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## Biosecurity – preparing for new and old risks.

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### Biosecurity – the context

Biosecurity may be defined as the policies and measures taken to protect from biological harm. It encompasses the prevention and mitigation from diseases, pests, and bioterrorism, of economy, environment and public health. It includes food and water supply, agricultural resources and production, pollution management, blood and blood product supplies, and warrantly attempts to ensure that ecologies sustaining either people or animals are maintained.

Human lives have always been affected by other life forms. Protecting ourselves, our food supply and our environment against diseases has been a major challenge in all human history. Improved knowledge and understanding of harmful organisms and their mode of action has resulted in major achievements such as development of vaccines, eradication of diseases such as smallpox, improved hygiene in food production and resistance breeding in food crops and livestock. Current trading patterns, climate change and technological developments result in the emergence of new risks. Not only do we know too little about these new risks, but they also challenge our biosecurity governance.

Proposals for future biosecurity governance are outlined in the European Commission's Green Paper on Bio-preparedness<sup>1</sup>. Some of these proposals are also discussed in the present paper. However, the focus of the present paper is mainly new emerging risks that are not, or only to a limited extent, discussed in the Green Paper.

### The old risks – and the new ones

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<sup>1</sup> European Commission 2007. Green Paper on Bio-preparedness. Prepared for consultation July 11th 2007. Consultation concluded October 1st 2007.

### The prevailing focus

Traditionally, the most acknowledged risks in a biosecurity perspective have been posed by microbes that directly affect human health (for examples, see Table 1). Several of these could potentially be used in acts of bioterrorism. However, it has proven difficult to effectively launch a major bioterror attack with these microbes. First, the microbe must be isolated and propagated to obtain the quantity required for attack. Secondly, the potency of the microbe is highly dependent on the specific strain (genotype), and also often on the stage of its life-cycle, and therefore it may be difficult to obtain highly virulent material. Thirdly, an attack is not effective unless the microbe can be distributed and transmitted to the targeted populations (humans, animals or crops). Finally, the terrorists can easily be the first victims to the microbes even before the attack is launched, unless they possess the know-how and technology to protect themselves. Therefore, it is considered highly resource demanding to build the necessary capacity to launch a major bioterror attack, and only few laboratories have the necessary competence and resources to do so. Another well recognised risk is that of incidents affecting our food supply, including agrobioterror. Animal and plant diseases, as well as post-harvest contamination may affect the quality, quantity and safety of the food.

### The changing premises

Global trade and movement of humans and other living biological material is gradually leading to introduction of new species and genotypes (genetic variants). This is particularly true for microbes that due to their size can easily move along with traded goods, material and people. Free movement of goods and people is politically desired in most democratic nations. Quarantine or import bans may be used to prevent import of harmful agents. However, such measures may be difficult to justify according to international agreements, may require solid documentation of the presence of a significant risk, and are therefore mainly used in connection with the most potent biohazards such as virus diseases in animals (e.g. rabies and food-and-mouth disease).

### The evolving paradigm of microbes

Microbes are often associated with particular hosts and/or environments, and this has facilitated our ability to detect them and prevent harm. Unfortunately, they are also often more adaptive to change than their hosts. This is for example reflected in what may best be described as the constant arms race between plant and animal breeders on the one hand and pathogens on the plants and animals on the other. The flexibility of most microbes is linked with their genetics and short life cycles. Ability to rapidly turn on or off genes and to rearrange and incorporate genetic information from the environment are some of the features that may explain the adaptability of microbes. Bacteria with resistance to multiple antibiotics have emerged through uptake of genes encoding such resistance<sup>2, 3</sup>.

The relationship between a host and an organism that lives on the host (the “guest”) can be mutually beneficial or one can exploit the other. Often, the degree of exploitation and benefit is balanced by competition between a multitude of co-existing “guests”. This can be illustrated with reference to the human gut. Well being and efficient food digestion is facilitated by the presence of a good balance of gut microbes. Treatment of an infectious disease with antibiotics kills many of the gut bacteria and results in digestive disorder until the right combination of gut microbes is reestablished. Exposing “guests” for new potential hosts and environments facilitates host jumps and may alter the balancing competition between “guests”. New hosts may also lack resistance to a potential pathogen, while such resistance may be well established in the original host. The result

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<sup>2</sup> Ochman H., Lawrence J.G. & Groisman E.A. 2000. Lateral gene transfer and the nature of bacterial innovation. *Nature* 405, 299-304

<sup>3</sup> Rowe-Magnus D.A., Guerout A-M., Ploncard P, Dychinco B., Davies J. & Mazel D. 2001. The evolutionary history of chromosomal super-integrations provides an ancestry for multiresistant integrations. *Proc. Natl. Acad. Sci. U.S.A.* 98: 652-657

may be emergence of new diseases from what was not previously considered to be harmful species or genotypes. Host jumps are well recognised causes of new infectious diseases, affecting both plants<sup>4</sup>, animals and humans (zoonoses)<sup>5</sup>.

### Nordic challenges

People in the Nordic countries travel more and rely more on imports than the populations of most other countries. The Nordic countries have few protective barriers against microbial diseases, except for a relatively cold climate. The biological effects of climate change are difficult to predict. However, it is predictable that it will be possible for a diversity of cold climate sensitive microbes, animals, plants and fungi to become established. Some of these emerging species pose a biosecurity risk. This is clearly illustrated by the significant increase in reported incidents of Lyme borreliosis from ticks carrying the bacterium *Borrelia burgdorferi*, several new noxious invertebrates (e.g. the deer ked/deer fly *Lipoptena cervi* and flukes/cercariae in lakes), new weedy and toxic plants and significant changes in the fungal biodiversity on commercial crops<sup>6</sup>. Increased border control, quarantining imported products for limited time and targeted eradication of individuals and small populations can be applied to prevent establishment of some of the larger species and possibly of their associated microbes. But for the majority of potentially immigrating species, this is probably not feasible.

### Gene technology – a new risk

Gene technology is a technology that allow us to study and modify genetic information at a very detailed and targeted level. The technology is rapidly developing, and the potential applications become broader and cheaper. Specific biological properties can now be linked to specific genes, these genes can be described and also isolated, copied and transmitted from its original source to a totally unrelated species, e.g. from a bacterium to an animal or vice versa. The result is then referred to as a genetically modified organism (GMO). Recently, it has been demonstrated that a complete genome (the entire genetic information of an organism) can be synthesised in a laboratory<sup>7</sup> and preparations have been launched to transmit this artificial genome to an “empty” cell in which it is then meant to function normally<sup>8</sup>. If successful, this in effect means that it is technically possible to create entirely new life-forms.

### Gene technology may also promote biosecurity

Gene technology enables better predictability with respect to the genetic changes and effects of the intended product development than conventional breeding technologies. The potential reduction in unintended side effects may result in safer products. Furthermore, the technology can be used to provide detailed information about the characteristics of plant or animal breeds, as well as putative pathogens and beneficial organisms, and consequently may improve our ability to perform comprehensive risk assessments.

Gene technology can also be used prophylactically or therapeutically, e.g. for the production of effective vaccines in large quantities in short time. However, as vaccine production is increasingly done by private commercial companies who are mainly concerned with expected profits, the preparedness against unpredicted diseases may be insufficient.

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<sup>4</sup> Anderson P.K. & al. 2004. Emerging infectious diseases of plants: pathogen pollution, climate change and agrotechnology drivers. *Trends in Ecology and Evolution* 19: 535-544.

<sup>5</sup> Woolhouse M.E.J. et al. 2005. Emerging pathogens: the epidemiology and evolution of species jumps. *Trends in Ecology and Evolution* 20: 238-244

<sup>6</sup> See e.g. The Norwegian Biodiversity Information Centre (Artsdatabanken) 2007. The Norwegian Blacklist. Ecological risk analysis of alien species. [http://www.artsdatabanken.no/dm\\_linkinternal.aspx?amid=3572](http://www.artsdatabanken.no/dm_linkinternal.aspx?amid=3572)

<sup>7</sup> Gibson D.G. et al. 2008. Complete chemical synthesis, assembly, and cloning of a *Mycoplasma genitalium* genome. *Science* 319: 1215-1220

<sup>8</sup> Anon 2008. Press release from the J. Craig Venter Institute January 24<sup>th</sup> 2008.

<http://www.jcvi.org/cms/research/projects/synthetic-bacterial-genome/press-release/>

Very few food plants contribute to a majority of global food supply. Gene technology solutions to protect against diseases caused by insects, fungi and viruses are developed and marketed. Gene technology solutions are also to some extent being developed to respond to climatic factors. The dramatic increase in food prices on the global market over the last two years has issued a clear warning of a potential global food security crisis. Such a crisis will mainly affect the people in developing countries, but will subsequently affect also the developed countries. Species of the fungal genera *Aspergillus* and *Fusarium* alone are estimated to cause annual crop losses in the U.S.A. of several billion USD. In Africa south of Sahara, the impact of these fungi is even higher. There, infected grain of staple food crops used for consumption often contain high levels of toxins produced by the fungi. Fungal infections occur in the field as well as in storage, and insect wounds on plants are thought to be a major infection route. Gene technology facilitates the development of plants and animals with inherent (genetic) protection against pests and diseases, and consequently has great potential for contributing to improved food security.

#### Dual-use of gene technology

Historically, the resource requirements for development of a GMO were huge, and the competence to do so was limited to publicly controlled academic institutions and large reputable companies. Depending on the organism/species, the type of genetic modification and the intended application of the new GMO, it may no longer require very large resources or particularly high competence to develop a potentially harmful genetically modified microorganism (GMMO, e.g. bacterium), while the development of a potentially harmful GMO (e.g. plant or animal) may be somewhat more challenging. A GMMO may therefore be developed by a small group of hostile people, while a GMO will require a larger organisation. It is also possible to create the GMO or GMMO so that it will mimic a non-GMO both to the eye and to the analytical controls.

Illegal exploitation of the technology may be desired for commercial as well as hostile purposes. The likelihood of such dual-use of gene technology is mainly depending on a cost-benefit estimate. If the cost of developing and the risk of being detected is considered lower than the possible outcome/achievement, then there is a significant likelihood that someone will make an attempt. Development of a GMO/GMMO for hostile purposes may also expose the developers and their allies to the GMO/GMMO. It may therefore be most attractive to try to develop a GMO/GMMO that is unlikely to expose the developers and their allies to harm. This may e.g. be achieved by targeting a particular food crop or domesticated animal species.

Since GMO scepticism is widespread it is difficult to market GMOs, in particular in Europe. The costs of authorising a single GMO, e.g. a GMO maize line, have been estimated to approximately €3.5 – 15 million<sup>9</sup>. It may therefore be tempting to try to develop an attractive high-yield GMO and market it as non-GMO. It may be difficult to avoid that the GMO nature is revealed in the long run. Yet, it could be imagined that lack of public control, the use of straw men or complex company ownership structures, and high short term profits, can result in the marketing of unofficial GMOs as non-GMOs.

Other scenarios involving dual-use of gene technology can be outlined. However, our main intention here is to visualise the emergent gaps in biosecurity governance, and to call for appropriate corrective action.

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<sup>9</sup> Kalaitzandonakes N. et al. 2007. Compliance costs for regulatory approval of new biotech crops. Nature Biotechnology 25: 509-511

## **Biosecurity governance**

### Tracing microbes to their source

Laboratory strains of pathogens are usually well characterised with respect to their genetic fingerprint. This means that when a laboratory strain is involved in any act of terror or accidentally released, it can usually be traced back to the responsible laboratory. This can be illustrated with the anthrax letters in the USA immediately after September 11<sup>th</sup> 2001, and with the foot-and-mouth disease incident in the UK in 2007. The anthrax spores found in the letters in late 2001 were traced back to a specific strain at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) biological weapons laboratory at Fort Detrick in Frederick, Maryland<sup>10, 11</sup>. The foot-and-mouth disease is caused by a virus, and the virus found in diseased animals was traced back to a strain (FMDV BFS 1860 O<sub>1</sub> 1967) used to produce a vaccine against the foot-and-mouth disease in a UK laboratory (Institute for Animal Health and Merial Animal Health Ltd at Pirbright)<sup>12</sup>.

### Governing the threats from microbes

In forensics, the suspects and victims of criminal acts are often identified on the basis of their genetic fingerprints. Microbes can be identified in a similar way. However, genetic fingerprints always need to be matched against reference fingerprints (see e.g. <sup>11</sup>). The establishment of reference fingerprint databases and rapid communication systems to check the profile of a strain isolated from an outbreak or possible bioterror attack against the references will therefore be important precautionary measures. Not only will this facilitate the identification of the origin of an isolated strain, but it is also likely to provide useful information about the specific characteristics of the isolated strain that may offer guidance to the most effective countermeasures.

Unfortunately, detailed information about the genetic composition of harmful microbes can be subject to dual-use. Gene technology can be used to screen strains to select highly potent strains, i.e. strains possessing the most virulent gene varieties. This technology can also be used to increase the potency of strains by modification or insertion of virulent gene varieties. And finally it can be used to mimic the genetic fingerprint of other strains by modification of the fingerprint markers, e.g. to camouflage a highly potent strain behind the fingerprint of less potent and possibly native strains. Consequently, the public availability of this type of information has been restricted considerably since September 2001. While this means that it may be more difficult for possible bioterrorists to obtain the information, it may simultaneously make it more difficult for national security personnel to trace the source and implement the most appropriate countermeasures. Close international collaboration is therefore needed to ensure that the national security interests are not compromised by measures to prevent bioterrorists from obtaining exploitable information.

### Regulation of gene technology and GMOs

The general framework of the sanitary and phytosanitary (SPS) agreement of the World Trade Organisation (WTO) allows for protective measures to ensure plant and animal health, even at the expense of international trade<sup>13</sup>. Gene technology is regulated by national and international

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<sup>10</sup> Van Ert M.N. et al. 2007. Strain specific single-nucleotide polymorphism assay for the *Bacillus anthracis* Ames strain. *J. Clin. Microbiol.* 45: 47-53

<sup>11</sup> Enserink M. 2008. Full-genome sequencing paved the way from spores to a suspect. *Science* 321: 898-899

<sup>12</sup> Department for Environment, Food and Rural Affairs (DEFRA), UK. 2007. Epidemiology report on the probable release of FMD virus at the Pirbright site and the transmission of infection to the first infected cattle herd, from investigations up to 29 August 2007 (Day 26).

[http://www.defra.gov.uk/animalh/diseases/fmd/investigations/pdf/fmd\\_epidreport2007.pdf](http://www.defra.gov.uk/animalh/diseases/fmd/investigations/pdf/fmd_epidreport2007.pdf)

<sup>13</sup> World Trade Organisation. The WTO agreement on the application of Sanitary and Phytosanitary Measures (SPS Agreement). [http://www.wto.org/english/tratop\\_e/sps\\_e/spsagr\\_e.htm](http://www.wto.org/english/tratop_e/sps_e/spsagr_e.htm)

agreements and laws. The Cartagena protocol on Biosafety<sup>14</sup> is the most widely adopted international agreement, and among others define rules for the release, containment, traceability and transport of genetically modified material. However, approximately 1/3 of all nations, among these is the U.S.A., have not yet signed/or ratified the Cartagena protocol. At the national level, developing countries generally have strict regulations, and in principle release into the environment or introduction to the food chain of a GMO or its derived products will only take place after a risk assessment procedure demonstrating that the GMO or product is safe. Regulations commonly distinguish between GMOs and GMMOs. Within EU and the Nordic countries (except Iceland) the presence of GMO-derived material is only legal if the original GMO is authorised within the jurisdiction. For authorisation in these countries it is also provisional with a quantitative and specific detection method, to ensure that the product can be traced and identified after being marketed.

### Detecting GMOs

The monitoring and surveillance of GMOs is based on application of highly targeted analytical methods in combination with documentary based traceability. Analytical control is applied mainly to verify seed purity by commercial seed producers, and for monitoring compliance with labelling requirements in EU, Japan and some other countries. The labelling requirements concern only authorised GMOs. The methods applied for detection of GMOs are largely unable to identify the presence of non-authorised GMOs, and often they are not even able to detect material from these GMOs. Consequently, the current governance is based on trust and technology designed for detection of safe GMOs. Illegal GMOs may be safe, but this can only be determined after conducting a thorough risk assessment. The lack of appropriate technologies for detecting and identifying illegal GMOs is therefore posing a new and emerging biosecurity risk.

### Discussion

#### Societal effects and preparedness

Until now, there are relatively few examples of bioterrorism from modern time, and even fewer that have had large scale biological or societal effects. Many potential risk scenarios involving gene technology have been described. Yet, no negative health effects of GMOs have so far materialised and the environmental effects associated with GMOs are comparable to those of conventional agriculture products.

Despite this, it may be feasible to create fear and potentially destabilise socio-economic structures. Intended or unintended effects can be immediate (acute) or long term. All known attempts to launch bioterror attacks have applied material with acute effect, e.g. highly virulent microbes. Long term effects may involve mechanisms of accumulation or amplification of harmful biological material or biochemical compounds including toxins, where the effect is expressed above a certain threshold. Alternatively harmful effects may be induced through catalytic conversion of harmless to harmful compounds.

In Norway and some other Nordic countries the drinking water supplies are often open watercourses with limited treatment of the water prior to distribution to consumers. Thus, contamination of drinking water is a realistic scenario, as demonstrated recently in the Norwegian city of Bergen<sup>15, 16</sup>. Modern medicine and industrialised agriculture are highly dependent on application of chemical warfare against undesired competitors (e.g. cancer cells or weedy plants) and pathogens (e.g. bacteria or fungi). The possibility to apply gene technology to construct

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<sup>14</sup> <http://www.cbd.int/biosafety/>

<sup>15</sup> Steen K. & Damsgaard E. 2007. Giardiaepidemien i 2004 og Bergen Legevakt. Tidsskr. Norske Lægeforen. 127: 187-189

<sup>16</sup> Robberstad H. 2007. Plagsomme parasitter truer helsa. <http://www.forskning.no/artikler/2007/mars/1174557305.41>

competitors and pathogens with multiple resistance to practically all effective chemicals is realistic. Because chemical treatment would selectively favour the resistant competitors or pathogens, this could potentially affect the industrialised countries more than the developing countries.

#### Biosafety frameworks may backfire

The basic premise for societal security is to protect against risk and crisis. However, since both risk and crisis are partly constructed, socially protective measures and biosecurity governance may as well create risks and crisis.

Historically, the food safety of plants developed through plant breeding was not really questioned until GMO plants came into commercial production in the 1990-ies. A large number of food crop varieties cultivated during the last century were developed using technologies that resulted in the presence of new genetic material in the affected breed. At the genetic level this is comparable to the effect of genetic modification. A comprehensive comparison of the risks associated with these traditional techniques and those associated with gene technology has never been conducted. Despite this, an extensive national and international biosecurity framework has been established in the course of the last 15 years to protect against potential harms of GMOs. According to this framework, all new varieties which are developed using gene technology, are required to be subject to extensive safety research and public safety assessment, followed by regulatory authorisation before they are accepted for cultivation or as food or feed. Moreover, in many countries including the EU and Norway, authorised varieties have to be labelled as GMO. This rather strict regulatory framework was partly developed to ensure consumer confidence after extensive societal distrust in GMOs. A distrust partly generated through ethical and religious perception of gene technology as intervening and “manipulating” the natural order.

The regulative framework initially did not create major problems. GMOs were singled out as a societal threat, and the strict framework would ensure that only the authorised GMOs would arrive on the market (where they would be labelled). However, as more and more GMOs are developed globally, inevitably products containing non-authorised GMOs may also reach the market. Recent incidents affecting both U.S.A., China and Europe have demonstrated that despite the strict regulations unintended release of non-authorised products and GMOs may take place (see e.g.<sup>17</sup>). There are also unconfirmed claims about illegal presence in developing countries in South-America, Asia and eastern Europe.

The recent violations to the EU legislative framework have generated several crisis situations. Both consumers, companies, authorities and international trade has been severely influenced by these incidents (see e.g.<sup>17</sup> and references therein). However, the harms so far have not been caused by the biological agents themselves but the biosecurity regimes that *de facto* define the agents as harmful. Moreover, the development of new GMOs with potential societal benefits may have been hampered and delayed by the substantial costs to provide the required documentation to prove the absence of risks (see<sup>9</sup>).

There are at least three recognised main sources of such illegal presence. Illegal imports of seed or thefts of seeds or seedlings from experimental field trials by poor and uneducated/ignorant farmers is thought to be a possible source of illegal presence, that may result in a substantial quantity of illegal GMO in individual fields. Field trials are extensively used as part of the safety assessment prior to authorisation. Unintended spread of pollen from field trials is a likely dissemination route in some of the known cases of illegal presence. Finally, as authorisations differ among jurisdictions, GMOs authorised in e.g. the U.S.A. but not in the EU are recognised

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<sup>17</sup> Holst-Jensen A. 2008. GMO testing – trade, labeling or safety first? *Nature Biotechnology* 26: 858-859.

as a major possible source of illegal import to the EU. In both the latter scenarios, the level of illegal presence is likely to be very low. Field trials and laboratories need to be protected against trespassers who may intentionally or unintentionally spread viable GMOs to a less controlled environment. Field trials must be planned, performed and monitored so that the risk of unintended distribution of viable material is minimised. Provisional *a priori* information on field trials in data bases accessible by stakeholders responsible for biosecurity is desirable, in particular if it could include detailed information about the genetic structure of the GMO, detection methods, etc. However, intellectual property rights may be challenged by such a system.

The dilemma is not easy to solve. How to prevent harmful use of gene technology without preventing important societal benefits of the same technology? Indeed, the very same technologies may provide societal harms as well as benefits. More research is needed to investigate if the current biosecurity frameworks themselves may generate more social threats than they prevent.

### **Conclusions**

Preparedness against the old and new biosecurity threats may involve:

- Scenario experts and discussion groups
  - for identification of likely scenarios
  - for assessment of negative societal effects of biosecurity regimes
  - based on technological and societal developments
- Active intelligence, monitoring/surveillance and communication between parties responsible for different sectors, including but not limited to
  - public health
  - the food production chain
  - education and science
  - international trade and politics
  - national security and crime prevention
- Systems for rapid data compilation, processing, interpretation and dissemination
  - accessible 24h, 365d/y for all relevant parties (international collaboration)
  - allowing traceability to known strains and detailed genetic information
  - including information on field trials and laboratory experiments
  - barriers against dissemination to third parties and respecting intellectual property rights while protecting and prioritising biosecurity interests
- Development of suitable tools for biohazard:
  - monitoring/surveillance
  - detection, identification and characterisation
  - isolating and/or containing and eradicating biohazards at all levels from naturally occurring microbes to sophisticated gene technology products
  - probably requiring establishment of high-tech nodes with ability to synthesise biochemical molecules and tools without relying on external laboratories
- Expert teams combining scientific and analytic expertise with security personnel and decision and policy makers for
  - establishment of emergency measures
  - efficient communication and biosecurity governance
  - crisis management
- Initiation of relevant research projects/activities based on the needs identified via one or more of the bulletpoints above

The traditional microbes with potential to be used as agents of bioterror have been regulated and controlled without extensive negative societal costs. New biosecurity threats emerge as a consequence of potential dual-use of the very powerful gene technology. In addition, the

extensive use of gene technology and rapid increase in the development of GMOs generates very difficult dual-use dilemmas. While governance regimes were developed against the old biosecurity threats without great negative societal side effects this will be much more difficult with new risks in the years to come.

The current framework regulates GMOs solely on the basis of the technology used to develop GMOs (gene technology), without respect to the actual biohazards associated with the products. This regime may take resources away from work to prevent, detect and control the more serious threats posed by gene technology and other new and emerging biosecurity risks.

**Table 1. Examples of microbes<sup>18</sup> posing an emergent risk to human health<sup>19</sup>.**

<b>Viruses</b>	<b>Disease associated</b>	<b>Mortality rate</b>	<b>Source or suspected source (host)</b>
Influenza viruses (Orthomyxoviridae)	Flu	0.1% (immunocompromised)	Birds and mammals
Influenza virus A(H1N1)	Spanish flu	2-20% (>50% of † were adults)	
Influenza virus A(H5N1)	Bird flu	>50%	Birds
Ebola virus	Haemorrhagic (bleeding) fever	approx. 50% on average	Bats and monkeys
HIV	AIDS	Very high but long latency period. Deaths are caused by secondary infections, e.g. fungi or bacteria causing pneumonia.	Monkeys?
<b>Bacteria</b>	<b>Disease associated</b>	<b>Mortality rate</b>	<b>Source or suspected source (host)</b>
<i>Bacillus anthracis</i>	Anthrax		Livestock (soil)
<i>Escherichia coli</i> O157:H7	“Hamburger disease” (gut bleeding)		Livestock feces and soil
<i>Clostridium botulinum</i>	Botulism (response to toxin)	Depending on type and treatment. Below 10% in developed countries.	
<i>Yersinia pestis</i>	Plague	Depending on type. Low (bubonic) to very high (pneumonic)	Rats (fleas)
<b>Eukaryote parasites</b>	<b>Disease associated</b>	<b>Mortality rate</b>	<b>Source or suspected source (host)</b>
<i>Plasmodium falciparum</i>	Malaria	Usually low	Mosquitoes
<i>Toxoplasma gondii</i>	Toxoplasmosis	Usually very low, but can be severe to unborn foetus	Mainly cats

<sup>18</sup> These agents are called microbes because a microscope is required to see them.

<sup>19</sup> Other potential biohazards come from less harmful food spoilage bacteria (e.g. *Salmonella* spp. and *Campylobacter* spp.), plant and animal pathogens (bacteria, fungi, protozoa, nematodes, insects) and toxin producing organisms, in particular some fungal species that primarily may affect food quality and availability, as well as economy and trade.

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