases from spreading, and almost impossible to keep highly infectious diseases controlled.[1] Opposed to what happened with previous pandemics, such as bubonic plague or Spanish flu, which took months to spread, recent events like SARS and avian flu indicate that today's pathogens either are more easily spread or have more opportunities to do so. Currently, we are witnesses of the coexistence of intensive farming methods, including the centralization of animal markets and high-density livestock rearing, with traditional agriculture. This reality may provide the ideal opportunity for the emergence of new pathogens and their quick spread through animal and human populations.

However, many developed nations have not experienced a major human or animal disease outbreak in over half a century – meaning that their people and governments are unused to coping politically and socially with large-scale infectious disease, whether it may be natural or intentionally caused.[1]

Since the beginning of the XXI century, a variety of extremist groups has shown interest in using biological weapons. Although, so far, most of their attempts have ended in failure, the 2001 'anthrax letters' episode, in the US, exemplifies how it is certainly conceivable that these actors might attain biological weapons offensives. Also, it is expected that they might employ or target animals as part of their implementation of a terrorist attack, due to the economic consequences that such action might bring.[1]

Additionally, rapid developments in synthetic biology and the advent of microbiological kits may improve capabilities of both state and non-state actors, regarding biological warfare. No terrorist has ever synthesised a pathogen from scratch, but this does not mean it will never happen.[1] There is a general concern that synthetic biology will lead to further simplification of laboratory work protocols and that, combined with open access to the genomic DNA sequences of pathogenic organisms, and the reduction of price for DNA synthesis, will make biology increasingly accessible to people operation outside well-equipped professional research laboratories, including people with malevolent intentions.[23] Human threats are even more dynamic than evolutionary factors, in that human beings can adapt their behaviour instantaneously, can strategize to avoid defences and can concentrate their efforts on vulnerabilities.[1] Nowadays, synthetic biology has been subject to a common narrative, supported by public health officers and government actors, regarding the biosecurity threat it poses. This framing may lead to some misconceptions, mainly from a public opinion

perspective. It is believed that, besides simplifying biology and making it accessible for common people without special facilities, the growth of Do-It-Yourself biology may offer dual-use knowledge. Also, the decrease in price of DNA synthesis would make it easier to create new pathogens, which could be used as biological weapons for high consequence, mass casualty attacks.[23]

Myth busters

Experts on biological threats studies, such as Sonia Ben Ouagrham-Gormley and Katherine Vogel, defend that the previously mentioned views overestimate the real bioterrorist threat. [23, 43] Due to their technical complexity and high developmental costs, as well as their reliance on living microorganisms that are highly sensitive to their environmental and handling conditions, the attempted use of biological agents is unpredictable in its outcomes. As shown by past governmental programs and independent terrorist plans — the failures in the developmental process cause extensive delays in program advancement. Furthermore, the stages of a bioweapon lifecycle — research, development, production, scale-up, weaponization, and testing — are highly interdependent, and the successful passage from one stage to the next requires organizational and managerial conditions that promote coordination, cooperation, and information exchange among the various teams of experts involved, which are particularly difficult to achieve. As a result, most past state and non-state bioweapons programs have been unsuccessful at reaching their goals.[23, 43]

Perhaps, the most important point in the analysis of the possible development of synthetic biological agents is the consideration of how 'tacit knowledge' is implied in the process. Broadly, tacit knowledge refers to skills and techniques that cannot be readily codified but, rather, acquired by a process of 'learning by doing' or 'learning by example' and often take considerate time and effort to gain.[23] Training by experienced professional researchers and specialist skills acquired by trial and error, as well as the enculturation in laboratory practices, are still highly relevant to the success of synthetic biology projects.[23]

On what concerns DNA synthesis, the public opinion disquietude about online orders of DNA sequences by common individuals – the *de novo* synthesis of poliovirus in 2002 and the "reconstruction" of Spanish flu virus in 2005 – specialists' opinion is reassuring. Firstly, it is important to differentiate the synthesis of oligonucleotides (less than 100 nucleotides is length), from "gene synthesis" (*de novo* synthesis of "gene-length" DNA sequences, typically 200 to 3000 base pairs), and from the assembly of *de novo* synthetized gene-length fragments into genetic circuits and whole genomes. Obtaining the oligonucleotides is only the first step in a complicated process – even specialized DNA synthesis companies cannot synthetize *de novo*

any desired DNA sequence. DNA synthesis is error prone and some sequences are recalcitrant to chemical synthesis. [23]

So, we are still better at reading DNA than actually writing it. In fact, the real challenge regarding the creation or virulence and transmissibility enhancement of biological agents is not their DNA synthesis, but rather the assembly of DNA fragments.[23] It is a painstakingly difficult process that requires expertise, adequate laboratory materials and a seemingly infinite succession of trial and error experiments, in order to build a functional genome, instead of constructing a genome-sized DNA fragment. Besides, although this cannot be taken as a definitive rule, as viruses suffer passages though host organisms during their production process in the laboratory, they tend to accumulate mutations that generate an attenuated strain. Similarly, bacteria cultured in laboratories tend to lose virulence.[23]

Given these points, it is clear that public opinion and some governmental statements overlook significant difficulties faced with the process of designing or producing a pathogen, as they focus mainly on material features. Thus, missing important socio-technical factors, such as tacit knowledge and DNA synthesis and assembly specificities that go beyond currently automated processes, might be a gullible perspective.[23]

6. Conclusions

Writing this report was a great opportunity to extend my knowledge to an unlikely field relating to Veterinary Medicine. While doing my research, I found myself rephrasing the report's title several times, as my perception on the subject changed, and so changed the focus I wanted it to have.

All things considered, the threats which humans, animals and the environment face, regarding biological agents are broad on their nature, on their sources, and on their likely impact and duration. The bioterrorist threat definitely exists, although it may not be as easily achievable as one might think, due to the technical constraints related to creating 'weapons' and not only 'pathogens'. In fact, this type of threat ends up taking a bigger toll on one's psyche than on concrete matters, due to the unpredictability associated with isolated individuals or with small extremist groups, rather than populations – which have foreseeable behaviour patterns.

Moreover, the threat posed by laboratories and investigation centres must be carefully weighed in. Despite the application of strict biosafety rules, accidents have happened more than a few times. Although this may seem unavoidable or poorly relevant regarding the amount of existing facilities, that is not the case. One release or accidental escape of a highly virulent pathogen, for which quick response systems are not prepared, may represent the trigger of a pandemic.

Additionally, the deliberate or accidental introduction of new species of animals and plants can disrupt entire ecosystems. Previous deliberate introductions have resulted in sanitary chaos, due to the lack of foresight regarding their evolution in the new environment. Also, accidental introductions tend to occur more frequently, due to increased international trade and increased transportation of people around the globe.

In the final analysis, the importance of efficient surveillance methods and quick response strategies cannot be overstated. It may seem more relevant to be prepared for specific threats, for their consequences are already well known among us. However, the biggest turning points in history have been unexpected events. Thus, it makes sense to be prepared to the unexpected, through generalist surveillance systems and simulation exercises which involve stakeholders from different fields of knowledge, able to perform diverse response types, besides the traditional contingency plans aimed at specific disease events.

"This idea that in order to make a decision you need to focus on the consequences (which you can know) rather than the probability (which you can't know) is the central idea of uncertainty."

Nassim Nicholas Taleb, *The Black Swan: The Impact of the Highly Improbable*

References

1. Ackerman G: **It is hard to predict the future: the evolving nature of threats and vulnerabilities**. *Rev Sci Tech* 2006, **25**(1):353-360.
2. Asia WROfS-E: **A brief guide to emerging infectious diseases and zoonoses**; 2014.
3. Asokan G, Asokan V: **Bradford Hill's criteria, emerging zoonoses, and One Health**. *J Epidemiol Glob Health* 2015.
4. Campbell-Lendrum D, Manga L, Bagayoko M, Sommerfeld J: **Climate change and vector-borne diseases: what are the implications for public health research and policy?** *Philos Trans R Soc Lond B Biol Sci* 2015, **370**(1665).
5. CDC: **Section IV—Laboratory Biosafety Level Criteria**. In: *Biosafety in Microbiological and Biomedical Laboratories.* edn.; 2009.
6. **CDC A-Z Index** [http://www.cdc.gov/az]
7. Chomel B, Sun B: **Bioterrorism and invasive species**. *Rev Sci Tech* 2010, **29**(2):193-199.
8. Clarke N, Rinderknecht J: **Bioterrorism: intentional introduction of animal disease**. *Rev Sci Tech* 2011, **30**(1):131-138.
9. Corning S: **World Organisation for Animal Health: strengthening Veterinary Services for effective One Health collaboration**. *Rev Sci Tech* 2014, **33**(2):639-650.
10. **Reducing Australia's carp Invasion** [http://www.csiro.au/en/Research/BF/Areas/Managing-the-impacts-of-invasive-species/Biological-control/Biocontrol-of-carp]
11. Cunha B, Burillo A, Bouza E: **Legionnaires' disease**. *The Lancet* 2016, **387**(10016):376-385.
12. Dudley J, Woodford M: **Bioweapons, bioterrorism and biodiversity: potential impacts of biological weapons attacks on agricultural and biological diversity**. *Rev Sci Tech* 2002.
13. Dufour B, Hendrikx P, Toma B: **Élaboration et mise en place de systèmes de surveillance épidémiologique des maladies à haut risque dans les pays développé**. *Rev Sci Tech* 2006, **1**(25):187-198.
14. Dvorak G: **Bioterrorism and High Consequence Pathogen Wallchart**. In. http://www.cfsph.iastate.edu/Products/resources/WallChart.pdf: Center for Food Security and Pubic Health; 2015.
15. FAO–OIE–WHO: **GLEWS+The Joint FAO–OIE–WHO Global Early Warning System for health threats and emerging risks at the human–animal–ecosystems interface**. In.; 2013.
16. **Food and Agriculture Organization of the United Nations** [www.fao.org]

17. Friend M: **Biowarfare, Bioterrorism, and Animal Diseases as Bioweapons**. In: *Disease Emergence and Resurgence: The Wildlife-Human Connection. Volume Circular 1285*, edn. Reston, Virginia: U.S. Geological Survey; 2006: 400.
18. Frischknecht F: **The History of Biological Warfare**. In: *Decontamination of Warefare Agents.* edn.: WILEY-VCH Verlag GmbH & Co. KGaA; 2008.
19. Furmanski M: **Threatened pandemics and laboratory escapes: Self-fulfilling prophecies**. In: *Bulletin of the Atomic Scientists.* 2014.
20. **The Australia Group** [http://www.australiagroup.net/en/origins.html]
21. Initiative TNAKF: **Synthetic Biology: Building a Nation's Inspiration: Interdisciplinary Research Team Summaries**. Washington, DC: The National Academies Press; 2010.
22. **ProMed Mail Post** [http://www.promedmail.org]
23. Jefferson C, Lentzos F, Marris C: **Synthetic biology and biosecurity: challenging the "myths"**. *Frontiers in Public Health* 2014, **2**:115.
24. Karesh W, Dobson A, Lloyd-Smith J, Lubroth J, Dixon M, Bennett M, Aldrich S, Harrington T, Formenty P, Loh E *et al*: **Ecology of zoonoses: natural and unnatural histories**. *The Lancet* 2012, **380**(9857):1936-1945.
25. Kilpatrick A, Randolph S: **Drivers, dynamics, and control of emerging vector-borne zoonotic diseases**. *The Lancet* 2012, **380**(9857):1946-1955.
26. Marí Saéz A, Weiss S, Nowak K, Lapeyre V, Zimmermann F, Düx A, Kühl H, Kaba M, Regnaut S, Merkel K *et al*: **Investigating the zoonotic origin of the West African Ebola epidemic**. *EMBO Molecular Medicine* 2015, **7**(1):17-23.
27. Monceau K, Bonnard O, Thiéry D: **Vespa velutina: a new invasive predator of honeybees in Europe**. *Journal of Pest Science* 2013, **87**(1):1-16.
28. Morse S, Mazet J, Woolhouse M, Parrish C, Carroll D, Karesh W, Zambrana-Torrelio C, Lipkin W, Daszak P: **Prediction and prevention of the next pandemic zoonosis**. *The Lancet* 2012, **380**(9857):1956-1965.
29. Moutou F, Pastoret P: **Defining an invasive species**. *Rev Sci Tech* 2010, **29**(1):37-45, 27-35, 47-56.
30. Nations Lo: **Geneva Protocol**. In. Geneva; 1925.
31. Nations U: **Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction** 1972.
32. **What are Biological and Toxin Weapons?** [http://www.unog.ch]
33. Negev M, Paz S, Clermont A, Pri-Or N, Shalom U, Yeger T, Green M: **Impacts of Climate Change on Vector Borne Diseases in the Mediterranean Basin -**

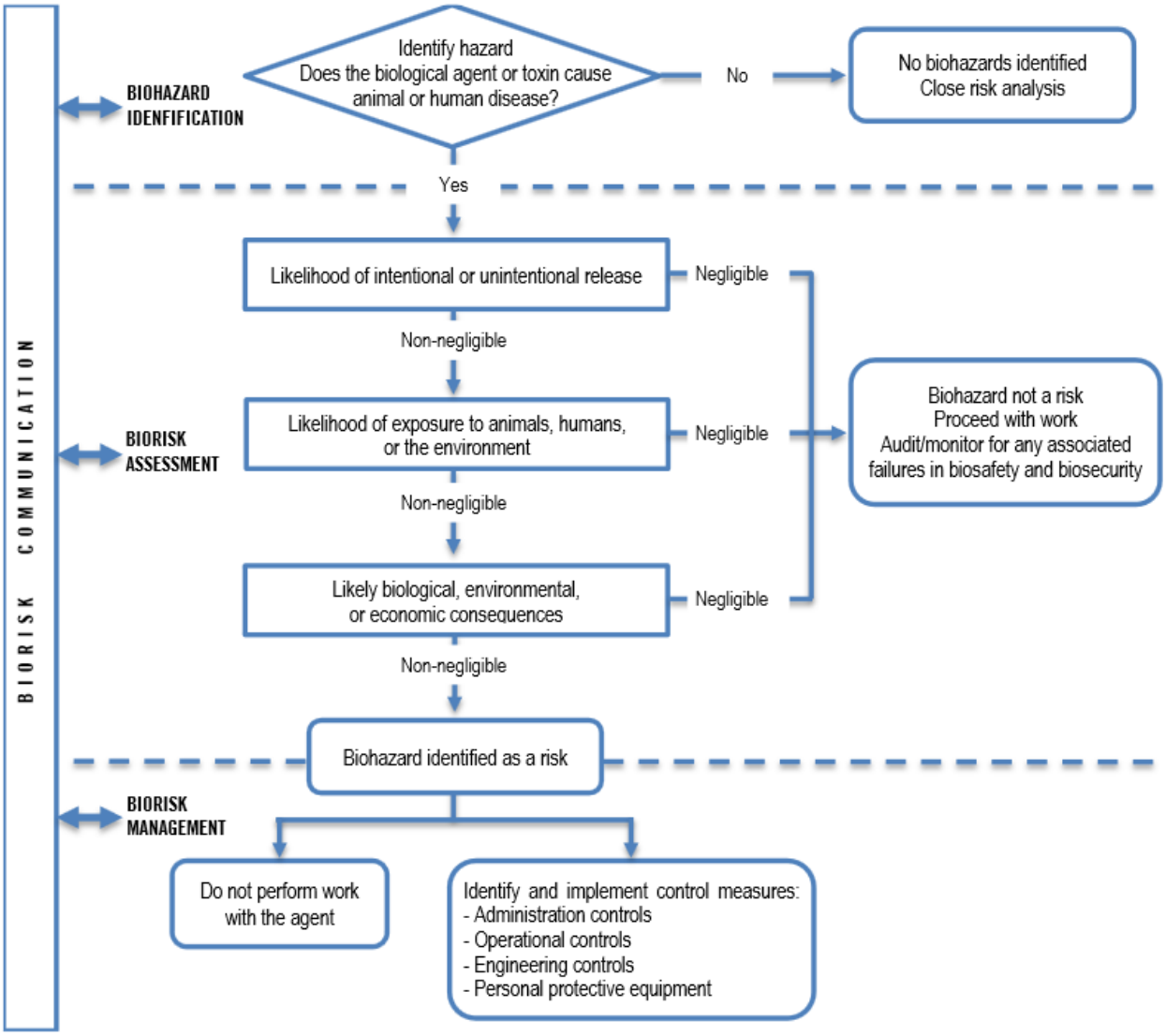
Implications for Preparedness and Adaptation Policy. *Int J Environ Res Public Health* 2015, **12**(6):6745-6770.

34. Nigam P, Nigam A: **Botulinum Toxin**. *Indian Journal of Dermatology* 2010, **55**(1):8-14.
35. Nuttall I, Miyagishima K, Roth C, de La Rocque S: **The United Nations and One Health: the International Health Regulations (2005) and global health security**. *Rev Sci Tech* 2014, **33**(2):659-668.
36. OIE: **Biothreat Reduction Strategy**. In: *Strengthening global biological security.* 2015.
37. OIE: **Factsheet on Bioterrorism**. 2015.
38. OIE: **Manual of Diagnostic Tests and Vaccines for Terrestrial Animals**. In., edn.; 2015.
39. **OIE website** [www.oie.int]
40. **WAHID - Disease Occurrence Timelines** [http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/Diseasetimelines]
41. Ouagrham-Gormley S: **Amerithrax review: Lessons for future investigations**. In: *Bulletin of the Atomic Scientists.* vol. 2016; 2011: Opinion article.
42. Ouagrham-Gormley S: **The Pandora's Box of Biology**. *The Global Studies Review* 2012, **8**(1).
43. Ouagrham-Gormley S: **Bioweapons not an alternative to nuclear weapons**. *Bulletin of the Atomic Scientists* 2015.
44. Papa A, Mirazimi A, Koksal I, Estrada-Pena A, Feldmann H: **Recent advances in research on Crimean-Congo hemorrhagic fever**. *J Clin Virol* 2015, **64**:137-143.
45. Scholte E, Schaffner F: **Waiting for the tiger: establishment and spread of the Aedes albopictus mosquito in Europe**. In: *ecology and control of vector-borne diseases, Volume 1.* edn. Wageningen: Wageningen Academic Publishers; 2007: 241-260.
46. Schwab K: **Course: Biological Agents of Water and Foodborne Bioterrorism**. In.: Johns Hopkins Center For Public Health Preparedness; 2006.
47. Shimura J, Coates D, Mulongoy J: **The role of international organisations in controlling invasive species and preserving biodiversity**. *Rev Sci Tech* 2010, **29**(2):405-410.
48. Shivaji T, Sousa Pinto C, San-Bento A, Oliveira Serra L, Valente J, Machado J, Marques T, Carvalho L, Nogueira P, Nunes B *et al*: **A large community outbreak of Legionnaires' disease in Vila Franca de Xira, Portugal, October to November 2014**. *Eurosurveillance* 2014, **19**(50).
49. Sidwell R, Smee D: **Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control**. *Antiviral Res* 2003, **57**(1-2):101-111.

50. Sjodin A, Broman T, Melefors O, Andersson G, Rasmusson B, Knutsson R, Forsman M: **The need for high-quality whole-genome sequence databases in microbial forensics**. *Biosecur Bioterror* 2013, **11 Suppl 1**:S78-86.
51. Spickler A: **Animal Diseases Technical Factsheets**. *Iowa State University - Centre for Food Secutity and Public Health* 2015.
52. **Sendai Framework for Disaster Risk Reduction** [http://www.unisdr.org/we/coordinate/sendai-framework]
53. Vallat B, Pinto J, Schudel A: **International organisations and their role in helping to protect the worldwide community against natural and intentional biological disasters**. *Rev Sci Tech* 2006, **25**(1):163-172.
54. van Rijn S: **Capabilities Analysis of Bioterrorism: Roadblocks Facing Non-State Actors' Use of Bioweapons**. In: *Global Biodefense.* 2014.
55. Webster JP, Gower CM, Knowles SC, Molyneux DH, Fenton A: **One health - an ecological and evolutionary framework for tackling Neglected Zoonotic Diseases**. *Evol Appl* 2016, **9**(2):313-333.
56. Wheelis M: **Biological warfare at the 1346 siege of Caffa**. *Emerg Infect Dis* 2002.
57. WHO: **Laboratory biosafety manual**. In., 3rd edn.; 2004: 5-8.
58. WHO: **Responsible life sciences research for global health security**; 2010.
59. **WHO website** [http://www.who.int]
60. Wilson T, Gregg D, King D, Noah D, Perkins L, Swayne D, Inskeep W: **Agroterrorism, biological crimes, and biowarfare targeting animal agriculture. The clinical, pathologic, diagnostic, and epidemiologic features of some important animal diseases**. *Clin Lab Med* 2001, **21**(3):549-591.

Annexes

Biological Risk Analysis Process



Note: The biological risk management process should address all laboratory processes and procedures associated with the specific hazard (biological agent or toxin). The biological risk assessment and biological risk control planning involves a team of individuals who understand the organisational aspects of the laboratory, the biology and pathogenesis of the agent, and the impacts of exposures and accidental or intentional release of the biological agent or toxin.

Flowchart 1 - Biological Risk Analysis Process. Source – OIE, 2015, Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Laboratory Biosafety Levels

BSL	Agents	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)
1	Not known to consistently cause diseases in healthy adults	Standard microbiological practices	No primary barriers required. PPE: laboratory coats and gloves; eye and face protection, as needed	Laboratory bench and sink required
2	Agents associated with human disease. Routes of transmission include percutaneous injury, ingestion and mucous membrane exposure.	BSL-1 practice plus limited access, biohazard warning signs, 'Sharps' precautions, Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: BSCs or other physical containment ; devices used for all manipulations of agents that cause splashes or aerosols of infectious materials PPE: Laboratory coats, gloves, face and eye protection, as needed	BSL-1 plus autoclave available
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure.	BSL-2 practice plus controlled access, decontamination of all waste, decontamination of laboratory clothing before laundering	Primary barriers: BSCs or other physical containment devices used for all open manipulations of agents PPE: Protective laboratory clothing, gloves, face, eye and respiratory protection, as needed	BSL-2 plus physical separation from access, self-closing, double-door access, exhausted air not recirculated, negative airflow, entry through airlock or anteroom, hand washing sink near laboratory exit
4	Dangerous/exotic agents which pose high individual risk of aerosol-transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatments	BSL-3 practices plus clothing change before entering, shower upon exit All material decontaminated on exit from the facility.	Primary barriers: All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit.	BSL-3 plus separate building or isolated zone, dedicated supply and exhaust, vacuum, and decontamination systems

Table 1 - Summary of Recommended Biosafety Levels for Infectious Agents

Source: CDC: Section IV—Laboratory Biosafety Level Criteria. In: *Biosafety in Microbiological and Biomedical Laboratories.* edn.; 2009. [5]

Internship projects

Technical disease cards updated

Disease	Last updated in
African Horse sickness	2013
African swine fever	2013
Bluetongue	2013
Bovine babesiosis	2013
Classical swine fever	2009
Contagious bovine pleuropneumonia	2009
Contagious caprine pleuropneumonia	2009
Dourine	2013
Epizootic haemorrhagic disease	2009
Equine piroplasmosis	2009
Foot and mouth disease	2013
Glanders	2013
Haemorrhagic septicaemia	2013
Heartwater	2009
Highly pathogenic avian influenza	2009
Japanese encephalitis	2013
Lumpy skin disease	2013
Malignant catarrhal fever	2013
Newcastle disease	2013
Nipah (virus encephalitis)	2009
Peste des petits ruminants (TDC + DIS)	2013
Rabbit haemorrhagic disease	2015
Rabies	2014
Rift Valley fever	2009
Rinderpest (TDC + DIS)	2013
Screwworm	2013
Sheep pox and goat pox	2013
Swine influenza	2009
Swine vesicular disease	2013
Theileriosis	2009
Trypanosoma evansi infections (including SURRA)	2013
Trypanosomosis (tsetse-transmitted)	2013
Venezuelan equine encephalitis	2013
Vesicular stomatitis	2013
MERS-CoV Factsheet	2014

http://www.oie.int/en/animal-health-in-the-world/technical-disease-cards/

Biothreat Watch, Issue 1, Jan – May 2016

General

- **Insights into the preparation of BWC review** Jan/Feb 2016 http://www.armscontrol.org/ACT/206_0102/News/BWC-Parties-Prepare-for-Review-Meeting
- **New Developments in Biological and Chemical Terrorism Countermeasures;** Ronald J. Kendall, Steven M. Presley, Seshadri S. Ramkumar, CRC Press, Feb. 2016 - 185 pages https://books.google.fr/books?id=l3SmCwAAQBAJ&hl=fr&source=gbs_navlinks_s
- **Preparing for non-traditional biothreats** Feb 2016 http://online.liebertpub.com/doi/pdfplus/10.1089/hs.2015.0045
- **Contextual Factors Among Indiscriminate or Large Attacks on Food or Water Supplies**, 1946-2015 Feb 2016 http://online.liebertpub.com/doi/pdfplus/10.1089/hs.2015.0056
- **From over 90 000 cases to zero in two decades: the European Region is malaria free** Apr 2016 http://www.euro.who.int/en/media-centre/sections/press-releases/2016/04/from-over-90-000-cases-to-zero-in-two-decades-the-european-region-is-malaria-free
- **The Department of Homeland Security Will Test Bioterror Airflow in New York Subway System** May 2016 http://nymag.com/daily/intelligencer/2016/05/dhs-will-test-bioterror-airflow-in-nyc-subway.html#

Diagnostic methods

- **Expansion of Microbial Forensics**. Schmedes SE, et al. J Clin Microbiol. Feb 2016. Unofficial online version) https://www.researchgate.net/search.Search.html?type=publication&query=Expansion%20of%20Microbial%20Forensics&tabViewId=57309dfded99e1394a514117&previous=researcher
- **Are public health microbiology laboratories in the European Union prepared for tracking infectious diseases? The first EULabCap report published,** Feb 2016 http://ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?ID=1359&List=8db7286c-fe2d-476c-9133-18ff4cb1b568&Source=http%3A%2F%2Fecdc.europa.eu%2Fen%2Fhealthtopics%2Fmicrobiology%2Fmicrobiology-activities%2Flaboratory-capability%2FPages%2Fdefault.aspx
- Dong, M., et al. (Mar 2016), **Standardized methods to generate mock (spiked) clinical specimens by spiking blood or plasma with cultured pathogens**. J Appl Microbiol, 120: 1119–1129. doi:10.1111/jam.13082 (The development of diagnostic platforms for detection of low prevalence pathogens such as biothreat or emerging agents is challenged by the lack of clinical specimens for performance evaluation. This deficit can be overcome using mock clinical specimens made by spiking cultured pathogens into human matrices.) http://onlinelibrary.wiley.com/doi/10.1111/jam.13082/abstract?systemMessage=Wiley+Online+Library+will+be+unavailable+on+Saturday+14th+May+11%3A00-14%3A00+BST+%2F+06%3A00-09%3A00+EDT+%2F+18%3A00-21%3A00+SGT+for+essential+maintenance.Apologies+for+the+inconvenience.

- **Mass spectrometry for the detection of bioterrorism agents: from environmental to clinical applications.** Duriez E, et al. Mar 2016 http://www.ncbi.nlm.nih.gov/pubmed/26956386 (Restricted access)
- **First Commercial Zika Virus Test Gets FDA Approval,** May 2016 http://globalbiodefense.com/2016/05/02/first-commercial-zika-virus-test-gets-fda-approval/

Emerging Diseases/ Emerging threats

- **Kenyan Police 'Foiled' Anthrax Attack Linked to IS Group**, May 2016 http://www.voanews.com/content/kenyan-police-foiled-anthrax-attack-linked-to-is-group/3315042.html
- **European Union SHIPSAN ACT Joint Action publishes interim guidance on maritime transport and Zika virus disease** http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21453
- **Zika virus: 2.2 billion people in 'at risk' areas** http://www.bbc.com/news/health-36090650
- Edmonds, J et al. "**Multigeneration Cross-Contamination of Mail with *Bacillus Anthracis* Spores**." Ed. Raymond Schuch. *PLoS ONE* 11.4 (2016): e0152225. *PMC*. Web. 9 May 2016. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4849716/
- Zeitlin, Larry et al. "**Monoclonal Antibody Therapy for Junin Virus Infection.**" *Proceedings of the National Academy of Sciences of the United States of America* 113.16 (2016): 4458–4463. *PMC*. Web. 9 May 2016. (**Argentinian Haemorrhagic Fever**) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4843420/?report=classic

Vaccines

- Eurosurveillance, Volume 21, Issue 6, 11 February 2016 - News **European Commission Horizon 2020 programme call for vaccine development research into malaria and neglected infectious diseases, including Zika virus** http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21376
- **Infographic about Zika vaccine development process** March 2016 http://blog.dicksondata.com/2016/03/vaccinating-a-pandemic-the-hurdles-ahead-for-the-zika-virus/
- **Zika vaccine efficacy trials could start in 2017**, May 2016 http://www.sciencemag.org/news/2016/05/zika-vaccine-efficacy-trials-could-start-2017
- **Defending against smallpox: a focus on vaccines,** Emily A. Voigt et al. (Restricted Access) Expert Review of Vaccines http://www.tandfonline.com/doi/abs/10.1080/14760584.2016.1175305?journalCode=ierv20
- **Pakistan polio: Seven killed in anti-vaccination attack** April 2016 http://www.bbc.com/news/world-asia-36090891
- **Particulate delivery systems for vaccination against bioterrorism agents and emerging infectious pathogens.** Fan, Y. and Moon, J. J. (April 2016), WIREs Nanomed Nanobiotechnol (Preview available) http://onlinelibrary.wiley.com/doi/10.1002/wnan.1403/abstract?systemMessage=Wiley+Online+Library+will+be+unavailable+on+Saturday+14th+May+11%3A00-

14%3A00+BST+%2F+06%3A00-09%3A00+EDT+%2F+18%3A00-21%3A00+SGT+for+essential+maintenance.Apologies+for+the+inconvenience.

Events

- **14th Annual CDC International Symposium on Biosafety,** Jan 30 – Feb 3, 2016, Atlanta, USA. "Biosafety Management: Planning for the Future by Learning from the Past" was this year's theme. http://globalbiodefense.com/event/cdc-international-symposium-on-biosafety-2016/
- The American Society of Microbiology **Biodefense and Emerging Infectious Diseases 2016 Research Meeting** Feb 8-10, 2016 in Arlington, Virginia, USA. http://www.asmbiodefense.org/
- **15th Medical Biodefense Conference** Apr 26-29, 2016, Munich, Germany. It focused on medical aspects of biodefense, presenting the latest research findings and products in the areas of diagnostics, treatment and prevention of diseases caused by highly dangerous infectious agents. http://www.biodefense2016.org/#sthash.UbR5VOWj.dpuf
- **14th Annual Vaccines + Therapeutics Conference 2016** – "Biodefense, AMR, Emerging Infectious Diseases", May 17-19, Washington DC, USA http://www.infocastinc.com/downloads_pdf/vaccines-therapeutics-2016-summit-agenda.pdf
- **NCT CBRNe USA 2016**, May 31st – June 2nd http://cbrneusa.com/program/
- **World Conference on Disaster Management** , June 7-8, 2016 in Toronto, Canada. http://www.wcdm.org/programs.html
- **The 12th International Symposium on Protection Against Chemical and Biological Warfare Agents, CBW Symposium 2016**, will be held June 8-10, 2016 in Stockholm, Sweden. http://www.foi.se/en/Our-Services/Conferences-and-Seminars/12th-CBW-Protection-Symposium/
- **Preventing & Treating Biological Exposures – An Occupational Health Colloquium** on June 13-15, 2016 in Austin, Texas. Hosted by the Eagleson Institute, in partnership with the Elizabeth R. Griffin Research Foundation http://www.eagleson.org/conferences/occupational-health-colloquium
- **2nd Biodefense World Summit**, June 27 – 30, Baltimore, USA http://www.biodefenseworldsummit.com/

Collaborating Centres Activities

- **Overview of the CSIRO Australian Animal Health Laboratory** Lowenthal, John (Restricted access) Journal of Infection and Public Health , Volume 0 , Issue 0 http://www.jiph.org/article/S1876-0341%2816%2930024-7/abstract

OIE Bulletin article

IVSA Animal Welfare Conference

Utrecht, The Netherlands, 22-24 April 2016

The International Veterinary Students Association (IVSA) is a non-profit organization of veterinary students, representing approximately 30,000 students in more than 60 countries. Among its core objectives are raising the overall standards of veterinary education, supporting measures to improve the standard of animal welfare worldwide and encouraging cooperation between members, veterinary student associations and international organizations. In 27th May 2014, IVSA and the OIE signed a cooperation agreement. This document promotes the collaboration of the parties in common interest areas, such as veterinary education, animal welfare and in the scope of IVSA Standing Committee on One Health. Also, both parties agreed to invite the other to conferences and consultancies in which common interests would be addressed.

With the support of the OIE, IVSA organized its first Animal Welfare Conference. This 3 day event was aimed at students from all over the world who have a special interest in this area. It represented an opportunity to learn about the current projects and research on this field, as well as to understand the role several organizations play in the welfare of animals and improving animal housing and transportation conditions, as well as raising the standards of animal welfare. Also, the conference allowed students to interact with representatives from international organizations, veterinary and other federations and associations, academia, policy makers and colleagues in general.

The event was attended by around 150 students and recently graduated veterinarians, representing the five continents, and had the participation of 22 speakers. The OIE was represented by Dr Alex Thiermann (former President of the OIE Code Commission), who gave a lecture on the implementation of OIE welfare standards worldwide. Dr Thiermann talked about the pioneer role of the OIE in the organization of Global Animal Welfare Conferences, the evolution of the subjects addressed in each conference and the inclusion of aquatic animal welfare. Also, the roles of each Scientific Commission were explained, with special attention to Aquatic Animal Health Standards Comission, and the broad spectrum of topics it comprises. In addition Dr Sirah Abdul Rahman, also represented the OIE and provided a point of view with respect to animal welfare and religious practices.

Participants found the event to be a success, especially regarding the presentations given by speakers from backgrounds other that veterinarian. The conference allowed to meet other cultures perspectives and realities on animal welfare and opened doors for future cooperation.

Cross referencing list

Cross referencing

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
A					
	Anthrax (Bacillus anthracis)	☑	☑	☑	Humans, cattle, sheep, goats, pigs, horses, dogs, cats, others (wild herbivores and carnivores, guinea pigs)
	Botulism (Clostridium botunilum toxin)	☐	☑	☑	Humans, cattle, sheep, goats, pigs, horses, dogs, cats, others (aquatic animals, foxes, mink)
	Plague (Yersinia pestis)	☐	☑	☑	Humans, dogs, cats, others (rodents, rock and ground squirrel, prairie dog)
	Smallpox (Variola major)	☐	☑	☐	Humans
	Tularemia (Francisella tularensis)	☑	☑	☐	Humans, sheep, pigs, horses, cats, dogs, birds, others (rabbits, rodents, aquatic animals)
	Viral Hemorragic Fevers (filoviruses: Eb	☐	☑	☑	Humans, others (non-human primates, guinea pigs, rodents - arenaviruses)
B					
	Brucellosis (B. melitensis)	☑	☑	☑	Humans, sheep, goats, cattle
	Viral Encephalitis (VEE, EEE, WEE)	☑	☑	☑	Humans, equine, others (rodents)
	Q fever (Coaxiella burnetii)	☑	☑	☑	Humans, dogs, cats, cattle, sheep, goats, aquatic animals
	Melioidosis (Burkholderia pseudomallei)	☐	☑	☑	Humans, sheeps, goats, pigs, cattle, cats, horses, dogs, other (rodents, rabbits, zoo animals, fish, non-human primates)
	Glanders (Burkholderia mallei)	☑	☑	☑	Humans, equine (horses, donkeys, mules), goats, dogs, birds, others (camels, guinea pigs, hamsters)
	Brucellosis (B. suis)	☑	☑	☑	Humans, pigs, horses
	Brucellosis (B. ovis)	☑	☑	☐	Sheep, others (cervids)
	Toxins (Ricinus communis, Clostridium p	☐	☑	☐	All
	Brucellosis (B. abortus)	☑	☑	☑	Humans, cattle, sheep, goats, horses, others

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
	Typhus Fever (Ricketsia prowazekii)	☐	☑	☑	Humans, other (flying squirrels)
	Brucellosis (B. canis)	☐	☑	☑	Humans, dogs
	Salmonella species	☐	☐	☐	Humans and animals
	Psittacosis/Avian chlamydiosis (Clamido	☑	☑	☑	Birds, other (parakeets, parrots, love birds)
	Shygella dysenteriae	☐	☐	☐	Human, non-human primates
	E. coli O157:H7	☐	☐	☐	Humans and animals
	Cholera (Vibrio cholerae)	☐	☐	☐	Humans. The surface of shellfish may act as a fomite.
	Cryptosporidiosis (Criptosporidium parv	☐	☐	☐	Humans and other mammals
C					
	Hantavirus	☐	☑	☑	Humans, rodents
	Nipah (Nipah virus)	☑	☑	☑	Humans, pigs, horses, goats, dogs, cats
none					
	Salmonid alphavirus	☑	☐	☐	Aquatic animals (Atlantic salmon, rainbow trout and brown trout)
	Aujeszky's disease virus	☑	☐	☐	Swine are natural host. Infects nearly all domesticated and wild mammals including cattle, sheep, goats, cats and dogs.
	Epizootic haemorrhagic disease	☑	☐	☐	Most wild and domestic ruminants (Ibaraki disease)
	Dourine	☑	☐	☐	Equidae
	Equine infectious anaemia	☑	☐	☐	Equidae
	Equine influenza	☑	☐	☐	Equidae
	Equine piroplasmosis	☑	☐	☐	Equidae
	Equine viral arteritis	☑	☐	☐	Equidae
	Equine rhinopneumonitis (EHV-1)	☑	☐	☐	Horses
	Porcine cysticercosis	☑	☐	☐	Swine
	Porcine reproductive and respiratory sy	☑	☐	☐	Domestic swine

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
	Avian infectious bronchitis	☑	☐	☐	Chicken
	Avian mycoplasmosis (Mycoplasma syn	☑	☐	☐	Chicken
	Avian mycoplasmosis (Mycoplasma galli	☑	☐	☐	Chicken
	Epizootic ulcerative syndrome (Aphano	☑	☐	☐	Aquatic animals (wild and farmed freshwater and estuarine fish)
	Gyrodactylus salaris infection	☑	☐	☐	Aquatic animals (Atlantic salmon)
	Rabies	☑	☐	☑	Humans, dogs, all mammals
	Duck viral hepatitis	☑	☐	☐	Ducks
	Fowl typhoid/Pullorum disease	☑	☐	☐	Birds
	Avian influenza (LPAI)	☑	☐	☑	Birds
	Infectious bursal disease (Gumboro dise	☑	☐	☐	Chicken
	Turkey rhinotracheitis	☑	☐	☐	Turkey and chicken
	Transmissible gastroenteritis	☑	☐	☐	Swine
	Myxomatosis	☑	☐	☐	Leporidae
	Rabbit haemorrhagic disease	☑	☐	☐	Rabbit
	Camelpox	☑	☐	☐	Camelids
	Leishmaniosis	☑	☐	☑	Humans, dogs, other domesticated animals
	Avian infectious laryngotracheitis	☑	☐	☐	Chicken and other birds
	Bovine genital campylobacteriosis	☑	☐	☑	Humans, cattle
	Trypanosomosis (tsetse-transmitted)	☑	☐	☐	Cattle and other mammals
	Paratuberculosis	☑	☐	☑	Ruminants, (Humans?)
	Surra (Trypanosoma evansi)	☑	☐	☐	Equids, camels, others
	Caprine arthritis/encephalitis	☑	☐	☐	Small ruminants
	Maedi-visna	☑	☐	☐	Small ruminants
	Contagious agalactia	☑	☐	☐	Small ruminants
	Ovine chlamydiosis	☑	☐	☐	Sheep

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
	Nairobi sheep disease	☑	☐	☐	Small ruminants
	Brucella ovis (ovine epididymitis)	☑	☐	☐	Sheep
	Paratyphoid Abortion	☑	☐	☐	Sheep
	Scrapie	☑	☐	☐	Sheep, goats and moufflon
	Sheep and Goat pox	☑	☐	☐	Sheep and goats
	Echinococcus granulosus (cystic hydatid	☑	☐	☑	Humans, dogs, cats, hyenas, others
	Bovine tuberculosis	☑	☐	☑	Humans, cattle, other mammals
	Echinococcus multilocularis (alveolar hy	☑	☐	☑	Humans, wild animals, dogs, cats, others
	Infection with Perkinsus olseni	☑	☐	☐	Mollusc
	Bovine babesiosis	☑	☐	☐	Cattle, African and water buffalo
	Infectious hematopoietic necrosis	☑	☐	☐	Aquatic animals (most species of salmonid fish reared in fresh water or sea water)
	Bovine anaplasmosis	☑	☐	☐	Cattle
	Screwworm myiasis	☑	☐	☑	Humans, all mammals, birds
	Trichinella spp. Infection	☑	☐	☑	Humans, other mammals, birds or reptiles
	Theileriosis	☑	☐	☐	Bovidae (domestic and wild)
	Infectious bovine rhinotracheitis/infecti	☑	☐	☐	Cattle (domestic and wild)
	Bovine viral diarrhoea	☑	☐	☐	Cattle
	Haemorrhagic septicaemia	☑	☐	☐	Cattle and water buffalos
	Enzootic bovine leukosis	☑	☐	☐	Cattle
	Trichomonosis	☑	☐	☐	Cattle
	Contagious equine metritis	☑	☐	☐	Horses
	Lumpy skin disease (virus)	☑	☑	☐	Cattle
	African swine fever (ASF virus)	☑	☑	☐	Domestic and wild pigs
	Akabane virus	☐	☑	☐	Cattle, sheep, goats

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
	Avian influenza virus (HPAI)	☑	☑	☑	Humans, chicken, turkey, wild birds, pigs, water fowl
	Bluetongue (BT virus)	☑	☑	☐	Sheep, goats, cattle, deer, elk, antelope
	Bovine spongiform encephalopaty (BSE	☑	☑	☑	Humans, cattle
	Classical swine fever (CSF virus)	☑	☑	☐	Swine
	Coccidioidomycosis (Coccidioides immit	☐	☑	☑	Humans, cattle, sheep, pigs, mammals
	Contagious bovine pleuropneumonia (	☑	☑	☐	Cattle
	Contagious caprine pleuropneumonia (	☑	☑	☐	Goats
	Foot-and-mouth disease (FMD virus)	☑	☑	☑	Humans, cattle, sheep, goats, pigs
	Goat pox and Sheepx pox (viruses)	☑	☑	☐	Goats, sheep
	Infection with Marteilia refringens	☑	☐	☐	Mollusc
	Japanese encephalitis (virus)	☑	☑	☑	Humans, horses, pigs
	Hendra (Hendra virus)	☐	☑	☑	Humans, horses, cats, other (guinea pigs)
	Malignant catarrhal fever (virus)	☐	☑	☐	Cattle, wild ruminants
	Menangle virus	☐	☑	☑	Humans, pigs
	Newcastle disease (virus, velogenic strai	☑	☑	☑	Humans, poultry, other avian species
	Peste des Petis Ruminants (virus)	☑	☑	☐	Goats, sheep
	Rinderpest	☑	☑	☐	Cattle, sheep, goats, pigs
	Screwworm myiasis (Cochliomyia homn	☑	☑	☑	Humans, other mammals, birds
	Swine vesicular disease (virus)	☐	☑	☑	Humans, pigs
	PENDING STATUS Bartonellosis	☐	☐	☑	Humans, cats, dogs, cattle, rodents, sheep, cervids, rodents, aquatic animals
	Epizootic Haematopoietic Necrosis	☑	☐	☐	Aquatic animals (redfin perch and rainbow trout)
	Infectious Salmon Anemia (HPR-del or H	☑	☐	☐	Aquatic animals (Salmonids)
	Spring viremia of the Carp	☑	☐	☐	Aquatic animals (Carp and other Cyprinidae)
	Viral Haemorragic Septicemia	☑	☐	☐	Aquatic animals (marine and freshwater fish)

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
	Heartwater (Erlichia ruminatum/Cowdri	☑	☑	☐	Cattle, sheep, goats, wild ruminants
	Infection with Batrachochytrium dendro	☑	☐	☐	Amphibians
	Red sea bream iridoviral disease	☑	☐	☐	Aquatic animals (farmed red sea bream and other fish)
	Infection of honey bees with Melissococ	☑	☐	☐	Honey bees
	Infection of honey bees with Paenibacill	☑	☐	☐	Honey bees
	Infestation of honey bees with Acarapis	☑	☐	☐	Honey bees
	Infestation of honey bees with Tropilael	☑	☐	☐	Honey bees
	Infestation of honey bees with Varroa s	☑	☐	☐	Honey bees
	Infestation with Aethina tumida (small h	☑	☐	☐	Honey bees
	Infection with abalone herpesvirus	☑	☐	☐	Mollusc
	Infection with Bonamia exitiosa	☑	☐	☐	Mollusc
	Infection with Bonamia ostrae	☑	☐	☐	Mollusc
	Crimean Congo haemorrhagic fever	☑	☐	☑	Humans, a wide range of wild and domestic animals such as cattle, sheep and goats.
	Infection with Perkinsus marinus	☑	☐	☐	Mollusc
	African horse sickness (AHS virus)	☑	☑	☐	Horses, zebras, donkey, mules, camels
	Infection with Xenohaliotis californiensi	☑	☐	☐	Mollusc
	Rift valley Fever (RVF virus)	☑	☑	☑	Humans, cattle, sheep, goats, dogs, cats, other (camels, monkeys)
	Infection with ranavirus	☑	☐	☐	Amphibians
	Acute hepatopancreatic necrosis diseas	☑	☐	☐	Crustacean
	Crayfish plague (Aphanomyces astaci)	☑	☐	☐	Crustacean
	Infection with Yellowhead virus	☑	☐	☐	Crustacean
	Infectious hypodermal and haematopoi	☑	☐	☐	Crustacean
	Infectious myonecrosis	☑	☐	☐	Crustacean
	Necrotising hepatopancreatitis	☑	☐	☐	Crustacean

CDC Classification	Disease or Agent	OIE listed	CFSPH chart	Zoonotic	Affected species
	Taura syndrome	☑	☐	☐	Crustacean
	White spot disease	☑	☐	☐	Crustacean
	White tail disease	☑	☐	☐	Crustacean
	West Nile Fever (WNF virus)	☑	☑	☑	Humans, horses, birds, cattle, sheep, goats, dogs, cats, ther (many mammals, and reptiles)
	Koi herpesvirus disease	☑	☐	☐	Aquatic animals (common carp and varieties such as koi carp and ghost carp)
	Vesicular stomatitis (virus)	☐	☑	☑	Humans, horses, donkeys, mules, cattle, pigs

Other projects

Not yet online

- PPR portal
- Rinderpest portal
- Biothreat reduction strategy portal

Confidential

- Laboratory twinning database
- Biothreat reduction conference – related research