The global proliferation of high-containment biological laboratories: understanding the phenomenon and its implications

This paper (No. 22102018-00132-EN) has been peer-reviewed, accepted, edited, and corrected by authors. It has not yet been formatted for printing. It will be published in December 2018 in issue **37** (3) of the *Scientific and Technical Review*

A. Peters

Infection Control Programme and World Health Organization (WHO) Collaborating Centre on Patient Safety, University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland

E-mail: alexandra.peters@hcuge.ch

Summary

Disease-causing pathogens have been with humanity for as long as the species has existed, but the world has changed. The human population is increasing and becoming more globalised. Meanwhile, the international system remains unstable and biotechnology is advancing at a breakneck speed. Humans are coming into contact with new and re-emerging pathogens as they spread into previously uninhabited environments. Pathogens play an increasingly global role, and infectious disease is becoming less confined by geographical or climatic boundaries.

In order to meet these new challenges, both states and the private sector have been building an increasing number of high containment biological laboratories (HCBLs) that work with biosafety level (BSL) 3 and 4 pathogens. This rate has increased sharply since 9/11, and most states that have the means to build such laboratories do so. Pathogens do not stop at borders, and the more prepared a state is to deal with them, the better for its national security. Although there is information available on the world's BSL-4 laboratories, none of it includes the proliferation of BSL-3 laboratories.

This paper attempts to create a working database of the state of global HCBL proliferation. It seeks to analyse the data and to understand how

we are dealing with this phenomenon, the risks involved, and the possible measures to be taken. The information is inevitably complex and certainly far from complete, but it is the author's hope that it will provide a sufficient basis from which to make useful, actionable inferences.

Keywords

Biosecurity – Bioterrorism – Epidemic – International security – Laboratory – Pathogen – Proliferation – Public health.

Introduction

Disease-causing pathogens have been with humanity for as long as the species has existed. We live in an age where the world's population is growing exponentially and humans are in constant contact with each other, with animals, and with the environment. The possibility of an epidemic travelling around the world at an unprecedented rate is becoming increasingly likely.

This interconnectivity, coupled with rapid advances in biotechnology and the emergence of violent extremist groups, makes for an increased biological threat to humanity. Some violent extremist groups have expressed direct interest in acquiring biological weapons, or have already tried to implement programmes for their development (see the section 'Bioterrorism: the threat posed by non-state actors'). High-containment biological laboratories (HCBLs) have become an indispensable part of many national security programmes because they can help counter the three types of biological insecurity: natural epidemics, intentional misuse, and accidental dissemination. The term refers to biosafety level (BSL) 3 and 4 laboratories, which are specifically designed to prevent pathogenic or infectious organisms from coming into contact with the environment, and to protect the people working with them. Most developed nations have such facilities, though their very existence raises important security issues. There is insufficient international oversight of the research conducted, and little research on the threat that these facilities and their contents pose. Both governments and industry hold stakes in researching high containment agents. Most states operate within a complex matrix of external and

internal pressures, including the information that governments receive, how they use it, and their people's interests and fears.

Since 9/11, there has been a marked proliferation of these laboratories worldwide (see Appendix). This proliferation increases the ability to understand and treat disease, and helps protect humans against pathogens. Paradoxically, this phenomenon also increases insecurity. The possibility of accidents, thefts or diversions, or malicious use of pathogens multiplies with every additional laboratory built. The more labs we build to protect ourselves, the more ostensibly unstable the situation becomes. While it is difficult to analyse precisely the increased risk of this proliferation in the context of the benefits to society, it is important to raise these questions before building new laboratories or when deciding where to allocate increased security measures. An increase in the number of HCBLs without improving standards for safety and oversight leads to an increased risk both for accidents in facilities and for potential pathogen diversion or recruitment of laboratory personnel by non-state actors (NSAs). An overview of HCBLs globally is useful both for analysis of the current situation and as a starting point for further research.

Currently, most states that can build laboratories do so. This has resulted in something akin to a free-for-all of construction without any systematic oversight – there is no comprehensive list of how many HCBLs exist globally. Although some of these issues are beginning to be explored, analysis is generally lacking both in scope and in depth, largely due to a lack of organised data. Information remains incomplete about the rate and extent of HCBL proliferation, the location of facilities, and their functions. This makes it difficult for measures to be taken on national or international levels, and for governments to focus on the most important issues such as national oversight, international standards for HCBL construction and maintenance, and screening and training of personnel. Addressing these issues would go a long way towards preventing both accidents and possible diversions of pathogens.

The recent global increase in the number of HCBLs has been driven by a 'perfect storm' of factors: a global increase in violent extremism, fear of biological weapon (BW) use by NSAs, the emergence of new

diseases, and the re-emergence of previously known diseases in new geographical areas. The global human population has more than doubled since 1960 (1), and increased population density and mobility have led to the 'globalisation of diseases' (2), enabling epidemics to spread much farther and faster than they could before (3, 4). Diseases such as cholera, tuberculosis, diphtheria, plague, yellow fever and dengue are reappearing (5). By having contact with previously uninhabited environments, humans can be exposed to zoonotic diseases with which they had no prior contact (6).

The HCBLs provide the safest possible environment to identify and research these pathogens. They are instrumental in preventing and responding to natural outbreaks, and offer the hope of better response to the threat of bioterrorism (7). However, their proliferation is a paradox: the more labs we build to protect ourselves, the more precarious the environment becomes. Although research on pathogens saves lives, something as small as a faulty air vent could create a global health crisis. Though they play a critical role in the study of emerging diseases and in biodefence efforts, HCBLs remain vulnerable to accidents, and could conceivably increase the risk of terrorist BW use by acting as a possible source of pathogens or knowledge. This paper seeks to synthesise a body of data on HCBL proliferation, analyse its implications, and offer policy recommendations.

Data collection for the paper

The main body of research consists of an Appendix that lists 86 states that possess or are currently building HCBLs, the number of laboratories known in these states, whether they had bioweapons programmes, and other relevant information where available (8). Where there is a gap in reliable data, the Appendix is marked with 'N/A' (not available).

An effort was made to gather as much information about the laboratories as possible in order to be able to accurately identify and assess patterns of proliferation. This information can help policymakers make informed decisions to reduce vulnerabilities.

It is worth noting that many of the world's HCBLs belong to private or academic institutions, many of which are not subject to governmental oversight. The information available varies significantly from state to state: often, facility location, activities and ownership are unknown, even to the government of the state in which the laboratory is located.

The author cannot claim that the Appendix is complete; in fact, it is guaranteed not to be, owing to the vast differences in reporting and the growing number of HCBLs (9). Although many countries seem to be quite forthcoming about their activities, one cannot assume that this is universally the case.

High-containment biological laboratories

The genesis of HCBLs is rooted in United States military research during World War II (WWII). Before biocontainment evolved, there was no reliable way to protect a researcher working with biological agents. Therefore, HCBLs became a necessary structure in which to research the most dangerous pathogens. They eventually came into use in hospitals, private industry and universities. They also remained in use for BW programmes. In most countries, laboratories are assigned a BSL between 1 and 4. The higher the number, the better the laboratory is equipped to work with the most virulent and infectious organisms. As used here, the term HCBL includes BSL-3 and BSL-4 laboratories only. The BSL-3 laboratories are designed to house organisms (usually viruses or bacteria) that infect humans through inhalation (aerosol) and can be lethal (10, 11). The BSL-4 laboratories house agents that transmit disease either by aerosol or in an unknown way, which are often fatal to humans, and for which there are generally no known treatments or vaccines (11). The laboratories themselves are subject to complex safety measures (10) and certifications (12), and are very expensive to build and maintain (12, 13).

Biosafety, biosecurity and biodefence

It is important to distinguish among biosafety, biosecurity and biodefence. Biosafety mainly concerns the safety of people working in a laboratory, and how well its containment functions (14). It includes equipment, the construction of the laboratory itself, as well as the

practices used by workers (15). Biosecurity is the protection of facilities or laboratories against theft or diversion of agents that could be used for bioterrorism or to proliferate BW (15).

Biodefence is the science, technology and policy of how to protect against both natural epidemics and those due to bioterrorism. However, individual states' definitions of biosecurity vary significantly: while some countries consider certain activities to be biodefence, others do not, and thus do not report them as such. Biodefence programmes range from mostly civilian to mostly military. Japan and Switzerland, for instance, have 'mostly civilian' biodefence activities; those of the United States of America (USA), Germany, India and South Africa are 'to a greater extent civilian'; and those of the United Kingdom (UK) are to 'a greater extent military' (8). In the Appendix, any activities or programmes considered by the state to be biodefence are labelled as such, but the difference in scope among the programmes can be significant, and this should be taken into consideration.

High-containment biological laboratories and biological weapons

While a state bioweapons programme needs an HCBL, there are instances of crude low-tech BW use by NSAs that did not necessarily use BSL-3 or -4 pathogens and were prepared without an HCBL. The HCBLs are developed for a number of legitimate reasons including studying endemic disease and potential epidemics, defence against bioterrorism, studying animal and plant pathogens, producing vaccines and working with genetically modified organisms (GMOs). The laboratories can exist in national centres, academic and private institutions, and hospitals.

Biological weapon production has three components: agent production, weaponisation, and storage. Of these, only weaponisation presupposes specialised technology and processes that are rarely used for legitimate purposes (16, 17). All other processes and equipment necessary in BW production are dual-use (18). Pathogens can be found in nature, and can be grown in petri dishes, in fermentation vats (bacteria) or in hosts (viruses). Toxins can also be produced artificially, by adding the DNA coding for the toxin to bacteria that produce it when they multiply (19).

Technology now allows the synthesis of viruses based on their genome, and genetic engineering can increase the pathogenicity of a bacterium or shorten the incubation period of a disease (19). Synthetic biology, where DNA is created from scratch, is also advancing rapidly. Purifying and storing pathogens is as useful for BW stockpiles as it is for vaccines. As far as the laboratories are concerned, the deciding factor between a state BW programme and legitimate research is the intent behind it.

Because HCBLs are necessary for a state weapons programme, it is expected that states with former weapons programmes will have them. This does not mean, however, that these labs are currently used for BW/defence research. It is true that if the targets are plants or animals (which could cause a great deal of disruption and economic loss) then not all state BW programmes would need HCBLs as many of those pathogens are not considered dangerous enough to humans to necessitate an HCBL. The states that had such programmes (the USA, UK, Germany, Russia, Canada, China, South Africa and France) contain the bulk of the world's HCBLs: together they have at least 2,595 such laboratories of the more than 3,204 worldwide. However, there are states without former weapons programmes that have a relatively large number of HCBLs: Sweden is an example.

Technically, a government biodefence HCBL could rather quickly be converted into an offensive BW programme. States with advanced biodefence programmes could be considered to have a latent BW capability, regardless of their intentions. The technology needed to disperse or weaponise such agents is often not very advanced and is used in other industries for perfectly normal applications.

Since the Biological Weapons Convention (BWC) was opened for signing in 1972, the overwhelming number of signatories made it clear that most countries were against the use of BW as a legitimate tool of war (20). By the time it went into effect, Canada, France, Germany, the UK and the USA had already unilaterally dismantled their offensive BW programmes. In the 1990s Russia and South Africa followed suit (21, 22). The author cannot rule out the existence of some offensive programmes (see Appendix), but the shared ethical norm that prevents state BW use may influence why governments are more concerned about BW use by NSAs than by states.

An analysis of the current situation

Although some information concerning dates of construction is incomplete, one can see a distinct pattern of global proliferation of HCBLs. States are often quite open about their laboratories. The notable exception is Israel, which does not confirm possession of HCBLs, although it regularly publishes defensive BW research (23). The Appendix shows that these laboratories are proliferating both horizontally and vertically: more states are building them, and the states that have them are building more of them. Of the 86 states analysed, close to 40 have explicitly described recent HCBL construction. Anecdotal evidence of new construction exists for numerous additional states, as does the expansion of existing programmes (see Appendix). For the remaining states that did not mention the dates of construction, the sources were recent, implying that the HCBLs were recent too. For example, in the USA, the number of HCBLs registered with the Centers for Disease Control and Prevention (CDC) tripled between 2004 and 2008 (this number does not include the laboratories working with pathogens that are dangerous but do not require registration, such as tuberculosis and severe acute respiratory syndrome [SARS]) (24). No states deliberately declare that they do not want any more laboratories, although Ireland maintains that no BSL-4 laboratories are planned, and Japan does not allow its BSL-4 facilities to operate at that level because of public opposition.

Issues with oversight: case study of the United States of America

The initial aim in compiling a table showing the proliferation of HCBLs was to list the numbers of BSL-3 and BSL-4 facilities in each country, permitting an exact analysis of the scope of HCBLs globally. Although this information is available for some states, exact numbers are unavailable for others, often due to a lack of national oversight. The most glaring example is the USA, which has well over 1,600 labs – by far the world's highest number of HCBLs (see Appendix). In 2007, the US Government Accountability Office (GAO) admitted to 'a major proliferation of high-containment BSL-3 and BSL-4 laboratories' (25). According to the GAO investigation, no agency of the 12 interviewed tracks the number of HCBLs in the USA, and 'consequently no agency

is responsible for determining the risks associated with the proliferation of these laboratories' (25).

Although the facilities that are federally funded or work with select agents (as listed in the CDC and US Department of Agriculture's Select Agents Program) are documented, many laboratories fall outside this group (26). According to the GAO report, while the USA had only 5 BSL-4 laboratories before 9/11, by 2007 they had 15, including at least 1 still being planned (25). According to the Federation of American Scientists (FAS), documentation exists for only 12 of them, 2 of which have an unconfirmed status, and 3 of which are under construction (27). Gronvall *et al.*'s 2007 list of BSL-4 laboratories stated that there were 11, including 4 that were due to be completed in 2008 (28). A 2008 GAO report to the Congressional Committee is titled 'Perimeter Security Assessment of the Nation's Five BSL-4 Laboratories'. It is not made clear why in this later GAO report only five laboratories are mentioned. On page 1 of the report, reference is made to the 2007 GAO report, but the number of BSL-4 laboratories in the 2008 report is one-third of the number given in 2007 (26). Despite the fact that all these BSL-4 facilities are known to the government through the Select Agents Program, there are major discrepancies in the reporting.

According to the latest (2015) GAO report (29) the situation has yet to be remedied. There is still no federal agency with comprehensive oversight of HCBLs, and the CDC's new Laboratory Science and Safety Office had, as of 2015, not yet fully implemented the GAO's earlier recommendations.

The official estimates for the numbers of BSL-3 laboratories vary even more, with discrepancies of up to 100% in 2005 (28). It is important to note the USA is not alone in its lack of oversight, it just has the largest number of HCBLs and easily available information regarding them.

High-containment biological laboratories and levels of economic development

To explore the connection between economics and HCBLs, the states in the Appendix were compared to those in the Financial Times Stock Exchange (FTSE) Global Equity Index Series. All of the 24 'developed

nations', 11 'advanced emerging nations', and 12 'secondary emerging nations' have HCBLs (Hong Kong is listed separately from China by the FTSE, but not in the Appendix to this paper) (30). Although correlation does not prove causation, it seems that most states with the financial means to build these laboratories do so. The HCBLs can also generate substantial income: for some states, biotechnology has been a boon to their economies (31, 32, 33, 34). The number of HCBLs owned by private institutions further illustrates their lucrativeness.

Threat

Threat is defined here as danger to the well-being of people or to the integrity of a state. In its most basic interpretation, threat concerns the release of a dangerous HCBL agent into an environment outside the laboratory. There are three ways in which this can occur: accidents, theft/diversions, and events that compromise the structural integrity of the HCBL (both natural disasters and intentional attacks) (35). The HCBL proliferation in and of itself also constitutes a threat: increased lab numbers mean more vulnerabilities.

Biological weapons: the threat posed by states

There are historical accounts of states using biological agents since ancient times (36, 37), but these were hardly what we would consider a BW today (36). In WWI, covert German operations in Romania infected livestock that were intended for export to Russia with anthrax and glanders (38). After WWI, the Geneva Protocol attempted to prohibit poisonous gases and biological warfare, and all the great powers except for the USA and Japan signed it (39). Japan conducted numerous operations in China, spraying agents causing cholera, salmonella, anthrax and plague from aircraft. These activities had various degrees of success (including infecting the Japanese troops themselves), but about 10,000 cholera cases in China were attributed to their activities (36). Besides these Japanese 'field trials', there is no other proven incident of a state using BW against another state (40, 41).

Although the stated reasons for building HCBLs are not necessarily the only reasons for building them, it is worth mentioning that no state has explicitly justified their biodefence programmes as a precaution against

the threat of state-deployed BW. The use of BW is considered illegitimate by most states (20), although some state-sponsored BW programmes allegedly could still exist.

There are a number of good reasons for a state to avoid using BW against another state. Because bioweapons are almost universally perceived as illegitimate, and compliance with the BWC has been very high, retaliation against a state using BW might be stronger than if it used conventional weapons. Furthermore, BW use could endanger a state's own army through either direct contamination or contagion. Considering these drawbacks, state access to conventional weaponry, and historical precedent, it is unlikely that states will use BW against each other.

Bioterrorism: the threat posed by non-state actors

At least 32 of the 78 states analysed possess some sort of biodefence programme. There are some states for which information is unavailable, but they are likely to have a biodefence programme if they have been accused of offensive research (see Appendix). Finland, Japan, South Korea, Switzerland, the Philippines, the United Kingdom and the United States have all explicitly mentioned bioterrorism as reasons for their biodefence programmes (42). There are isolated cases in which individuals and NSAs have attempted to deploy biological agents (43), and only two in which they have been weaponised (put into a form or delivery vehicle for use as a BW) and deployed – both with little success. The Rajneeshee cult infected salad bars with salmonella in 1984, and Aum Shinrikyo attempted to cause an inhalational anthrax epidemic in 1993, but neither event resulted in any casualties (43). The 1993 event in particular raised states' awareness of the threat of terrorist use of weapons of mass destruction (WMD) (44), but these events happened too early and were of too little human significance (in that there were no casualties) to explain the extent of states' preoccupation with bioterrorism.

This focus can be traced to two particular incidents in 2001. The first is 9/11, and the second is the anthrax letter attacks. Although 9/11 was an act of conventional terrorism, it demonstrated that even a nation like the USA was vulnerable to attack on its own soil. This significantly

increased awareness of all types of terrorism, including bioterrorism (45). Islamic terrorist groups have openly declared their intention to pursue BW capability (46, 47) and have developed rudimentary programmes (48). Although these efforts have been 'largely unsuccessful', they have been taken very seriously (49).

The anthrax attacks in 2001 were of limited scope, and there were only five casualties (50). Scientist Bruce Ivins was the primary suspect of the Federal Bureau of Investigation (FBI), based on circumstantial evidence, and the case was closed after he committed suicide. The inability to definitively resolve the question of who had sent the letters was alarming for two reasons. First, efforts were unsuccessful despite the significant resources expended. Second, the fact that the bacterial strain was domestic meant the government had ready access to facilities and staff, which would not have been the case had the strain been foreign in origin. The failure to resolve this case was a global wake-up call to the inadequacy of current biodefence resources (42, 49, 51, 52).

In 1988, terrorism expert Brian Jenkins speculated that terrorists 'want a lot of people watching, not a lot of people dead', and that terrorist groups avoid causing too much public revulsion for fear of alienating their constituents and inviting government retaliation (53) Although this may often still hold true, terrorism has evolved. In 2002, Islamic terrorist group spokesman Sulayman Abu Ghayth al-Libi claimed that his group's *fatwa* is to kill four million Americans, and that it justified the use of WMD (47). If terrorist ambitions have indeed shifted towards wanting a large number of people dead, then we need to re-examine our understanding of terrorist behaviour. Unlike a state, these groups do not have large conventional armies at their disposal, so pursuing WMD (including BW) could become a logical option. Currently, it is still easier and cheaper for terrorists to use conventional weapons, and they seem to be putting most of their resources into those. However, the psychological effect and mass panic that would ensue if a population were subjected to biological attack may be a motivator to pursue BW. In any case, bioterrorism has become a global concern; the US State Department considers potential terrorist WMD use to be one of the '"gravest threats" to the security of the United States and its allies' (54).

The HCBLs play a dual role in bioterrorism: they can function both as its source and as the primary line of defence against it. For terrorists to be successful in developing BW, they need access to at least a rudimentary version of an HCBL (or at the very least a BSL-2 lab), either for studying pathogens, or for producing the desired quantity. All known pathogens except for smallpox and the 1918 influenza pandemic virus are present in the environment. Attempts to make BW, presumably without the correct facilities, have not worked well in the past: in 2009, a 40-member terror cell working on BW was killed by bubonic plague (48). In the future, it is logical that the terrorist organisation would recruit trained scientists and use facilities already in place rather than trying to develop their own.

In order to have a pathogen viable for weaponisation, a terrorist group must either try to isolate a pathogen from nature or divert one that is already identified, purified and growing in a lab. When isolating from nature there may be fewer agents available, and the process may require additional technical resources or experience in order to isolate, culture and purify the desired pathogen. Furthermore, not all strains of a certain pathogen are equally virulent, as was seen when Aum Shinrikyo used the wrong strain of anthrax and consequently failed to achieve their objective (55). Since diversion is typically easier than isolation, biosecurity and personnel reliability programmes in laboratories are essential to protect pathogens. The HCBLs also play a crucial role in combating bioterrorism, since much of the world's biodefence focuses on pathogen identification, treatment development and vaccine production. A US Government assessment concluded that most accidents are due to human error. It found that people working in these laboratories can pose a risk, and that it is difficult to control inventories of biological agents with the technology available (56). Making it more difficult for employees to divert pathogens and making sure that the personnel working in the labs are highly trained and reliable are paramount to maintaining security.

Threats posed by accidents and natural disasters

Accidents and disasters happen, even among reputable scientists working in state-of-the-art laboratories (57). The fact that many labs have been built in areas of high population density further raises the

stakes in case of a mishap (58). It is believed that a large percentage of accidents in HCBLs go unreported, especially if there are no serious consequences (56, 59).

Examples

In 2006, at a Texas A&M BSL-3 laboratory, a worker became infected with *Brucella* after working on aerosolising the bacterium. She had neither the training nor the authorisation to work with that particular pathogen, and was diagnosed more than two months after exposure. The laboratory did not have the authorisation to aerosolise brucellosis and did not report the incident to the CDC. It was later also discovered that some vials of *Brucella* as well as some diseased laboratory animals had gone missing from the same lab (25). More recently, there were US government incidents involving the mishandling of anthrax in both 2014 (60) and 2015 (61). In 2014, the USA also discovered over 300 previously unknown vials of agents that had been kept undocumented in their storage facilities for decades; some of these included smallpox (62).

On a nationwide scale, the lack of oversight and reporting is even more evident: under the Federal Select Agent Program, US labs are required to report any accidents or accidental releases of specific agents. This programme oversees approximately 300 laboratories in the USA. It is unclear who oversees the rest (63), but oversight is probably privatised. Between 2006 and 2013, federal regulators were notified of approximately 1,500 incidents involving select agents, 800 of which required some medical evaluation or treatment (63). Incidents like these are surely not isolated and are probably underreported globally, especially in countries that do not have as clear a protocol on laboratory regulations and accident reporting as the USA does.

Sometimes the threat of accidental release lies in the physical structure of the laboratory. Depending on the regulations and financial means of a country, the building's structure may be more or less secure. Even if built to international standards, operational and annual maintenance must be done. Air filters need to be changed, and equipment becomes less reliable with age: seals can crack, and mechanical systems can fail.

A UK outbreak of foot and mouth disease in 2007 originated from contaminated wastewater, which had leaked from a damaged drainage system at the Pirbright HCBL (25). An investigation of the facility found evidence of a leaking drainage system, damaged pipes, displaced joints, debris build-up and damage from tree roots. It is thought that the disease spread via vehicles driving through contaminated mud and carrying the pathogen offsite (25). A previous outbreak of the disease in the UK in 2001 led to the culling of six million animals, and cost taxpayers over £3 billion and private enterprise £5 billion (64).

Laboratories in zones where natural disasters are common are particularly at risk. In June 2007 the CDC's newest BSL-4 laboratory in Atlanta suffered a thunderstorm and experienced a power outage whereby both its primary and backup energy systems failed. The power outage also shut down the negative air-pressure system (although this is not the only measure used in labs to keep a pathogen contained). Luckily, the facility had just been completed and there were no pathogens stored there at the time (25).

Accidents with mutated or genetically engineered pathogens can be even worse, as well-intentioned research is capable of producing virulent or transmissible organisms that do not exist in nature; for example, the US Government funded research on influenza that led to two papers written in 2012 on aerosol-transmissible mutations of the avian flu virus H5N1. Some argue that such research should never have been conducted, while others maintain that more must be done to correctly understand the disease (which naturally mutates on its own) (65). Since that time, a number of other papers have also been published on this topic and additional studies have been conducted.

As researchers and universities compete for recognition and funding, it is difficult to draw the line between what should and what should not be studied and published. Numerous governments have developed guidelines concerning the regulation of dual-use research, in an effort to balance prioritising research on pandemic and emerging diseases with regulations for responsible science.

The threat posed by the proliferation of high containment biological laboratories

More laboratories mean that there are more places where failure can occur or from which agents can be diverted. One must assess whether it is safer to build HCBL facilities in fewer places with more laboratories in each, or whether it is safer to disperse them.

It could be more difficult for governments to oversee and protect many separate facilities. Fewer facilities could mean better oversight; putting more laboratories in the same buildings would lower costs, possibly leaving more of the budget for additional security measures. Some states tend to do this: Canada, for instance, has over 35 individual BSL-3 laboratories at just one of their facilities. Romania and Belgium also have the majority of their BSL-3 laboratories housed together (see Appendix). On the other hand, if a natural disaster impacts a facility holding a large number of laboratories, the consequences could be worse than if the same event were to strike a smaller facility.

Another pertinent issue caused by HCBL proliferation concerns the competency of scientists working in them. Because the number of HCBLs is rising, more people are needed to staff them. In the USA, 8,335 individuals had clearance to work in HCBLs in 2004, and by 2008 that number had increased to 10,365 (59). What used to be a small group of the world's top scientists has now broadened to include people who are less educated or experienced: top scientists cannot be educated fast enough to meet the increasing demand. This is probably an even bigger issue in countries that do not have the infrastructure to train their own scientists. This may force laboratories to hire less well-qualified people, who may be more susceptible to human error than their more educated or experienced counterparts. The dramatic increase in trained HCBL scientists may also present a larger pool from which terrorists can recruit. Having access to researchers with a background of work in high containment facilities would be a boon to any terrorist BW programme.

Each person working in an HCBL is an independent variable whose actions cannot be guaranteed by even the most stringent and redundant biosecurity measures. More scientists mean that there is a greater probability that one of them could have malicious intent, or be

psychologically unstable. Background checks, psychological tests and certification may reduce these risks, but it is unclear how many countries implement these measures when hiring personnel. States may have limited control over laboratories that are not state run. Obliging them to comply with all the safety regulations is difficult in the first place; making them accountable for guaranteeing the intentions of each one of their researchers is impossible.

Measures taken thus far

Globally, there are 37 national and regional members of the International Federation of Biosafety Associations, and as many have 'observer' status (66, 67). A few examples are detailed below to show the range of situations and approaches regarding threat management.

Institutional level

Biosafety measures are the first line of defence against accidents and diversions. Most HCBLs have an extensive number of physical security measures in place, such as alarms, fences, cameras, etc. (68). Some have armed guards, or require that researchers are never alone in the laboratory. Institutions often voluntarily decide on extra security measures individually (59). Although biosafety measures are required for official laboratory certification, there is always the risk that some laboratories will work with pathogens that they are not certified for.

National level

The levels of standardisation and national oversight of HCBLs vary greatly from state to state. Many base their biosafety and biosecurity programmes on directives and guidelines issued by international organisations. The World Health Organization (WHO), the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) have all published such guidelines (9). Some states have protocols and standards to vet the personnel in governmental HCBLs, but others appear not to.

There are major problems with every national system examined (9, 56, 69, 70, 71, 72). Available information on the biosafety and biosecurity measures of most states is lacking, although many have some degree of

government oversight (see Appendix). This obviously requires more resources for states with many HCBLs than for states with fewer. Biosecurity protocols may be more rudimentary in states with less experience or less funding. Many states with former BW programmes or the states working closely with them seem to have more developed guidelines concerning biosecurity, perhaps because they have a longer history of working with these agents. More research needs to be done to determine the degree of correlation and its significance. No country examined currently has adequate oversight of their HCBLs.

Regional and international level

Along with the guidelines written by the aforementioned international organisations, there is a growing level of cooperation between states concerning biosafety and biosecurity. Some of these measures directly affect HCBLs, and others seem as though they should, but do not. Both broad international agreements as well as a few regional initiatives are examined briefly below.

All of the relevant international agreements concern BW, yet none addresses HCBLs specifically. The BWC has been a factor in reducing mistrust between nations and creating an international norm against state BW programmes (73, 74). There is nothing in the convention to monitor the proliferation of HCBLs or to make them safer. Article X even reaffirms its support for 'the fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes' (75).

The Australia Group's main objective is to control exports of certain chemicals, biological agents and equipment to ensure that they avoid both 'direct' and 'inadvertent involvement' in the spread of chemical and biological weapons (CBW) (76). The Australia Group consists of 41 states, the majority of which have HCBLs (77). Although this may make member states less likely to sell sensitive agents to states or groups that might misuse such agents, the Australia Group does not really have an impact on legitimate research being done in HCBLs.

United Nations (UN) Resolution 1540 goes a step further. Although it is concerned with preventing the spread of CBW, it focuses on the spread of agents and delivery systems to NSAs. Per the 2004 resolution, states are called to 'establish appropriate domestic controls over related materials to prevent their illicit trafficking' (78). Domestic controls for secure production, use and transport, physical protection measures and law enforcement against trafficking of agents are covered by the resolution (79). Licensing personnel, registration and certification of all pertinent facilities, as well as measures to ensure personnel reliability, although not expressly stated, could be considered measures that pertain to the resolution (80). It would be a major step forward if UN resolution 1540 were to be fully implemented by all states with HCBLs.

There have also been regional initiatives to increase cooperation and knowledge sharing, and to standardise practices and procedures. In Europe, the European Cooperation in Science and Technology (COST) Action B28 was enacted 'to increase knowledge on BSL3 and BSL4 agents in order to support the development of more accurate diagnostics, vaccines and therapeutics, and to better understand the epidemiology of these highly pathogenic microorganisms' (42). The original impetus for COST had its roots in the unpreparedness of European laboratories at the time of the 2001 anthrax letters event. After realising that most of the dangerous pathogen research was in the USA and, because most of it was classified, 'of little use for the European Union', the European Union (EU) decided to launch a collaborative effort to be globally competitive (42). Because the EU's HCBLs are distributed over a number of smaller states, they maximise productivity through collaboration.

The Middle East and North African (MENA) countries have formed the coalition of Region Network High Containment Laboratories (RNCL) in order to implement biosafety and biosecurity strategies at the national and regional levels, improve the infrastructure of laboratories and emphasise staff training. Their work addresses the threats of both natural pandemics and human-made risks (81). Coalitions can identify measures for improvement but lack the power of governments to implement them.

Recommendations: practical and political

Proliferation of HCBLs will undoubtedly continue, but one must ask how many of these laboratories the world needs. Recently the USA has begun thinking about reducing lab numbers. Human ambition and error are dangerous in even the most structurally sound laboratories. Terrorists will seek the easiest way to make BW, so oversight, background checks and redundant security systems are vital. Natural disasters or freak occurrences happen, and no laboratory can ever be completely prepared.

Biosecurity measures must be implemented and verified. Only laboratories that have been certified should house dangerous pathogens, and each state should have a single government agency responsible for monitoring and certifying all their HCBLs, including private laboratories. This could be done through a mandatory certification and inspection process, where the government has access to the relevant information on the type of research being conducted, although this could pose issues for companies working on proprietary research. Laboratories should be checked frequently for equipment failures, and be required to recertify periodically.

There must be clear protocols in place for emergency response procedures. All mishaps should be reported immediately to a single government agency, which should be responsible for documenting and responding to accidents, when needed. The governing state should know exactly what types of research are being carried out where, regardless of whether the laboratory is privately run or not. The intangible aspects of security must be addressed as well, including personnel background checks and psychological evaluations. In general, governments and biorisk associations have researched what needs to be done; the problem lies in the implementation of their findings. Government action often takes years, depending on the political system and the level of priority attached to HCBL safety.

Because of financial constraints, many developing states have difficulties building adequate HCBLs to study endemic diseases that affect their populations directly. It is imperative that these diseases are researched only in laboratories equipped for the dangers they pose.

Although accidents can happen anywhere, they are likely to happen less often and have less severe consequences in adequate facilities. Because states seem to be the least dangerous actors with regard to the use of BW, it would be wise to increase inter-state cooperation and knowledge sharing.

Concerning HCBL oversight, states must embrace a paradigm shift. Instead of viewing these labs solely as a question of national security, they should recognise them as a matter of global security. Increased cooperative measures may also discourage states that are still conducting questionable research, which may be done as much out of habit or political determinism as it may be done out of a perceived need for BW. The era when a significant group of states felt that they needed BW seems to be drawing to a close. Standards for biosafety and biosecurity in HCBLs must be internationally agreed upon, standardised and implemented.

Although important, this goal represents a major policy obstacle. Sharing oversight and/or ownership of research is not only expensive and difficult to implement, but it also raises issues of national sovereignty in this particular arena. In order to foster oversight, countries with possibly different values, priorities and research agendas are expected to share their information, and give up a degree of their control to an international body.

Asking the right question

The BSL-4 facilities have more government and international oversight than BSL-3 facilities. However, although the latter are too numerous to oversee easily, the majority of potential BW pathogens are BLS-3 agents (82). Of all the states that have ever had BW programmes, only the former Soviet Union and the USA have done any known research on or weaponisation of BSL-4 agents (83). In all the aforementioned instances of bioterrorism and attempted bioterrorism, no individual or NSA has ever weaponised or attempted to weaponise a BSL-4 agent.

Given the extremely virulent nature of BSL-4 agents, they are difficult to work with, and thus rather self-protecting (84, 85). It would be nearly impossible to safely freeze-dry, mill and weaponise such a pathogen

without an appropriate facility. The BSL-4 agents are not necessarily more contagious than their BSL-3 counterparts; they do, however, tend to have fewer countermeasures and/or vaccines developed to protect those working with them from exposure. The danger of an agent depends not only how lethal it is, but how well it transmits from person to person. States should keep this in mind when deciding on security features for HCBLs.

For these reasons, it is important to be vigilant of BSL-3 facilities in respect to bioterrorism. The pathogens they contain can be just as deadly, and are far easier to work with. Only approximately 2% of the world's HCBLs are BSL-4, and it is crucial that governments and international organisations shift their attention to the other 98%.

Conclusions

In order to accurately analyse the threats HCBL proliferation poses and minimise its risk, it is crucial to have an overview of what types of laboratories are proliferating in which states, and what types of research they are conducting.

Numerous states and interest groups are beginning to demand better oversight of their HCBL facilities, and there has been an increase in international cooperation as well as some attempt at standardisation of practices and facilities. Unfortunately, the measures that have been taken so far are not yet adequate, and the degree of oversight and control that states exert over their HCBLs varies considerably. Going forward it is important for states to implement strict national standards for safety and security, as well as working with each other to foster increased international trust, cooperation and oversight. Existing measures must be strengthened and new ones developed for both national and private laboratories. Pathogens do not recognise borders, and states must regard HCBL proliferation as the global issue it is.

References

1. World Bank (2012). – Population growth (annual percentage). World Bank Databank. Available at: https://data.worldbank.org/indicator/sp.pop.totl (accessed on 30 September 2018).

2. Shisana O. (2005). – Managing globalisation for health Human Sciences Research Council, Pretoria, South Africa, 23 pp. Available at: www.who.int/healthpromotion/hpr_6gchp_speech_shisana.pdf (accessed on 11 December 2017).

3. Garret L. (1994). – The coming plague: newly emerging diseases in a world out of balance. Farrar, Straus and Giroux, New York, United States of America, 768 pp.

4. Avert (2015). – Global HIV & AIDS statistics. Horsham, United Kingdom. Available at: www.avert.org/global-hiv-and-aids-statistics (accessed on 12 December 2017).

5. Gupta S.K., Gupta P., Sharma P., Shrivastava A.K. & Soni S.K. (2012). – Emerging and re-emerging infectious diseases, future challenges and strategy. *J. Clin. Diagn. Res.*, **6** (6), 1095–1100. Available at: www.jcdr.net/back_issues.asp?year=2012&month=August (accessed on 30 August 2018).

6. Barrett R. & Armelagos G. (2013). – An unnatural history of emerging infections. Oxford University Press, Oxford, United Kingdom, 154 pp.

7. Gottron F. & Shea D.A. (2009). – Oversight of high-containment biological laboratories: issues for Congress. Congressional Research Service, Washington, DC, United States of America, 33. Available at: https://fas.org/sgp/crs/terror/R40418.pdf (accessed on 11 December 2017).

8. BioWeapons Prevention Project (BWPP) (2011). – Bioweapons Monitor 2011 (I. Hunger, ed.). BioWeapons Prevention Project, Berlin, Germany, 142 pp. Available at: www.bwpp.org/documents/BWM%202011%20WEB.pdf (accessed on 11 December 2017).

9. Kallings I. & Summermatter K. (2012). – E2: high containment microbiology laboratories in Europe. *In* Biosecurity challenges of the global expansion of high-containment biological

laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). National Academies Press, Washington, DC, United States of America, 151–158. Available at: www.nap.edu/read/13315/chapter/20 (accessed on 8 October 2018).

10. Centers for Disease Control and Prevention (CDC) (2009). – Biosafety in microbiological and biomedical laboratories. 5th Ed. US Government Printing Office, Washington, DC, United States of America, 415 pp. Available at: www.cdc.gov/biosafety/publications/bmbl5/ (accessed on 11 December 2017).

11. United States Defense Science Board Task Force (2009). – Department of Defense Biological Safety and Security Program. Office for the Under Secretary of Defense for Acquisition, Technology, and Logistics, Washington, DC, United States of America, 93 pp. Available at: https://fas.org/irp/agency/dod/dsb/biosafety.pdf (accessed on 11 December 2017).

12. Wesel L. (2005). – UC Davis gets a handle on the true costs of BSL-3 labs. Tradeline, Orinda, California, United States of America. Available at: www.tradelineinc.com/reports/2005-8/uc-davis-gets-a-handle-true-costs-bsl-3-labs (accessed on 11 December 2017).

13. Neuman V.A. & Martin J.P. (2005). – Biosafety level 4 labs up close and personal. HPAC Engineering, New York, United States of America. Available at: www.hpac.com/iaq-amp-ventilation/biosafety-level-4-labs-close-and-personal (accessed on 11 December 2017).

14. American Biological Safety Association (ABSA) (2017). – What we do. Available at: https://absa.org/biosafety/ (accessed on 11 December 2017).

15. Salerno R.M. & Koelm J.G. (2002). – Biological laboratory and transportation security and the Biological Weapons Convention, SAND No. 2002-1067P. Sandia National Laboratories, Albuquerque, New Mexico, United States of America. Available at: www.sandia.gov/cooperative-monitoring-

center/_assets/documents/sand2002-1067p.pdf (accessed on 11 December 2017).

16. Katz R. (2004). – Biological weapons: a national security problem that requires a public health response. Office of Population Research (OPR) Working Paper Series, Princeton University, Princeton, New Jersey, United States of America, 38 pp. Available at: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.680.5464&rep=rep1&type=pdf (accessed on 30 August 2018).

17. United States (US) Patent and Trademark Office (2003). – Patent Number 6,523,478 B1. Rifle-launched non-lethal cargo dispenser. US Patent and Trademark Office, Washington, DC, United States of America. Available at: www.google.com/patents/US6523478 (accessed on 11 December 2017).

18. United States Department of Defense (US DoD) (1998). – The militarily critical technologies list. Part II: weapons of mass destruction technologies (ADA 330102). Office of the Under Secretary of Defense for Acquisition and Technology, US DoD, Arlington, Virginia, United States of America, 401 pp. Available at: https://fas.org/irp/threat/mctl98-2/mctl98-2.pdf (accessed on 11 December 2017).

19. Federation of American Scientists (FAS) (2012). – Introduction to biological weapons. FAS, Washington, DC, United States of America. Available at: www.fas.org/programs/bio/bwintro.html#production (accessed on 11 December 2017).

20. The Harvard Sussex Program on CBW Armament and Arms Limitation (HSP) (2001). – BWC signatures, ratifications and accessions. HSP, Sussex, United Kingdom. Available at: www.fas.harvard.edu/~hsp/bwcsig.html (accessed on 11 December 2017).

21. Nuclear Threat Initiative (NTI) (2015). – Russia: biological country profile. NTI, Washington, DC, United States of America. Available at: www.nti.org/learn/countries/russia/biological/ (accessed on 30 September 2018).

22. Nuclear Threat Initiative (NTI) (2015). – South Africa: nuclear country profile. NTI, Washington, DC, United States of America. Available at: www.nti.org/learn/countries/south-africa/nuclear/ (accessed on 30 September 2018).

23. Nuclear Threat Initiative (NTI) (2015). – Israel: biological country profile. NTI, Washington, DC, United States of America. Available at: www.nti.org/learn/countries/israel/biological/ (accessed on 8 October 2018).

24. Wadman M. (2009). – Booming biosafety labs probed: US lawmakers and scientists at odds over how to regulate high-containment labs. *Nature*, **461**, 577. doi:10.1038/461577a.

25. United States Government Accountability Office (GAO) (2007). – (GAO-08-108T) Testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives. High-containment biosafety laboratories: preliminary observations on the oversight of the proliferation of BSL-3 and BSL-4 laboratories in the United States. GAO, Washington, DC, United States of America, 39 pp. Available at: www.gao.gov/assets/120/117997.pdf (accessed on 11 December 2017).

26. United States Government Accountability Office (GAO) (2008). – (GAO-08-1092) Report to congressional committees. Biosafety laboratories: perimeter security assessment of the nation's five BSL-4 laboratories. GAO, Washington, DC, United States of America, 25 pp. Available at: www.gao.gov/new.items/d081092.pd (accessed on 11 December 2017).

27. Federation of American Scientists (FAS) (2011). – BSL-4 laboratories as of 2010–2011: Google fusion table. FAS, Washington, DC, United States of America. Available at: https://fusiontables.google.com/DataSource?snapid=S567513UnBn (accessed on 25 September 2018).

28. Gronvall G.K., Fitzgerald J., Chamberlain A., Inglesby T.V. & O'Toole T. (2007). – Meeting report: high-containment biodefense research laboratories: meeting report and center recommendations. *Biosecur. Bioterror.*, **5** (1), 75–85. doi:10.1089/bsp.2007.0902.

29. United States Government Accountability Office (GAO) (2015). – (GAO-15-792T) Testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives. High-containment laboratories: preliminary observations on federal efforts to address weaknesses exposed by recent safety lapses. GAO, Washington, DC, United States of America, 18 pp. Available at: www.gao.gov/assets/680/671678.pdf (accessed on 11 December 2017).

30. FTSE Russell (2017). – FTSE Annual Country Classification Review: September 2017. FTSE Russell, London, United Kingdom, 10 pp. Available at: www.ftse.com/products/downloads/FTSE-Country-Classification-Update-2017.pdf (accessed on 11 December 2017).

31. Enemark C. (2006). – Preventing accidental disease outbreaks: biosafety in East Asia. APSNet Policy Forum, Berkeley, California, United States of America. Available at: http://nautilus.org/apsnet/0631a-enemark-html/ (accessed on 11 December 2017).

32. Kenya Veterinary Vaccines Production Institute (KEVEVAPI) (2014). – About us. KEVEVAPI, Nairobi. Available at: www.kevevapi.org/index.php/about-us (accessed on 11 December 2017).

33. Jonsson T. (2007). – Competitiveness of the European biotechnology industry. European Commission, Brussels, Belgium, 26 pp. Available at: http://ec.europa.eu/DocsRoom/documents/1700/attachments/1/translations/en/renditions/pdf (accessed on 11 December 2017).

34. Biotechnology Innovation Organization (BIO) (2012). – About BIO. BIO, Washington, DC, United States of America. Available at: www.bio.org/articles/about-bio (accessed on 11 December 2017).

35. United States Government Accountability Office (GAO) (2009). – (GAO-09-747) Report to Congressional Committees. Biological Research: observations on DHS's analyses concerning whether FMD research can be done as safely on the mainland as on

Plum Island. GAO, Washington, DC, United States of America, 64 pp. Available at: www.gao.gov/new.items/d09747.pdf (accessed on 11 December 2017).

36. Johnson T.J. (2002) – A history of biological warfare from 300 B.C.E. to the present. American Association for Respiratory Care (AARC), Irving, Texas, United States of America. Available at: www.zarcommedia.com/index.php/research-documents/13014.html (accessed on 8 October 2017).

37. Fenn E.A. (2000). – Biological warfare in eighteenth-century North America: beyond Jeffrey Amherst. *J. Am. Hist.*, **86** (4), 1552–1580. doi:10.2307/2567577.

38. National Institute of Allergy and Infectious Diseases (NIAID) (2014). – Integrated research facility, NIAID, Bethesda, Maryland, United States of America. Available at: www.niaid.nih.gov/about/integrated-research-facility (accessed on 13 December 2017).

39. Federation of American Scientists (FAS) (2012). – Geneva Protocol. FAS, Washington, DC, United States of America. Available at: www.fas.org/nuke/control/geneva/intro.htm (accessed on 11 December 2017).

40. Stockholm International Peace Research Institute (SIPRI). – (1984). – Chemical warfare in the Iran–Iraq War. SIPRI, Solna, Sweden, 11 pp. Available at: www.sipri.org/sites/default/files/files/FS/SIPRIFS8405.pdf (accessed on 25 September 2018).

41. A. Cohen. (2001). – Israel and chemical/biological weapons: history, deterrence, and arms control. *Nonprolif. Rev.*, **8** (3), 27–53. doi:10.1080/10736700108436862.

42. European Cooperation in Science and Technology (COST) (2011). – BMBS COST Action B28: array technology for BSL3 and BSL4 pathogens. COST, Brussels, Belgium. Available at: www.cost.eu/COST_Actions/bmbs/B28 (accessed on 11 December 2017).

43. Carus W.S. (2000). – R.I.S.E. *In* Toxic terror: assessing terrorist use of chemical and biological weapons (J.B. Tucker, ed.). MIT Press, Cambridge, Massachusetts, United States of America, 55–70.

44. Cronin A.K. (2004). – Terrorist motivations for chemical and biological weapons use: placing the threat in context. *Def. Secur. Anal.* **20** (4), 313–20. doi: 10.1080/1475179042000305778.

45. United States Food and Drug Administration (US FDA) (2002). – Bioterrorism Act of 2002. US FDA, Washington, DC, United States of America.

46. Makalinao I. (2009). – Building local and global partnerships for biosafety and biosecurity: the Philippine experience. The Biological and Toxin Weapons Convention, Bradford, Yorkshire, United Kingdom, 30 pp. Available at: www.opbw.org/new_process/mx2009/BWC_MSP_2009_MX_Presentation_090827-AM_Philippines_E.pdf (accessed on 1 August 2012).

47. Mowatt-Larson R. (2010). – Al Qaeda weapons of mass destruction threat: hype or reality? Belfer Center for Science and International Affairs, Harvard Kennedy School, Cambridge, Massachusetts, United States of America. Available at: www.belfercenter.org/publication/al-qaeda-weapons-mass-destruction-threat-hype-or-reality (accessed on 11 December 2017).

48. Burke J. (2004). – Al Qaeda. *Foreign Pol.*, **142**, 18–26. doi:10.2307/4147572.

49. United States Department of Justice (US DoJ) (2010). – Amerithrax investigative summary: released pursuant to the Freedom of Information Act, 19 February 2010. US DoJ, Washington, DC, United States of America, 96 pp. Available at: www.justice.gov/archive/amerithrax/docs/amx-investigative-summary.pdf (accessed on 11 December 2017).

50. Council on Foreign Relations (CFR) (2006). – The anthrax letters. CFR, New York, United States of America. Available at: www.cfr.org/backgrounder/anthrax-letters#p1 (accessed on 11 December 2017).

51. Manjoo F. (2008). – The anthrax truth movement: the Web searches for holes in the FBI's latest lone-gunman theory. Slate, New York, United States of America. Available at: www.slate.com/articles/technology/technology/2008/08/the_anthrax_truth_movement.html (accessed on 11 December 2017).

52. British Broadcasting Corporation (BBC) News (2011). – FBI 'overstated' evidence used in anthrax letters case. BBC News, London, United Kingdom. Available at: www.bbc.co.uk/news/world-us-canada-12475920 (accessed on 11 December 2017).

53. University of California Irvine Libraries (1988). – Quest for peace interviews: Brian Jenkins interview transcript. UC Irvine Libraries, Irvine. Available at: www.youtube.com/watch?v=VPVaeB73GyY (accessed on 25 September 2018).

54. Nuclear Threat Initiative (NTI) (2010). – WMD terrorism remains grave threat, US says. NTI, Washington, DC, United States of America. Available at: www.nti.org/gsn/article/wmd-terrorism-remains-grave-threat-us-says/ (accessed on 11 December 2017).

55. Takahashi H., Keim P., Kaufmann A.F., Keys C., Smith K.L., Taniguchi K., Inouye S. & Kurata T. (2004). – *Bacillus anthracis* bioterrorism incident Kameido, Tokyo, 1993. *Emerg. Infect. Dis*., **10** (1), 117–120. doi:10.3201/eid1001.030238.

56. United States Government Accountability Office (GAO) (2009). – (GAO-09-574) Report to congressional requesters. High containment laboratories: national strategy for oversight is needed. GAO, Washington, DC, United States of America, 104 pp. Available at: www.gao.gov/assets/300/295543.pdf (accessed on 11 December 2017).

57. Begley S. & Steenhuysen J. (2012). – How secure are labs handling world's deadliest pathogens? Reuters, London, United Kingdom. Available at: www.reuters.com/article/2012/02/15/us-health-biosecurity-idUSTRE81E0R420120215 (accessed on 11 December 2017).

58. Van Boeckel T.P., Tildesley M.J., Linard C., Halloy J., Keeling M.J. & Gilbert M. (2013). – The Nosoi commute: a spatial perspective on the rise of BSL-4 laboratories in cities. arXiv:1312.3283. Arxiv.org, Ithaca, New York, United States of America, 16 pp. Available at: https://arxiv.org/pdf/1312.3283.pdf (accessed on 11 December 2017).

59. American Association for the Advancement of Science (AAAS) (2009). – Security in biological research: current oversight of high-containment laboratories. AAAS, Washington, DC, United States of America.

60. Centers for Disease Control and Prevention (CDC) (2014). – CDC lab incident: anthrax. CDC, Atlanta, Georgia, United States of America. Available at: www.cdc.gov/anthrax/news-multimedia/lab-incident/ (accessed on 11 December 2017).

61. Ackerman S. (2015). – Anthrax: Pentagon accidentally sent bioweapon to as many as nine states. Guardian, London, United Kingdom. Available at: www.theguardian.com/us-news/2015/may/27/pentagon-live-anthrax-accident (accessed on 11 December 2017).

62. Dennis B. & Sun L.H. (2014). – FDA found more than smallpox vials in storage room. Washington Post, Washington, DC, United States of America. Available at: www.washingtonpost.com/national/health-science/fda-found-more-than-smallpox-vials-in-storage-room/2014/07/16/850d4b12-0d22-11e4-8341-b8072b1e7348_story.html?noredirect=on&utm_term=.267e79b3e3e7 (accessed on 25 September 2018).

63. Young A. & Penzenstadler N. (2015). – Inside America's secretive biolabs. USA Today, McLean, Virginia, United States of America. Available at: www.usatoday.com/story/news/2015/05/28/biolabs-pathogens-location-incidents/26587505/ (accessed on 11 December 2017).

64. United Kingdom National Audit Office (2002). – The 2001 outbreak of foot and mouth disease, report by the Comptroller and

Auditor General. Her Majesty's Stationery Office (HMSO), London, United Kingdom, 138 pp. Available at: www.nao.org.uk/wp-content/uploads/2002/06/0102939.pdf (accessed on 11 December 2017).

65. Yong E. (2012). – Influenza: five questions on H5N1. *Nature* 486 (7404), 456. doi:10.1038/486456a.

66. International Federation of Biosafety Associations (IFBA) (2011). – Member associations. IFBA, Ottawa, Canada. Available at: www.internationalbiosafety.org/index.php/ifba-members/ifba-membership/member-associations (accessed on 11 December 2017).

67. International Federation of Biosafety Associations (IFBA) (2011). – Observer organizations. IFBA, Ottawa, Canada. Available at: www.internationalbiosafety.org/index.php/ifba-members/ifba-membership/observer-organizations (accessed on 11 December 2017).

68. Iowa Department of Public Safety (2003). – Iowa laboratories facilities: physical security plan. Iowa Department of Public Safety, Des Moines, Iowa, United States of America. Available at: www.legis.iowa.gov/docs/publications/SD/18010.pdf (accessed on 11 December 2017).

69. Urgumov M.V. & Netesov S. (2012). – E4: overview of high containment biological laboratories in Russia. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). National Academies Press, Washington, DC, United States of America, 161–164. Available at: www.nap.edu/read/13315/chapter/22 (accessed on 25 September 2018).

70. dos Santos Macedo L. (2012). – E1: overview of biosafety and biosecurity in high-containment labs in Brazil: a report of the Brazilian Biosafety Association. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). National Academies Press, Washington, DC, United States of America, 143–150. Available at:

www.nap.edu/read/13315/chapter/19 (accessed on 25 September 2018).

71. Auewarakul P. (2010). – Biosafety/Biosecurity Network Thailand (BSNT). Available at: www.tm.mahidol.ac.th/jitmm-2010/download/JITMM-3-12-2010-C10-Prasert-Auewarakul-Biosafety.pdf (accessed on 11 December 2017).

72. Nasim A. & Khan E. (2012). – E3: biotechnology and biosecurity initiatives in Pakistan: a country report. Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). National Academies Press, Washington, DC, United States of America, 159–160. Available at: www.nap.edu/read/13315/chapter/21 (accessed on 25 September 2018).

73. Countryman T. (2011). – The next five years of the Biological Weapons Convention. Center for Biosecurity of University of Pittsburgh Medical Center (UPMC), Washington, DC, United States of America. Available at: www.youtube.com/watch?v=zC8WxHEs-kk (accessed on 12 December 2017).

74. Jasper U. (2004). – The challenge of biological weapons: proposals for greater EU effectiveness. *Disarm. Diplom.*, **78**. Available at: www.acronym.org.uk/old/archive/dd/dd78/78uj.htm (accessed on 12 December 2017).

75. The Biological and Toxin Weapons Convention (1972). – Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction. Available at: www.state.gov/t/isn/4718.htm#treaty (accessed on 25 September 2018).

76. The Australia Group (2007). – Objectives of the group. The Australia Group, Canberra, Australia. Available at: www.australiagroup.net/en/objectives.html (accessed on 12 December 2017).

77. The Australia Group (2007). – Australia Group participants. The Australia Group, Canberra, Australia. Available at: www.australiagroup.net/en/participants.html (accessed on 12 December 2017).

78. United Nations (UN) (2004). – 1540 Committee: Security Council Committee established pursuant to Resolution 1540. Factsheet. UN, New York, United States of America. Available at: www.un.org/en/sc/1540/1540-fact-sheet.shtml (accessed on 12 December 2017).

79. United Nations Security Council (UNSC) (2004). – Resolution 1540 (S/RES/1540). UNSC, New York, United States of America. Available at: www.un.org/en/ga/search/view_doc.asp?symbol=S/RES/1540(2004) (accessed on 12 December 2017).

80. Perkins D. & Jamison S. (2012). – United Nations Security Council Resolution 1540 – a primer for armed forces medical laboratory scientists. *Society Scope*, **15** (1), 5–7. Available at: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.729.7222&rep=rep1&type=pdf (accessed on 30 August 2018).

81. Trevan T. (2010). – Building regional and national biosafety and biosecurity strategies for the Middle East and North Africa. The International Council for the Life Sciences (ICLS), Washington, DC, United States of America, 4 pp. Available at: www.stanleyfoundation.org/1540/ICLSBBICStanleyFoundation1.pdf (accessed on 12 December 2017).

82. Federation of American Scientists (FAS) (2011). – Biosafety level 4 labs and BSL information. FAS, Washington, DC, United States of America. Available at: www.fas.org/programs/bio/biosafetylevels.html (accessed on 12 December 2017).

83. James Martin Center for Nonproliferation Studies (2008). – Chemical and biological weapons: possession and programs past and present. James Martin Center for Nonproliferation Studies, Monterey, California, United States of America, 22 pp. Available at:

www.nonproliferation.org/wp-content/uploads/2016/03/2008-Chemical-and-Biological-Weapons_-Possession-and-Programs-Past-and-Present.pdf (accessed on 12 December 2017).

84. Feiveson H., Mian Z., Ramana M.V. & Von Hippel F. (2011). – Managing spent fuel from nuclear power reactors: experience and lessons from around the world. International Panel on Fissile Materials, Princeton, New Jersey, United States of America, 192 pp. Available at: http://fissilematerials.org/library/rr10.pdf (accessed on 12 December 2017).

85. Leitenberg M. (1984). – Studies of military R&D and weapons development. Ministry of Foreign Affairs, Stockholm, Sweden. Available at: https://fas.org/man/eprint/leitenberg/index.html (accessed on 30 September 2018).

86. World Health Organization (WHO) Regional Office Africa (2016). – Report on the status of EDPLN BSL-3 in select countries in the African region. WHO Regional Office Africa, Brazzaville, Republic of Congo, 57 pp. Available at: www.afro.who.int/sites/default/files/2017-08/Report%20on%20the%20Status%20of%20EDPLN%20BSL-3%20in%20Select%20Countries%20in%20the%20African%20Region.pdf (accessed on 13 December 2017).

87. National Health Service and Food Quality (SENASA) (2016). – International Reference Centers. SENASA, Buenos Aires, Argentina. Available at: www.senasa.gob.ar/informacion/centros-de-referencia-internacional (accessed on 12 December 2017).

88. Pan American Health Organization (PAHO) (1998). – Meeting to establish a network of laboratories for the surveillance of emerging infectious diseases (EID) in the Southern Cone region, PAHO/HCP/HCT/122/98. Regional Office of the World Health Organization (WHO), Buenos Aires, Argentina, 48 pp. Available at: www.paho.org/english/ad/dpc/cd/doc429.pdf (accessed on 12 December 2017).

89. Espona M.J. (2010). – Tracing infectious diseases in South America: an IQ challenge. Massachusetts Institute of Technology

Information Quality (MITIQ) Program, Cambridge, Massachusetts, United States of America, 11 pp. Available at: http://mitiq.mit.edu/ICIQ/Documents/IQ%20Conference%202010/Papers/1C3_Espona_Little_Rock_2010.pdf (accessed on 12 December 2017).

90. Lucero N.E. & Siñeriz F. (2005). – The Argentine experience in enhancing biosafety through good laboratory practices. *Asian Biotech. Dev. Rev.*, **8** (1), 99–120. Available at: https://pdfs.semanticscholar.org/3064/5c597826d4dd6ca43f6a3ec3d38573d107f6.pdf (accessed on 13 December 2017).

91. McGurk G.B. (2009). – A study of air-tightness in Australian high-level bio-containment facilities. *Appl. Biosaf.*, **14** (2), 72–80. doi:10.1177/153567600901400205.

92. Roffey R., Hart J. & Kuhlau F. (2006). – Critical guidance: A code of conduct for biodefense scientists. Arms Control Association, Washington, DC, United States of America. Available at: www.armscontrol.org/print/2099 (accessed on 12 December 2017).

93. National Tuberculosis Advisory Committee (2006). – Guidelines for Australian mycobacteriology laboratories. *Communic. Dis. Intell.*, **30** (1), 116–128. Available at: www.ncbi.nlm.nih.gov/pubmed/16637240 (accessed on 12 December 2017).

94. Butler D. (2009). – European biosafety labs set to grow. *Nature*, **462**, 146–147. doi:10.1038/462146a.

95. Austrian Life Sciences Directory (2009). – Medical University of Vienna: Institute of Neurology. Austrian Life Sciences Directory, Vienna, Austria. Available at: www.lifesciencesdirectory.at/index.php?file=show.php&ref=249 (accessed on 12 December 2017).

96. European Cooperation in Science and Technology (COST) (2011). – BMBS COST Action B28. COST, Brussels, Belgium. Available at: www.cost.eu/COST_Actions/bmbs/B28?management (accessed on 25 September 2018).

97. Johnson A., Akhundova G., Aliyeva S. & Strelow L. (2015). – Implementation and evaluation of a training program as part of the cooperative biological engagement program in Azerbaijan. *Front. Public Health*, **3**, 228. doi:10.3389/fpubh.2015.00228.

98. Federation of American Scientists (FAS) (2009). – Major biosafety level 3 and 4 (BSL-3 and 4) facilities around the world. FAS, Washington, DC, United States of America. Available at: www.fas.org/programs/bio/biolevel-old.html (accessed on 12 December 2017).

99. International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B). – Abstracts: 13th Annual Scientific Conference of ICDDR, B. Science to accelerate universal health coverage (A. Cravioto A, ed.), 14–17 March 2011, Dhaka, Bangladesh, 359 pp. Dhaka: International Centre for Diarrhoeal Disease Research, Bangladesh; 2011. Available at: http://dspace.icddrb.org/jspui/bitstream/123456789/6686/1/13%20Ascon%20Abstracts.pdf

100. The Republican Research and Practical Center for Epidemiology and Microbiology (2012). – About us. The Republican Research and Practical Center for Epidemiology and Microbiology, Minsk, Belarus. Available at: www.belriem.by/en/about-us (accessed on 12 December 2017).

101. International Science & Technology Center (ISTC) (2012). – Belarussian Research Institution for Epidemiology and Microbiology (RIEM). ISTC, Minsk, Belarus. Available at: www.istc.int/en/institute/7985 (accessed on 12 December 2017).

102. Veterinary and Agrochemical Research Centre (CODA–CERVA) (2012). – CODA–CERVA: plant and scientific equipment. CODA–-CERVA, Brussels, Belgium. Available at: www.aphaea.eu/partners/coda-cerva (accessed on 12 December 2017).

103. Fondation Mérieux (2016). – Inauguration of Charles Mérieux Infectiology Center of Brazil in Rio Branco. Fondation Mérieux, Lyon, France. Available at: www.fondation-

merieux.org/en/news/inauguration-of-charles-merieux-infectiology-center-of-brazil-in-rio-branco/ (accessed on 12 December 2017).

104. Petrunov B. (2008). – Letter to the chairman: Bulgarian delegation, 3 pp. Available at: https://unoda-web.s3-accelerate.amazonaws.com/wp-content/uploads/assets/media/BD9C86E6514AFEF2C12574B200362A98/file/BWC_MSP_2008_MX-Statement-Bulgaria-080818-PM.pdf (accessed on 12 December 2017).

105. United States Department of Defense (US DoD) (2011). – DoD Chemical and Biological Defense Program Annual Report to Congress. Federation of American Scientists (FAS), Washington, DC, United States of America, 15 pp. Available at: https://fas.org/irp/threat/cbw/cbd-2011.pdf (accessed on 12 December 2017).

106. Willyard C. (2009). – Biosafety bungle leads to bird flu contamination. *Nature Medicine*, **15** (4), 349. doi:10.1038/nm0409-349a.

107. Ingalls L. (2004). – Operating, maintaining, and certifying BSL-3 and -4 Labs: lessons learned at the Canadian Science Centre in Winnipeg. Tradeline, Orinda, Canada. Available at: www.tradelineinc.com/reports/2004-10/operating-maintaining-and-certifying-bsl-3-and-4-labs (accessed on 26 September 2018).

108. Simon Fraser University (SFU) (2012). – The Pantophlet Laboratory. SFU, Burnaby, Canada. Available at: www.sfu.ca/~rpa19/researchpage.htm (accessed on 12 December 2017).

109. Public Health Agency of Canada (2012). – National Microbiology Laboratory (NML). Available at: www.canada.ca/en/public-health/programs/national-microbiology-laboratory.html (accessed on 26 September 2018).

110. Cryanoski D. (2017). – Inside the Chinese lab poised to study world's most dangerous pathogens. *Nature*, **542** (7642), 399–400. doi:10.1038/nature.2017.21487.

111. Wang Q. (trans.) (2003). – SARS lab in safety query. Available at: www.china.org.cn/english/2003/Oct/78627.htm (accessed on 12 December 2017).

112. Hottes A.K., Rusek B. & Sharples F. (2012). – Paths from assessments to functional labs (breakout sessions). *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). National Academies Press, Washington, DC, United States of America, 39–80. Available at: www.nap.edu/read/13315/chapter/7 (accessed on 8 October 2018).

113. World Health Organization (WHO) Bulletin (2009). – Labs form a new front against deadly pathogens. *Bull. WHO*, **87** (4), 245–324. Available at: www.who.int/bulletin/volumes/87/4/09-010409/en/ (accessed on 12 December 2017).

114. Kimball D. (2011). – Chemical and biological weapons status at a glance. Arms Control Association, Washington, DC, United States of America. Available at: www.armscontrol.org/factsheets/cbwprolif (accessed on 26 September 2018).

115. Nuclear Threat Initiative (NTI) (2012). – China: biological country profile. NTI, Washington, DC, United States of America. Available at: www.nti.org/country-profiles/china/biological/ (accessed on 12 December 2017).

116. Wu W., Lee L., Chen W., Yang S., Wu H., Shih W. & Kuo S.H. (2007). – Development of laboratory biosafety management: the Taiwan experience. *Appl. Biosaf.*, **12** (1), 18–25. doi:10.1177/153567600701200104.

117. Gobierno de Colombia: Instituto Nacional de Salud (INS). (2017). – Virologia. Gobierno de Colombia: INS, Bogota, Colombia. Available at: www.ins.gov.co/TyS/examenes-de-interes-en-salud-publica/Paginas/Virologia.aspx (accessed on 26 September 2018).

118. Ekaza E., Kouassi N'Guessan R., Kacou-N'Douba A., Aka N., Kouakou J., Le Vacon F., Altare F., Potel G. & de-La-Cochetière M.-F. (2013). – Emergence in Western African countries of MDR-TB, focus on Côte d'Ivoire. *Biomed. Res. Int*., 2013, Article ID 426709, 9 pp. doi:10.1155/2013/426709.

119. Global Biodefense (2012). – Europe CBRN centres of excellence seeking proposals. Global Biodefense, Seattle, Washington, United States of America. Available at: http://globalbiodefense.com/2012/03/06/europe-cbrn-centres-of-excellence-seeking-proposals/ (accessed on 12 December 2017).

120. Krebs M. (2003). – Individual report. *In* Cuban biotechnology: a firsthand report (G. Baker, ed.). Center for Defense Information, Washington, DC, United States of America, 14–23.

121. Wilhelm C. (2003). – Individual report. *In* Cuban biotechnology: a firsthand report (G. Baker, ed.). Center for Defense Information, Washington, DC, United States of America, 26–31.

122. Steinbruner J. (2003). – Individual report. *In* Cuban biotechnology: a firsthand report (G. Baker, ed.). Center for Defense Information, Washington, DC, United States of America, 32–33.

123. Warrick J. (2017). – Microbes by the ton: officials see weapons threat as North Korea gains biotech expertise. *Washington Post*, 10 December 2017. Available at: www.washingtonpost.com/world/national-security/microbes-by-the-ton-officials-see-weapons-threat-as-north-korea-gains-biotech-expertise/2017/12/10/9b9d5f9e-d5f0-11e7-95bf-df7c19270879_story.html?noredirect=on&utm_term=.de7e4b405e87 (accessed on 26 September 2018).

124. Lee Y.H., Yoon S.J., Kim Y.A., Yeom J.W. & Oh I.H. (2013). – Overview of the burden of diseases in North Korea. *J. Prev. Med. Public Health*, **46** (3), 111–117. doi:10.3961/jpmph.2013.46.3.111.

125. Bork K.H., Halkjaer-Knudsen V., Hansen J.S. & Heegaard E.D. (2007). – Biosecurity in Scandinavia. *Biosecur. Bioterror.*, **5** (1), 62–71. doi:10.1089/bsp.2006.0026.

126. Koenen F., Uttenthal Å. & Meindl-Böhmer A. (2007). – Real-time laboratory exercises to test contingency plans for classical swine fever: experiences from two national laboratories. *Rev. Sci. Tech. Off. Int. Epiz.*, **26** (3), 629–638. doi:10.20506/rst.26.3.1769.

127. Institute of Medicine (US) Committee to Review the Department of Defense Global Emerging Infections Surveillance and Response System (2001). – 5 GEIS at Naval Medical Research Unit 3, Egypt. *In* Perspectives on the Department of Defense Global Emerging Infections Surveillance and Response System: a program review (P.S. Brachman, H.C. O'Maonaigh, R.N. Miller, eds). National Academies Press (US), Washington, DC, United States of America. Available at: www.ncbi.nlm.nih.gov/books/NBK223705/ (accessed on 26 September 2018).

128. Nuclear Threat Initiative (NTI) (2012). – The biological threat: germs don't respect borders, so biological threats—manmade and naturally occurring—can quickly have global impacts. NTI, Washington, DC, United States of America. Available at: www.nti.org/learn/biological/ (accessed on 26 September 2018).

129. Ethiopian Ministry of Agriculture: Animal and Plant Health Regulatory Directorate (2010). – Ethiopian animal health year book 2009–2010, 63 pp. Ministry of Agriculture, Addis Ababa, Ethiopia. Available at: www.fao.org/fileadmin/user_upload/drought/docs/Ethiopian%20Animal%20Health%20Year%20Book%202009-%2020101.pdf (accessed on 12 December 2017).

130. World Health Organization (WHO) Regional Office Africa (2015). – WHO supports Ethiopia to obtain biosafety level 3 mobile laboratory. WHO Regional Office Africa, Brazzaville, Republic of Congo. Available at: www.afro.who.int/news/who-supports-ethiopia-obtain-biosafety-level-3-mobile-laboratory (accessed on 13 December 2017).

131. Finnish Food Safety Authority (EVIRA) (2012). – About us. EVIRA, Helsinki, Finland. Available at: www.evira.fi/en/about-evira/about-us/ (accessed on 12 December 2017).

132. United Nations Office at Geneva (UNOG) (2017). – Revised forms for the submission of confidence building measures. Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, 10 April 1972. UNOG, Geneva, Switzerland, 22 pp. Available at: www.unog.ch/80256EDD006B8954/(httpAssets)/46173D981857D251C125810100487906/$file/BWC_CBM_2017_Finland.pdf (accessed on 12 December 2017).

133. Fondation Mérieux (2011). – Jean Mérieux BSL-4 Laboratory. Fondation Mérieux, Lyon, France. Available at: www.fondation-merieux.org/en/what-we-do/enhancing-research-capabilities/research-laboratories/jean-merieux-inserm-p4-laboratory/ (accessed on 12 December 2017).

134. Comité français d'accréditation (Cofrac) (2010). – Rapport d'activité 2010 (2010 Annual Report). Cofrac, Paris, France. Available at: www.cofrac.fr/communication/rapports/Rapport_2010.pdf (accessed on 12 December 2017).

135.The Network of Animal Disease Infectiology Research Facilities (NADIR) (2009). – Concept and objectives. NADIR, Nouzilly, France. Available at: www.nadir-project.eu/The-project/Concept-and-objectives (accessed on 12 December 2017).

136. Soares J.M. (2012). – The birth of a laboratory. United States Army. Available at: www.army.mil/article/82553/The_Birth_of_a_Laboratory (accessed on 13 December 2017).

137. Kneist S. (2007). – Genlabor mit höchster gefahrenstufe (Genlabor with highest security level). Der Tagesspiegel, Berlin, Germany. Available at: www.tagesspiegel.de/berlin/genlabor-mit-

hoechster-gefahrenstufe/963614.html (accessed on 12 December 2017).

138. Riedel S. (2004). – Biological warfare and bioterrorism: a historical review. *Proc. Bayl. Univ. Med. Cent.*, **17** (4), 400–406. doi:10.1080/08998280.2004.11928002.

139. Gresz-Seregdy A. (2011). – Hungarian biosafety laboratory. *HČJZ*, **7** (28), 1 p. Available at: https://hcjz.hr/index.php/hcjz/article/viewFile/359/351 (accessed on 12 December 2017).

140. Global Biodefense (2013). – India completes first biodefense level 4 lab. Global Biodefense, Seattle, Washington, United States of America. Available at: http://globalbiodefense.com/2013/03/11/india-completes-first-biodefense-level-4-lab/ (accessed on 12 December 2017).

141. Nature (2007). – India gets high-security lab for human diseases [news in brief]. *Nature* **449** (7163), 649. doi:10.1038/449649e.

142. Biosafe Lab Pvt Ltd (2017). – Biosafety lab. Biosafe Lab Pvt Ltd, New Dehli, India. Available at: www.indiamart.com/biosafelabindia/biosafety-lab.html (accessed on 13 December 2017).

143. Sendow I. (2011). – The development of biosafety and biosecurity in an Indonesian veterinary laboratory. Indonesian Research Center for Veterinary Science (IRCVS), Jakarta, Indonesia, 28 pp. Available at: https://absaconference.org/pdf54/SessionIV-SendowGriffin.pdf (accessed on 12 December 2017).

144. Farnia P., Masjedi M.R. […] M. & Velayati A.A. (2003). – The results of three years surveillance on sputum smear microscopy in 285 district and regional tuberculosis laboratories of Iran. *Tanaffos*, **2** (5), 29–36. Available at: www.tanaffosjournal.ir/files_site/paperlist/r_529_120927090121.pdf (accessed on 12 December 2017).

145. United States Central Intelligence Agency (CIA) (2007). – Iraq WMD 2004: Biological warfare. US CIA, Langley, Virginia, United States of America.

146. Nuclear Threat Initiative (NTI) (2015). – Libya: biological country profile. NTI, Washington, DC, United States of America. Available at: www.nti.org/learn/countries/libya/biological/ (accessed on 11 December 2017)./

147. The Biological and Toxin Weapons Convention (2011). – Report by Ireland in accordance with the final declaration of the Third Review Conference of the parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction. The Biological and Toxin Weapons Convention, Bradford, Yorkshire, United Kingdom, 13 pp. Available at: www.opbw.org/cbms/annual_cbms/Ireland_cbm_2007.pdf (accessed on 12 December 2017).

148. Israel Institute for Biological Research (IIBR) (2009). – Biological sciences. IIBR, Ness-Ziona, Israel. Available at: www.iibr.gov.il/Biological-Sciences.aspx (accessed on 12 December 2017).

149. Network of Animal Disease Infectiology Research Facilities (NADIR) (2009). – Kimron Veterinary Institute. NADIR, Nouzilly, France. Available at: www.nadir-project.eu/Call-for-access/Open-facilities-available-for-access/Kimron-Veterinary-Institute (accessed on 12 December 2017).

150. Virtual Biosecurity Center (2010). – Italy: National Institute of Infectious Diseases. Virtual Biosecurity Center, Washington, DC, United States of America. Available at: http://virtualbiosecuritycenter.org/governments/italy (accessed on 12 December 2017).

151. National Institute of Infectious Disease (INMI) (2012). – Ricerca. INMI, Candiolo, Italy. Available at: www.inmi.it/ (accessed on 12 December 2017).

152. Williams P. & Wallace D. (1989). – Unit 731: Japan's secret biological warfare in World War II. Free Press, New York, United States of America, 303 pp.

153. Sugishima M. (2003). – Aum Shinrikyo and the Japanese law on bioterrorism. *Prehosp. Disaster Med.*, **18** (3), 179–183. doi:10.1017/S1049023X00001023.

154. Luxembourg Times (2015). – New facilities for Luxembourg Health Institute, 5 May 2015. Luxembourg Times. Luxembourg. Available at: www.wort.lu/en/luxembourg/esch-alzette-new-facilities-for-luxembourg-health-institute-55487de00c88b46a8ce58a5d (accessed on 12 December 2017).

155. Kassenova T. (2011). – Policy analysis brief. 1540 in practice: challenges and opportunities for Southeast Asia. The Stanley Foundation, Muscatine, Iowa, United States of America, 16 pp. Available at: www.stanleyfoundation.org/publications/pab/KassenovaPAB611.pdf (accessed on 12 December 2017).

156. Global Biodefense (2012). – Malaysia Defence Ministry reviewing Bioweapons Bill. Global Biodefense, Seattle, Washington, United States of America. Available at: http://globalbiodefense.com/2012/04/26/malaysia-defence-ministry-reviewing-bioweapons-bill/ (accessed on 13 December 2017).

157. European Virus Archive goes global (EVAg) (2017) – CICM – ML: Associated Partner, BSL3, non EU. EVAg, Marseille, France. Available at: www.european-virus-archive.com/associated-partner9 (accessed on 13 December 2017).

158. Avery D.H. (2010). – The North American plan for avian and pandemic influenza: a case study of regional health security in the 21st century. *Global Hlth Gov.*, **3** (2), 1–26. Available at: https://blogs.shu.edu/ghg/2010/04/01/the-north-american-plan-for-avian-and-pandemic-influenza-a-case-study-of-regional-health-security-in-the-21st-century/ (accessed on 13 December 2017).

159. Temsamani K. (2010). – Report of the training course. First Moroccan Biosafety Association training course on biological risk management. Moroccan Biosafety Association, Tetouan, Morocco, 9 pp. Available at: www.mobsa.org/doc/Report%20Tetouan.pdf (accessed on 13 December 2017).

160. Amdiouni H., Faouzi A., Fariat N., Hassar M., Soukri A. & Nourlil J. (2012). – Detection and molecular identification of human adenoviruses and enteroviruses in wastewater from Morocco. *Lett. Appl. Microbiol.*, **54** (4), 359–366. doi:10.1111/j.1472-765X.2012.03220.x.

161. Klein M. (2009). – Dutch high containment facilities for biopreparedness and outbreak response. National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands. Available at: www.unog.ch/80256EDD006B8954/(httpAssets)/8DFFEEE4D714FDAAC125768E0055933D/$file/MSP+-+NL+RIVM+(101209)+ver4.pdf (accessed on 13 December 2017)

162. RKD Architects (2012). – Insights: Netherlands RIVM appointment. RKD Architects, Dublin, Ireland. Available at: www.rkdarchitects.com/insights/article/netherlands-rivm-appointment (accessed on 13 December 2017).

163. New Zealand Ministry for Primary Industries (2012). – Plant Health & Environment Laboratory. New Zealand Ministry for Primary Industries, Wellington, New Zealand. Available at: www.mpi.govt.nz/protection-and-response/laboratories/plant-health-and-environment-laboratory/ (accessed on 13 December 2017).

164. News-Medical (2010). – New multimillion dollar BSL-3 laboratory complex at Nigerian National TB and Leprosy Training Center. News Medical.net, Manchester, United Kingdom. Available at: www.news-medical.net/news/20100618/New-multimillion-dollar-BSL-3-laboratory-complex-at-Nigerian-National-TB-and-Leprosy-Training-Center.aspx?page=2 (accessed on 13 December 2017).

165. Committee for the Assessment of DoD-GEIS Influenza Surveillance and Response Programs (2007). – Chapter 7. Naval

Medical Research Center: detachment Peru: avian and pandemic influenza activities. *In* Review of the DoD-GEIS Influenza Programs: Strengthening Global Surveillance and Response (Committee for the Assessment of DoD-GEIS Influenza Surveillance and Response Programs, eds), The National Academies Press, Washington, DC, United States of America, 147–166. Available at: www.nap.edu/read/11974/chapter/9 (accessed on 30 August 2018).

166. Poland National Institute of Public Health (PZH) (2015). – Kursy BSL-3. PZH, Warsaw, Poland. Available at: www.pzh.gov.pl/en/training-and-courses/kursy-bsl-3/ (accessed on 13 December 2017).

167. Portugal Institute of Molecular Medicine (IMM) (2017). – Biosafety level 3 laboratory. IMM, Lisbon, Portugal. Available at: https://imm.medicina.ulisboa.pt/en/servicos-e-recursos/technical-facilities/pathology-laboratory/ (accessed on 13 December 2017).

168. Da-sol K. (2017). – Korea to open first deadly virus biosafety laboratory. *Korea Herald,* Seoul, Republic of Korea. Available at: www.koreaherald.com/view.php?ud=20170316000902 (accessed on 13 December 2017).

169. International Vaccine Institute (IVI) (2008). – First Lady assumes Honorary Presidency of Korea Support Committee for IVI. IVI, Seoul, Republic of Korea. Available at: www.ivi.int/?pageid=19&page_id=12463&uid=108&mod=document (accessed on 13 December 2017).

170. Institut Pasteur Korea (2012). – Home. Institut Pasteur Korea, Gyeonggi-do, Republic of Korea. Available at: www.ip-korea.org/ (accessed on 13 December 2017).

171. Nuclear Threat Initiative (NTI) (2012) – South Korea to ramp up biodefense efforts. NTI, Washington, DC, United States of America. Available at: www.nti.org/gsn/article/south-korea-ramp-biodefense-efforts/ (accessed on 13 December 2017).

172. United Nations Office for Disarmament Affairs (UNODA). (2014). – Romania: confidence building measure return

(covering data for 2013). Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, 10 April 1972, 15 pp. Available at: https://unoda-web.s3-accelerate.amazonaws.com/wp-content/uploads/assets/geneva/BWC_CBM_2014_Romania.pdf (accessed on 13 December 2017).

173. Federal Service for Supervision of Consumer Rights Protection and Human Welfare (2012). – Federal Agency. Federal Service for Supervision of Consumer Rights Protection and Human Welfare, Moscow, Russia. Available at: www.rospotrebnadzor.ru/en/ (accessed on 13 December 2017).

174. European Commission (EC) (2011). – Final report on the 4th task force meeting of the 'Classical Swine Fever' sub-group, Belgrade, Serbia, 6–7 April 2011. EC, Brussel, Belgium, 6 pp. Available at: https://ec.europa.eu/food/sites/food/files/animals/docs/diseases_erad_csfs_report_serbia_0607042011_en.pdf (accessed on 13 December 2017).

175. European Virus Archive Goes Global (EVAg) (2018). – Institute of Virology (IVSAS–SK) Core Partner, BSL3, European Union (EU). Available at: www.european-virus-archive.com/partner8 (accessed on 13 December 2017).

176. University of Ljubljana Institute of Microbiology and Immunology (2018). – IC BSL-3+ Infrastructural centre for research of biosafety level 3 pathogenic microorganisms. University of Ljubljana Institute of Microbiology and Immunology. Available at: www.imi.si/raziskovalna-dejavnost-en/tekoci-projekti/infrastructural-centre/ic-bsl-3-infrastructural-centre-for-research-of-biosafety-level-3-pathogenic-microorganisms (accessed on 13 December 2017).

177. National Health Laboratory Service (2012). – National Institute for Communicable Diseases: Services. National Health Laboratory Service, Johannesburg, South Africa. Available at:

www.nicd.ac.za/?page=services&id=51 (accessed on 13 December 2017).

178. Loyd G. (2009). – European network of P4 laboratories (ENP4 Lab) work package 4: report checklist biosafety and biosecurity harmonisation. Health Protection Agency, London, United Kingdom, 19 pp. Available at: www.euronetp4.eu/Docs/Report%20Checklist.pdf (accessed on 13 December 2017).

179. Network of Animal Disease Infectiology Research Facilities (NADIR) (2009). – Centro de Investigación en Sanidad Animal/Animal Health Research Center (CISA). NADIR, Nouzilly. Available at: www.nadir-project.eu/Call-for-access/Open-facilities-available-for-access/Centro-de-Investigacion-en-Sanidad-Animal-CISA (accessed on 13 December 2017).

180. Olero L.E.M. & Escartín F.S. (2006). – Red de Laboratorios de Alerta Biólogica. Laboratorio, Madrid, Spain, 4 pp. Available at: www.colvema.org/PDF/RELAB.pdf (accessed on 13 December 2017).

181. Clínica Universidad de Navarra (2012). – Laboratorio de Bioseguridad. Clinica Universidad de Navarra, Navarre. Available at: www.cun.es/la-clinica/servicios-medicos/departamento/microbiologia-clinica/laboratorio-bioseguridad (accessed on 13 December 2017).

182. Fernandez M. (2003). – Barcelona abre el Cresa, el segundo centro de investigación en sanidad animal en España. Fundación Eroski, Elorrio. Available at: www.consumer.es/seguridad-alimentaria/ciencia-y-tecnologia/2003/09/23/8425.php (accessed on 13 December 2017).

183. Kallings I. (2012). – E5: high containment laboratories – Sweden case study. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). The National Academies Press, Washington, DC, United States of America, 165–168. Available

at: www.nap.edu/read/13315/chapter/23 (accessed on 30 September 2017).

184. Thelaus J., Lindberg A., Thisted Lambertz S., Byström M., Forsman M., Lindmark H., R. Knutsson, V. Båverud, A. Bråve, P. Jureen, A. Lundin Zumpe A & Ö. Melefors. (2017). – Network experiences from a cross-sector biosafety level-3 laboratory collaboration: a Swedish forum for biopreparedness diagnostics. *Health Secur.* **15** (4), 384–391. doi:10.1089/hs.2016.0082.

185. Smittskyddsinstitutet (Swedish Institute for Communicable Disease Control) (2012). – Welcome to Smittskyddsinstitutet. Smittskyddsinstitutet, Stockholm, Sweden. Available at: www.smittskyddsinstitutet.se/in-english/ (accessed on 13 December 2017).

186. Schweizerische Eidgenossenschaft (Swiss Federation) (2012). – Das Labor Spiez (The Spiez Laboratory). Swiss Federation, Bern, Switzerland. Available at: www.labor-spiez.ch/de/lab/index.htm (accessed on 13 December 2017).

187. Le Duc J. (2012). – Requirements for and challenges associated with BSL-4 labs (plenary session). *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). National Academies Press, Washington, DC, United States of America, 81: Table 8-1. Available at: www.nap.edu/read/13315/chapter/10 (accessed on 8 October 2018).

188. Pauli U., Kündig M., Haldemann F. & Summermatter K. (2011). – Installation of BSL-3 laboratories and ABSL-3 animal experimentation rooms in a preexisting BSL-3Ag facility: Design, implementation, validation, time requirements, and costs. *Appl. Biosaf.*, **16** (2), 103–111. Available at: http://journals.sagepub.com/doi/abs/10.1177/153567601101600206 (accessed on 13 December 2017).

189. Buchser C. (2010). – Killer viruses bound for the Bernese Oberland. SwissInfo, Bern, Switzerland. Available at:

www.swissinfo.ch/eng/science_technology/Killer_viruses_bound_for_the_Bernese_Oberland.html?cid=15348372 (accessed on 13 December 2017).

190. Evolva Holding S.A. (2017). – Evolva sells EV-035 series to emergent biosolutions. Available at: www.evolva.com/press-release/evolva-sells-ev-035-series-to-emergent-biosolutions/ (accessed on 13 December 2017).

191. Federal Office for Civilian Protection (2011). – Spiez Laboratory Annual Report 2010. Swiss Confederation, Spiez, Switzerland, 40 pp. Available at: www.labor-spiez.ch/pdf/en/dok/jab/Jahresbericht_LS_2010_e.pdf (accessed on 13 December 2017).

192. Gordon J. (2007). – Syria's bio-warfare threat: an interview with Dr Jill Dekker. New English Review, Nashville, Tennessee, United States of America. Available at: www.newenglishreview.org/custpage.cfm/frm/13108/sec_id/13108 (accessed on 13 December 2017).

193. Fondation Mérieux (2013). – The President of Tajikistan inaugurates National Reference Laboratory for Public Health designed by Fondation Mérieux experts. Available at: www.fondation-merieux.org/en/news/the-president-of-tajikistan-inaugurates-national-reference-laboratory-for-public-health-designed-by-fondation-merieux-experts/ (accessed on 13 December 2017).

194. Ifakara Health Institute (2016). – Biosafety levels II & III laboratories. Available at: http://ihi.or.tz/biosafety-level-3-laboratory/ (accessed on 13 December 2017).

195. Global Biodefense (2014). – New BSL-3 facility in Caribbean will boost regional biosecurity. Available at: http://globalbiodefense.com/2014/05/26/new-bsl-3-facility-in-caribbean-will-boost-regional-biosecurity/ (accessed on 13 December 2017).

196. Institut Pasteur de Tunis (2018). – Accueil. Available at: www.pasteur.tn/ (accessed on 2 October 2018).

197. Öktem H.A. (2012). – E6: country overview for Turkey: biosecurity laws and regulations in Turkey. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). The National Academies Press, Washington, DC, United States of America, 169–170. Available from: www.nap.edu/read/13315/chapter/24 (accessed on 26 September 2018).

198. College of Health Sciences, Makerere University (2017). – BSL3 (mycobacteriology) lab. Mbl.Mak.Ac.Ug. Available at: http://mbl.mak.ac.ug/index.php?option=com_content&view=article&id=17&Itemid=120 (accessed on 13 December 2017).

199. Kysil O. & Komisarenko S. (2012). – E7: high containment laboratories in Ukraine: local resources and regulations. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds.), The National Academies Press, Washington, DC, United States of America, 171–174. Available from: www.nap.edu/read/13315/chapter/25 (accessed on 13 December 2017).

200. Nuclear Threat Initiative (NTI) (2015) – United Arab Emirates. Available at: www.nti.org/learn/countries/united-arab-emirates/ (accessed on 13 December 2017).

201. Davison N. & Lentzos F. (2012). – E8: high containment laboratories – UK case study. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). The National Academies Press, Washington, DC, United States of America, 175–192. Available at: www.nap.edu/read/13315/chapter/26 (accessed on 13 December 2017).

202. United Kingdom House of Commons (HC) (2008). – HC 360 I. Biosecurity in UK research laboratories, Innovation, Universities, Science and Skills Committee, sixth report of session

2007–2008, Volume 1. HC, London, United Kingdom, 61 pp. Available at: https://publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf (accessed on 13 December 2017).

203. United Kingdom Parliamentary Office of Science and Technology (2001). – Bio-terrorism. *POSTnote*, **166**, 4 pp. Available at: http://researchbriefings.parliament.uk/ResearchBriefing/Summary/POST-PN-166 (accessed on 13 December 2017).

204. United States Homeland Security (2015). – National Biodefense Analysis and Countermeasures Center. United States Homeland Security, Washington, DC, United States of America. Available at: www.dhs.gov/science-and-technology/national-biodefense-analysis-and-countermeasures-center (accessed on 13 December 2017).

205. United States Research Council Staff (2012). – E9: United States high-containment biological labs and regulations. *In* Biosecurity challenges of the global expansion of high-containment biological laboratories (Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories, eds). The National Academies Press, Washington, DC, United States of America, 193–204. Available at: www.nap.edu/read/13315/chapter/27 (accessed on 26 September 2018).

206. WSP Parsons Brinckerhoff (2015). – University of Texas Medical Branch BSL4 laboratory: Shope Laboratory. WSP Parsons Brinckerhoff, New York, United States of America. Available at: www.wsp-pb.com/en/WSP-USA/What-we-do-USA/Projects/University-of-Texas-Medical-Branch-BSL4-Laboratory---Shope-Laboratory/ (accessed on 13 December 2017).

207. United States Army Medical Research Institute of Infectious Diseases (USAMRIID) (2015). – Biodefense solutions to protect our nation. USAMRIID, Frederick, Maryland, United States of

America. Available at: www.usamriid.army.mil/ (accessed on 13 December 2017).

208. Texas Biomedical Research Institute (2016). – Texas Biomedical Research Institute, San Antonio. Available at: www.txbiomed.org/ (accessed on 13 December 2017).

209. Crowley M. (2001). – Disease by design: de-mystifying the biological weapons debate. British American Security Information Council, London, United Kingdom, & Washington, DC, United States of America, 75 pp.

210. Japan International Cooperation Agency (JICA) (2011). – Japan supports capacity development for laboratory network in Vietnam [press release]. JICA, Tokyo, Japan, 2 pp. Available at: www.jica.go.jp/vietnam/office/information/press/pdf/press2010/20111 01_02e.pdf (accessed on 13 December 2017).

Appendix

State	BSL-4 laboratories	BSL-3 laboratories	BW/BDP(85)	Activities/additional information
Algeria	N/A	1 in 2014 (86)	Evidence of past offensive research, but not of production (83)	Virology in association with Institute Pasteur (86)
Argentina	1 (87)	1 in 1998 (88) and between 2 and 9 now (89, 90)	N/A	Human pathogens (89)
Australia	3 (82)	More than 40 (91)	BDP (92)	Epidemics, tuberculosis (93)
Austria	1 under discussion as of 2009 (94)	At least 1 (95)	BDP (42, 96)	The BSL-3 lab specialises in prion diseases (95)
Azerbaijan	N/A	1 under construction (97)	N/A	Disease surveillance, United States support (97)
Bangladesh	0	1 in 2010 (98)	N/A	Uses CDC guidelines. Endemic diseases (TB, HIV, influenza) with IP (99)
Belarus	1 (28, 100)	N/A	N/A	HIV, virus research and genetic research (101)
Belgium	0	4, with multiple BSL-3s at one facility (102)	BDP (96)	Animal and human pathogens (102)
Bolivia	0	1 planned (89)	N/A	Planned construction of BSL-3 with ANLIS Laboratory in Argentina (89)
Brazil	Ongoing discussion (70)	12 Public Health Laboratories and 8 Agricultural Laboratories (70, 89)	N/A	Zoonotic disease including avian influenza IP support (70, 103)
Bulgaria	0	Probably 1; the NRLIARD was constructing a BSL-3 facility (104)	BDP (96, 105)	Influenza, hepatitis, other viruses (106)
Cameroon	0	1 in 2003 (86)	N/A	Centre Pasteur, public health and national reference laboratory (86)
Canada	1 (4 BSL-4 laboratories in the same facility) (107)	More than 3 facilities and at least 32 BSL-3 laboratories in one facility (98,107). Latest built in 2012 (108)	Former offensive programme (ended 1945) (83). Biodefence programme (92)	Public health, disease prevention and control (109)
Central African Republic	0	1 in 2011 (86)	N/A	Arbovirus, haemorrhagic fever viruses with IP (86)
Chile	0	1 (pre-1998) (88, 89)	N/A	Emerging diseases (89)
China	1 (27); plan to build 5–7 more by 2025 (110)	10 before SARS, many more after (111). Currently around 30 are certified (112, 113)	BDP, likely maintains an offensive capability. Allegations that some research has breached the BWC (114, 115)	Public health, vaccines (110). WHO involvement in lab construction (111). Economic incentives (31)
Chinese Taipei	2: 1 confirmed, 1 unconfirmed (27, 116)	3 Before 2003, 20 by 2005. Prior to 2003, all HCBLs were foreign-built; later domestically with foreign advisors (116)	Possible research programme (83, 114).	Communicable diseases, SARS a priority (116)

Colombia	1 level 3/4 in planning (117)	1 in 2003 (117)	N/A	Public health (117)
Côte d'Ivoire	N/A	1 (118)	N/A	Tuberculosis (118)
Croatia	0	At least 1 (112)	BDP (119)	Human pathogens; there is much international cooperation, partly because of sample analysis costs (112)
Cuba	A few at a single facility that have never been used as such (120, 121)	5 (121)	Probable offensive research (83, 122)	HIV vaccine research (122)
Czech Republic	1 (27)	N/A	BDP (96, 105) biopreparedness (106)	Vaccines (106)
Democratic People's Republic of Korea	N/A	N/A	Offensive research with possible production of agents (83, 123)	Endemic tuberculosis and malaria (124)
Denmark	0	At least 5 in 2009 (125)	BDP (96)	Zoonotic disease (swine flu) (126)
Egypt	1 BSL 3–4 as part of US DoD (11, 127)	A few planned, unclear how many are built (112)	Possible former offensive programme. Not BWC member (128), but seems compliant (114)	To produce vaccines for endemic diseases (112). USA involved in lab construction (11, 127)
Ethiopia	0	2: 1 with USA in 2010 (129), 1 mobile with WHO (130)	N/A	Endemic animal diseases (129)
Finland	0	At least 13, 6 of which are BSL-3+ (131, 132)	BDP (132)	Focus on terrorism and infectious diseases (132)
France	2 (98, 133)	More than 12 BSL-3 (134). Recent construction (135)	Former offensive programme (indigenous programme ended in 1934, and programme under German occupation ended in 1945) (83). BDP (96)	Infectious diseases, host–pathogen interactions (133, 135)
Gabon	1 (27, 94)	First built in1982 (later became the BSL-4 facility) (112). Probably more, but N/A	No evidence of BDP (112)	Endemic and emerging diseases, public health, parasitology, etc. (112)
Georgia	0	At least 1 with US support, probably a few in same building (136)	N/A	Infectious diseases, both animal and human (136)
Germany	6: 4 are operational, 1 planned, and 1 under construction (27). 8 self-reported (9)	At least 97 (8), in 2007 there were 8 in Berlin alone (137)	Former offensive programme (138). BDP, military biodefence budget has doubled in the last decade (8)	Ranks fifth globally and first in Western Europe for life sciences and biotechnology (8)
Ghana	0	1 in 1999 (86)	N/A	Emerging pathogens (86)
Greece	0	2 (98)	BD (96)	Both BSL-3 laboratories are in hospitals, they are likely to specialise in human pathogens (98)
Hungary	1, but operated under BSL-3 conditions (139); 2 self-reported (9)	Unclear. 8 NLRs that would require BSL-3 facilities (139)	BDP (105)	Emergence and re-emergence of pathogens. Staff often trained in other EU laboratories (139)

India	4 (27, 140, 141)	Approximately 6 (8). Private company offering turnkey laboratory construction (142)	BDP (140)	One of the biggest global vaccine producers (8)
Indonesia	0	2 for zoonotic diseases (first in 2007) (143), plans to build 'numerous research facilities' (31)	N/A	Tuberculosis and avian influenza are endemic; the BSL-2 laboratories were proving insufficient (143)
Iran	0	Probably a few, but none listed as such (144)	Probable BDP. Dual-use R&D, no evidence of BWC non-compliance (114)	Tuberculosis is a high priority (144)
Iraq	1 former (145)	N/A, but most likely none (unlikely following US involvement)	Former offensive programme, dismantled before 2003 (114)	Production of foot and mouth vaccine, later for BW agent production (146)
Ireland	0, and none is planned (147)	Approximately 34 (147)	Possible former programme. No BDP, but the Department of Defence undertakes training on BW protection (147)	Public health and monitoring for marine biotoxins (147)
Israel	N/A, but probably the IIBR (148)	1 for animal diseases, but no further information (149)	Offensive research programme with possible production (83). BDP (23). Not a member of the BWC (128)	Vaccine production, disease detection, etc. Much joint research with the USA, including the CDC and US Army Medical Research and Development Command (148)
Italy	2 (27, 94)	5 within one of their BSL-4 facilities, at least 2 more; information is lacking (150)	BDP (96),	Research on human illnesses and vaccines (151)
Japan	2 that do not operate on BSL-4 level due to public opposition (27)	Approximately 200 (8)	Former BW programme (36,152). BDP (8)	One of the biggest global vaccine producers, sees bioterrorism as a major threat (8, 153)
Kenya	0	Approximately 6 (8)	No BDP (8)	Malaria and AIDS, and animal vaccine production, USA involved in lab construction (8)
Libya	N/A	N/A	Former offensive programme, ended 2003 (83, 114)	N/A
Luxembourg	0	At least one, which opened in 2007 (154)	BDP (96),	Specifically focused on the H5N1 influenza threat (154)
Madagascar	0	1 in 2008 (86)	N/A	Virology with IP (86)
Malaysia	Indication that they might build a BSL-4 in the future (155)	At least 3 with more planned (155)	BDP (156)	Economic incentive through biotechnology investment (31)
Mali	0	1 in 2005 (157)	N/A	Built with IP support, for infectious endemic disease (157)
Mexico	0	4, and 14 small ones in the same facility (89)	In cooperation with Pan-American biodefence, no evidence of own programme (158)	Biomedical research and some institutes especially for respiratory diseases (89)
Morocco	0	At least 3 (159)	N/A	Public health, endemic disease (160)
Netherlands	1 (58)	A few are mentioned but no total numbers; at least one mobile (161) and currently	BDP (96),	Biopreparedness and response to outbreaks, especially emerging diseases (161)

		building an 'extensive suite' of them (162)		
New Zealand	0	At least 1 (163)	N/A	Mostly focused on pests and diseases in plants (163)
Nigeria	0	1 built in 2010 (164)	N/A	Endemic disease, especially TB (164)
Norway	0	At least 2 before 2009 (125)	N/A	N/A
Pakistan	0	2 current and more planned (72)	Possible (83)	Diagnosing and treating endemic diseases such as TB (72)
Panama	0	2 (89)	N/A	N/A
Peru	1 BSL-3–4 as part of US DoD (11)	3 (89, 165)	N/A	Especially diseases that may threaten military operations in the region. USA involved in laboratory construction. The report also describes 'disease surveillance programs' in 10 South American nations (11)
Philippines	0	1 (46)	N/A	Public health and concerned about bioterrorism. (Mujahedeen Poisons Handbook identifying possible BW was found in Mindanao, Philippines) (46)
Poland	0	1 (166)	BDP (105)	Human pathogens (166)
Portugal	0	At least 1 (167)	N/A	Public health, especially TB and HIV (167)
Republic of Korea	1 ready to open in 2017 (168). Some BSL-3–4 (3+) in conjunction with the IVI (169)	At least 1 officially validated by the Korean Centers for Disease Control and Prevention in 2006 (170)	BDP (171)	Economic, through biotechnology investment (31), agent identification (170), and endemic diseases and vaccination production (169). Very concerned with bioterrorism (171)
Romania	0	At least 1 facility (172)	BDP (96, 105)	Diagnostic and applied research for public health (172)
Russia	3 (69)	84 regional offices and Hygienic and Epidemiological Centers, 29 research institutes, 14 anti-plague control stations (173). 19 are WHO Collaborating Centers. Difference in the Russian classification system, but many are equivalent of BSL-3 (69)	Former offensive (ended 1992). BDP. Likely that some current research goes beyond 'legitimate defence activities' (83)	Public health (173)
Senegal	0	1 in 2000 (86)		Virology laboratory with IP (86)
Serbia-Montenegro	0	At least 1 (174)	BDP (96)	Zoonotic diseases, including swine flu (174)
Singapore	1 (27). A 2011 article states that Singapore's BSL-4 Defense Science Organization was a BSL-3 operating at BSL-4 standards (152)	10, proliferation is recent (113)	N/A	Economic, through biotechnology investment (31)

Slovak Republic	0	1 (175)	BDP (105)	Zoonotic viruses, especially tick- and rodent-borne (175)
Slovenia	1 BSL-3+ (176)	N/A	N/A	Epidemiology and immunopathogenesis studies (176)
South Africa	1 (27)	Approximately 6 (8)	Former offensive (ended 1993) (88); BDP (8)	Public health and endemic diseases including 'respiratory and diarrheal diseases, meningitis, HIV/AIDS, TB, and malaria' (177)
Spain	1 (28,178), although the lab claims it is 3+ (179)	More than 7 for the Ministry of Defence (180). Only 3 BSL-3 mentioned (181, 182)	BDP; 9/11 and biosecurity cited as reasons (96), (180)	The BSL-4 lab is a veterinary lab focusing on animal and zoonotic diseases (178)
Sudan	0	N/A	Possible interest in offensive research (83)	N/A
Sweden	1 (27)	40 (125, 183)	BDP (184)	To monitor, protect and prevent against communicable diseases (185)
Switzerland	3, one is a glove box (27, 186, 187). There is also an additional BSL-3Ag facility (188)	At least 26 (8)	BDP (189,190)	Biodefence and public health (191)
Syria	N/A	N/A. Syrian Scientific Research Council seems to oversee sensitive biological research (192)	Offensive research programme with possible agent production. Noncompliant with BWC (83). Not a BWC member state and President Assad hinted at BW capability in 2010 (128)	May have help from Russia (and previously from the USSR), Democratic People's Republic of Korea, Iran and the former regime in Iraq (192)
Tajikistan	0	1 (193)	N/A	TB, built with IP (193)
Tanzania	0	1 (194)	N/A	TB and haemorrhagic fevers (194)
Thailand	1 BSL 3–4 as part of US DoD (11)	23 human health laboratories (including 7 mobile units), and 4 animal laboratories (71)	N/A	USA involvement in lab construction (11)
Trinidad and Tobago	0	1 (195)	N/A	Endemic diseases such as chikungunya, global threats such as Ebola and MERS (195)
Tunisia	0	1 (196)	N/A	IP support (196)
Turkey	0	7 (197)	BDP (96)	GMOs, agricultural and veterinary issues, disease surveillance and prevention (197)
Uganda	0	1 (198)	N/A	TB (198)

Ukraine	0	3 have BSL-3 certification (199). Unclear how many work with BSL-3 and -4 agents. Legally, 2 may work with 'group 1' pathogens and 402 can work with group 2. Technically these are different criteria, but they may work with the same or similar agents	Has participated in proposals for European CBRN projects, but no evidence of involvement or of own programme (119)	Human pathogens (in cooperation with the USA), food and agriculture laboratories (199)
United Arab Emirates	0	A few built in 2010 at DuBiotech for pharmaceutical companies (200)	N/A	Biotech industry, research (200)
United Kingdom	9 (201)	Approximately 600. 150 are operated by research institutes, 150 by universities, 75 by private companies, 170 by the NHS (201). Other figures are lower (8)	Former offensive programme (ended 1956) (83). Two BDP (civilian and military) (8)	'Existing and emergent infectious diseases of both humans and animals' (202). Concerned about bioterrorism (203)
United States	15: 14 operational, 1 under construction. According to the US Research Council Staff there are 6 operational and 6 planned or under construction as of September 2011 (27), (38, 204, 205, 206, 207, 208)	1,643 as of 2008 (56)	Former offensive programme (ended 1969), BDP (7). Allegations of questionable biodefence research, including the Jefferson Project, Project Bacchus and Project Clear Vision (209)	National safety, vaccines, medication development, anti-BW terrorism (205). One of the biggest global vaccine producers
Vietnam	0	At least 2 (one under construction in 2011) (155)	N/A	Japan is helping with their second BSL-3 lab (155, 210)

AIDS: acquired immune deficiency syndrome

ANLIS: National Laboratories and Health Institutes Administration

BDP: biodefence programme

BSL: biosafety level

BW: biological weapon

BWC: Biological Weapons Convention

CBRN: Chemical, Biological, Radiological and Nuclear Risk Mitigation

CDC: Centers for Disease Control and Prevention

EU: European Union

GMO: genetically modified organism

HCBL: high-containment biological laboratory

HIV: human immunodeficiency virus

IIBR: Israeli Institute for Biological Research

IP: Institut Pasteur

IVI: International Vaccine Institute

MERS: Middle East respiratory syndrome

N/A: information not available

NHS: National Health Service (UK)

NLR: national reference laboratory

NRLIARD: National Reference Laboratory for Influenza and Acute Respiratory Diseases

R&D: research and development

SARS: severe acute respiratory syndrome

TB: tuberculosis

US DoD: United States Department of Defense

USA: United States of America

USSR: Union of Soviet Socialist Republics

WHO: World Health Organization