The role of laboratories in mitigating the threat of Security Sensitive Biological Agents to animal health and agriculture

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Abstract. The aim of Australia's Security Sensitive Biological Agents (SSBAs) Regulatory Scheme is to limit opportunities for acts of bioterrorism or criminal acts using harmful biological agents. The scheme is based on a two-tiered list of agents, of which many can cause disease in animals and thereby have the potential to significantly impact Australian agricultural industries and the economy. Laboratories handling these agents have clear responsibilities for their biocontainment, biosafety and biosecurity. Importantly, through research and ongoing improvements to diagnostic assays and techniques, these facilities also play an integral role in threat preparedness, mitigation, diagnosis and control of natural, accidental or deliberate outbreaks of disease.

In December 2002, the Council of Australian Governments (COAG) agreed to a national review of the regulation, reporting and security around the storage, sale and handling of hazardous materials, including biological materials. The review was one of several government initiatives in the chemical, biological, radiological and nuclear security domain and formed a part of the broader National CBRN Security Strategy.

The resultant 2006 COAG Report on the Regulation and Control of Biological Agents identified that the regulations in place at the time focused on safety rather than security; and that there was a need to regulate the secure storage, possession, use and transport of security sensitive biological materials. In 2007, COAG agreed to the establishment of a national regulatory scheme for biological agents of security concern, in order to minimise the risk of their use for terrorism or criminal purposes. It was determined that the most effective and efficient means of minimising security risks posed by these materials was to establish a national regulatory scheme comprising a two-tiered list of Security Sensitive Biological Agents (SSBAs).

At a national level, all entities and facilities handling SSBAs must comply with the *National Health Security Act 2007*[1], the *National Health Security Regulations 2018*[2] and the SSBA Standards[3]. The SSBA Standards set out the minimum security requirements for entities and facilities that handle suspected or known SSBAs and deal with risk assessment, risk management, personnel security, physical security, storage, information security, inactivation, decontamination, disposal, transport, and management systems.

High biocontainment facilities by necessity of the materials that they hold must often abide by multiple sets of regulations – in Australia these also include regulations relating to Approved Arrangements (Department of Agriculture, Water and the Environment), Office of the Gene Technology Regulator (Department of Health) and Defence Export Controls (Department of Defence). In meeting all these regulatory requirements there is an underlying need for facilities holding these materials to have a strong biosafety, biosecurity and responsible conduct in life sciences culture, supported by regular and contemporaneous staff training; internal risk assessment by an institutional biosafety committee; security screening of staff, students and visitors; and an independent advisory body for all aspects of biosafety, biosecurity and biocontainment. An international standard developed in 2019; ISO 35001 Biorisk management for laboratories and other related organisations, will further assist laboratories in meeting their obligations[4].

The contribution of laboratories in controlling biothreats is also highlighted internationally, including in the World Organisation for Animal Health (OIE)'s Biological Threat Reduction Strategy (2015)[5]. This strategy identifies the need for security and health sectors to focus on biothreats, defined as accidental or deliberate

release of animal toxins and pathogens, including zoonotic agents. The role of laboratories is highlighted in four of five defined areas in the strategy, including maintaining high levels of biosafety and biosecurity, risk-based assessment (congruent with that of public health laboratories) for biosafety, biosecurity and sample shipment, and enhancing scientific and biosafety practices in developing countries through OIE Laboratory Twinning Programs.

Through meeting the requirements of the SSBA scheme laboratories also contribute to the United Nations Biological and Toxin Weapons Convention (BWC), of which Australia is a State Party. The BWC effectively 'prohibits the development, production, acquisition, transfer, stockpiling and use of biological and toxin weapons and is a key element in the international community's efforts to address the proliferation of weapons of mass destruction'[6]. Compliance with the articles of the convention necessitate laboratory biosafety and biosecurity measures aimed at preventing the accidental exposure to or release of biological agents and preventing their theft or loss or unauthorised possession, whilst also encouraging peaceful use of agents for biological science and technology.

With respect to animal health specifically, the significant representation of animal pathogens on the SSBA lists reflects the potential impacts on Australian livestock, agriculture and the economy through their intentional release. Of the twelve agents on tier 1 SSBA list, two are animal only pathogens, with another four pathogens or toxins recognised as causing disease in animals, and three are known to have a wildlife animal reservoir. Of the eight agents currently on the tier 2 list, five are animal only pathogens, with an additional two recognised as causing disease in animals. Laboratories and other facilities holding these agents have significant responsibility, both in terms of their obligations to safely and securely hold and handle the materials to prevent their misuse, but importantly to also conduct or support essential research for threat preparedness, mitigation and response against these agents, where appropriate resources are available.

A pertinent example of the role of laboratories in mitigating the threat of SSBAs to animals and agriculture is rinderpest. Rinderpest, caused by a tier 1 SSBA (rinderpest virus), was globally eradicated from the livestock populations in May 2011, making it only the second infectious disease (after smallpox, another tier 1 agent) for which this international milestone has been reached. Historically the disease has killed millions of livestock, with resultant impacts on livelihoods and food security. The OIE has a post-eradication 'Vigilance' campaign, of which one of the three objectives is to guide laboratories in the removal of any rinderpest virus-containing materials and stocks. Only four facilities internationally are considered Food and Agricultural Organization (FAO)-OIE approved Rinderpest Holding Facilities (RHF), allowed to handle rinderpest virus containing material (RVCM) and/or vaccine stocks. Significant effort has been invested in working with governments and institutions to raise awareness of the implications of holding RVCM in non-approved facilities and providing guidance on the destruction of such material to prevent its inadvertent or deliberate release. The RHFs hold considerable responsibility, and are therefore under significant international scrutiny, to safely contain the remaining material. Non-RHFs also continue to report to the OIE on suspected RVCM or disease cases, and therefore also have responsibility for countering rinderpest related biothreats.

Beyond ensuring biocontainment, biosafety and biosecurity, laboratories are also essential for preparedness, mitigation and response to biothreats. As an example, African swine fever (ASF) is an important viral disease of domestic and wild pigs, caused by ASF virus, a tier 2 SSBA. The disease is endemic in sub-Saharan Africa, with several incursions occurring outside of this continent in the 1960s and 1970s. It was introduced to Georgia in 2007 with subsequent spread to neighbouring countries and westward to the European Union states by 2014. In August 2018, the disease was first reported in China, and since that time has spread rapidly throughout Asia, with the current distribution of the virus now extending to more than 50 countries across three continents. By the end of 2019, official estimates indicated that ASF had claimed 25% of Chinese pigs, with some industry estimates indicating likely higher values[7] – in a country that has half the world's pig population[8]. This has seen increased demand for alternate protein sources within China, a shift in global trade patterns in animal proteins and concern raised regarding food security in some south-east Asian countries.

Despite extensive research efforts, a safe and effective ASF vaccine remains elusive. Laboratories around the world are conducting research on this tier 2 SSBA, with a focus on improved understanding of the virus and its interaction with the host. The development of vaccines and cell lines requires further knowledge on factors such as how the virus modulates immune function, correlates of host protection and the viral proteins involved in cellular entry, replication and morphogenesis[2]. Such research is essential for improved ASF control, and therefore for mitigating the threat that it poses from greater geographical spread through natural means (both legal and illegal movement

of animals and products) as well as intentional use as a biothreat agent.

In addition to conducting fundamental research to mitigate against the risks that SSBAs pose, laboratories are essential for diagnostic preparedness. This includes not only the diagnosis itself but the ongoing development and validation of accurate and fit-for-purpose diagnostic assays and platforms. Rapid diagnosis and confirmation of outbreaks is an essential component of disease control. Diagnostic expertise is also required in distinguishing these agents from more common pathogens and determining if the use of an agent is more likely attributable to accidental or deliberate use, rather than natural causes. The latter may require both epidemiological and laboratory evaluation through techniques such as whole genome sequencing and bioinformatics analysis. Laboratories also play a role in detecting and reporting new pathogens, which may ultimately be categorised as SSBAs, or new variants of SSBAs, and can also conduct research into and provide guidance on inactivation and decontamination strategies.

Laboratories holding and handling SSBAs that can impact on animal health have significant accountability to the Australian public and livestock industries in ensuring their biocontainment, biosafety and biosecurity. They also have considerable obligation and opportunity, when appropriately resourced, to contribute to improved understanding of these agents for better mitigation, preparedness and response to these ongoing threats.

Conflicts of interest

The author declares no conflicts of interest.

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Biography

Debbie Eagles is the Deputy Director of the CSIRO Australian Centre for Disease Preparedness. She is a veterinarian with specialist interest in the field/epidemiology/laboratory interface, an OIE Reference Laboratory Expert for Bluetongue Disease and a listed expert on the roster for the United Nations Secretary-General's Mechanism for investigation of alleged use of chemical and biological weapons.