



# Biological Agents and Toxins Act: Development and Enforcement of Biosafety and Biosecurity in Singapore

Tin Tun, Kristen E. Sadler, and James P. Tam

Nanyang Technological University, School of Biological Sciences, Singapore

## Abstract

*Biosafety and Biosecurity are very important issues in the present climate where emerging infectious diseases and threats of bioterrorism and biological attacks are of global concern. Biological safety requires the strengthening of the regulatory requirements and operational and safety programs. Singapore's first-ever law on the use of biological agents and toxins has come into force. The law clearly defines facility requirements for handling of them; develops the comprehensive system of control; prevents bioterrorism by controlling the use of high-risk hazardous agents; and, establishes a strong national biosafety culture. Singapore has made significant progress in the development and enforcement of biosafety and biosecurity measures. This progress certainly facilitates the safe expansion of our emerging biomedical industry and research development in life sciences. For the benefit of other facilities and future users, we report the impacts and contents of the new act in a simple and understandable presentation.*

## Introduction

The Biological Agents and Toxins Act (BATA) came into force on 3 January 2006 in Singapore (Ministry of Health, 7 December 2005). In writing the legislation, recommendations from the National Biosafety Committee (NBC) and its Technical Working Committee (TWC), which are represented by related government agencies, research institutions, hospitals and key industry players were taken into considerations. A public consultation exercise was conducted by the Ministry of Health (MOH) for the draft BATA from 11 April 2005 to 14 May 2005. Singapore's first-ever law on the use of biological agents (BA) and toxins were approved by the Parliament on 18 October 2005 (The Straits Time, 19 October 2005).

On recommendation of the NBC the MOH has adopted the Laboratory Biosafety Manual, 3rd edition (World Health Organization, 2004) as the national guidelines for biosafety to supplement the BATA. The World Health Organization (WHO) has long recognized that biosafety and biosecurity are important international is-

ssues. The WHO manual encourages countries to prepare specific codes of practices for the safe handling of potentially hazardous agents and provides expert guidance for developing such codes of practices. The importance of personal responsibility for safe laboratory activities is stressed throughout the manual. A safe and healthful laboratory environment is the product of individuals who are trained and technically proficient in safe practices.

Previously, the MOH adopted guidelines regarding human pathogens, and these guidelines were used to determine the level of biosafety required for specific purposes. The guidelines included regulations regarding the import, transport, transfer, handling, and disposal of human pathogens and their risk group classifications (Disease Control Branch, 2004). Those regulations have been integrated into the sections of the present BATA.

## Biological Agents and Toxins Act (BATA)

The BATA prohibits and otherwise regulates the possession, use, import, transshipment, transfer and transportation of biological agents, inactivated biological agents and toxins that are of public health concern (Singapore Statutes online, 2006). Its objectives include preventing acts of bioterrorism, establishing a strong national biosafety culture and facilitating emerging bioscience industry in Singapore. The important objectives of the BATA are provision of safety practices in handling of BA and toxins and promotion of biosafety training.

Major components of the BATA include lists of BA and toxins, controls for importation, possession, transshipment and transfer, and transport requirements. It also defines the facility requirements for high risk biological agents and toxins. The BATA adopts a schedule system for risk group classification of biological agents.

The BATA is relevant to companies and institutions involved in biomedical and life sciences research working with biological agents and toxins listed in schedules. Courier service providers should also be aware of the requirements for the transfer, transportation, transshipment and importation of biological agents and toxins. Any person who contravenes the sections of the Act shall be guilty of an offense and shall be liable on conviction to be pun-

ished with a very heavy fine or with imprisonment or with both.

### Schedules versus Risk Groups

The risk group classification of hazardous agents does vary from country to country, even though there are global standard laboratory practices and many aspects of laboratory culture are shared throughout the world. An agent classified into Risk Group 2 in one country may be classified as Risk Group 3 in another. Dengue Virus Type 1-4 was classified as Risk Group 2 in Singapore (previously), Canada and Australia but classified as Risk Group 3 in Belgium and European Union (Tun et al., 2006). Under the present BATA, biological agents and toxins are classified into schedules.

The BATA differentiates between higher risk group and lower risk group BA, and also those with potential to be weaponized. Five schedules in BATA cover a wide spectrum of biological agents and toxins and different levels of controls have been adopted for each schedule. Table 1 shows an overview of the schedules with corresponding risk groups, descriptions of schedules, facility requirements and number of BA in each schedule (MOH Biosafety, 2006). Schedule 1 is separated into part I and part II based on their potential to be weaponized. Schedule 1 (part II) and schedule 2 biological agents are deemed to be of bioterrorism potential and facilities wishing to work with these BA must be officially recognized as a protected place under the Protected Areas and Protected Places Act.

**Table 1**

Five schedules in BATA with their descriptions, corresponding Risk Group, number of BA in each schedule and Facility Requirements.

<b>Schedule Classification</b>	<b>Risk Group</b>	<b>Descriptions of Schedule</b>	<b>No. of BA</b>	<b>Facility Requirements</b>
Schedule 1 (Part I)	3	(1) Potential to cause serious disease which is high risk to individual	56	BSL3 Certified (Uncertified facility can appeal)
Schedule 1 (Part II)	3	(1) Potential to cause serious disease which is high risk to individual (2) Potential to be weaponized	23	BSL3 Certified and Protected Place (Uncertified facility and protected place can appeal)
Schedule 2	4	(1) Can cause severe/lethal disease, high risk to individual and community (2) Potential to be weaponized	14	BSL3 Certified and Protected Place with Special Approval granted by the Director (Medical Services)
Schedule 3	2	(1) Can infect humans (2) Need special attention in large scale production	3	Specified in the Approval by the Director (Medical Services)
Schedule 4	2	(1) Can infect humans	250 +	Conditions of a Permit granted by the Director (Medical Services)
Schedule 5	—	(1) Microbial toxins with potential to be weaponized	5	Protected Place and Conditions of an Approval granted by the Director (Medical Services)

## Biosafety Branch

The MOH established the Biosafety Branch in 2005 to account for all biosafety matters in a sustainable and organized manner. The branch administers the BATA; promotes high standards of biosafety in the research and biomedical community; maintains selected BA lists in schedules; assesses certification bodies and training providers; maintains a biosafety Information Technology (IT) system; coordinates containment measures and investigations; promotes links with other international and national biosafety organization; and, prevents bioterrorism by controlling the use of high risk biological agents.

According to the BATA requirements, a list of BA which is of importance to public health concerns and categorized in schedules based on their risk assessments, has been developed and updated. The branch keeps lists of Approved Facility Certifiers (AFC) and Approved Training Providers (ATP), and also sets the topics for biosafety training and the checklists for facility certification and for biosafety audit purpose. A webpage has been created and all relevant information is available online for the Biosafety Level 3 (BSL-3) facilities in Singapore (MOH Biosafety, 2006). The biosafety IT system allows all users to perform activities such as registering the facility, applications for permits and approvals, notification of transfers, receipt, inactivation and disposal, reporting of incident and inventory for biological agents, etc.

## Possession Control

Approval to possess biological agents in schedules 1 and 2 and toxins in schedule 5 are agent-specific and granted by the Director of Medical Services. No approval to possess is required for BA in schedules 3 and 4. There is no expiration date for the approval; however, the validity of the approval is tied to the facility being a certified BSL-3 facility. The approvals to possess BA in schedule 1 (part II) and schedule 2 are granted to a certified BSL-3 facility which are also officially recognized as a protected place under the Protected Areas and Protected Places Act. The approval to possess toxins in schedule 5 is granted to a certified or uncertified facility which is officially recognized as a protected place.

A special approval to handle materials is applicable to schedule 2 BA and is only granted by the director under the circumstances that the use of the schedule 2 BA is necessary in public interest; and the person who requires the schedule 2 BA has put in place adequate measures to contain the risks to public health and security posed by the agent. The approval to possess a schedule 1 BA may be granted to an operator of uncertified facility if the director is satisfied that the activity involving the use of schedule 1 BA will be carried out at such facility in a safe and proper manner. Therefore, appeal for exemption to handle the

BA under schedule 1 at an uncertified facility can be submitted to the MOH for approval from the Institutional Biosafety Committee (IBC) with risk assessment, documents to include research proposals and protocols, and proof that the facility is officially recognized as a protected place in case of schedule 1 (part II) biological agents.

To work with zoonotic agents, approval for possession of BAs from Agri-Food Veterinary Authority (AVA) of Singapore is required. The AVA inspects the facility before granting an approval. For genetically modified organisms (GMO), approval must be sought from Genetic Modification Advisory Committee (GMAC) before submitting an application for approval and permit to MOH.

In instances where a person possesses (and works with) a biological agent in contravention of sections in the BATA, the director may order the immediate cessation of any activity; the closure or cordoning off of the facility until such time as the director is satisfied that the facility may safely resume operation; the destruction of the BA at the facility; and, the decontamination of the facility. The person at the facility should undergo medical examination and medical treatment or may be quarantined at such place and for such period as specified in the order.

## Import Control

All biological agents in the schedules require import permit. The applications for import permits can be submitted online at Singapore Customs Tradenet System (Singapore Customs, 2006). The importer of the BA into Singapore must have approval to possess the BA. The importer or the end-user is responsible for ensuring that a valid permit is obtained before bringing the BA into Singapore. Even when engaging a courier service provider to apply for the import permit on behalf of the institution, the importer must verify that the correct permit has been obtained from the MOH.

Transshipment of BAs under the BATA must be carried out in accordance with the conditions of a permit granted by the director. Transshipment refers to instances where Singapore acts as a port of transfer for BAs and where the BAs arrive and are stored temporarily at any given location in Singapore. This is regardless of whether the BAs remain on the original conveyance (i.e., plane) upon which they arrive in country or are transferred to another conveyance (i.e., another flight). Every permit to import or transship a biological agent is valid only for the one specific consignment of the BA for which the permit has been granted, and can not be used for other consignments. Under the BATA the importer has to notify the MOH of any failure to receive schedules 1 (part II) and schedule 2 biological agents and schedule 5 toxins within 24 hours of such time as reasonably estimated for the receipt.

When temporary storage is required at any location

for imported BA before it is delivered to the destined facility in Singapore or for transshipment from Singapore, the permit holder must ensure the storage of the BA is in accordance with requirements as prescribed by the BATA.

For importation of zoonotic agents, the importer is required to obtain import permits from both the AVA and the MOH. The AVA and MOH have streamlined the import permit processing on Singapore Customs Tradenet System. Importer is required to declare a set of MOH-AVA product code for each zoonotic agent (AVA, 2005).

The BATA does not have requirements for export of biological agents and toxins. Export of high-risk biological agents and toxins is controlled by the Strategic Goods Control Act administered by Singapore Customs.

### Transfer Control and Transport Control

For transfer of schedule 1 and schedule 2 BA or schedule 5 toxins between facilities within Singapore, the BATA requires that both transferor and transferee must have valid approval to possess that agent. The transferor is responsible to notify the MOH of the proposed transfer. Transferor needs to notify the transferee of an estimated time of receipt of the agent and provide the carrier of the agent with a 24-hour emergency contact number of a person who is responsible for the transfer process. In the event of failure to receive the agent, the transferee must notify the MOH. Table 2 shows the approvals, permits and requirements to handle the BA under the BATA.

Packaging of the BA uses a basic triple packaging system which comprises a primary receptacle, secondary packaging and an outer packaging. Biological agents are packaged to meet International Air Transport Association (IATA) regulations.

Transportation of biological agents by postal mail or public transportation is strictly prohibited. The carrier ensures that any conveyance used must be affixed with infectious substance biohazard label for transportation of BA in the schedule 1, 2, or 3 (quantities aggregating 10 liters or more) and affixed with toxic substance biohazard label for transportation of schedule 5 toxins and that there are no unnecessary delays in transportation. A driver who is involved in the transportation must be trained and possess a valid Hazardous Materials Transportation Driver permit. It is applied to researchers who transport schedule 1 and schedule 2 biological agents and schedule 5 toxin in own vehicle.

### Facility Requirements

BSL-3 facility must be certified by a MOH-approved facility certifier (AFC) before applying for approval to possess schedule 1 and schedule 2 biological agents. The facility needs re-certification yearly or upon any design or structural change made to the facility. The MOH Biosafety keeps a checklist for certification process which is derived from the WHO Laboratory Biosafety Manual third edition and additional items recommended by the NBC as well as legislative requirements by the BATA. The facility that wants to handle schedule 1 (part II), schedule 2 biological agents and schedule 5 toxins, must be declared as a protected place under the Protected Areas and Protected Places. Additional criteria may be required by the AVA for Animal BSL-3 facility.

It is a requirement for a BSL-3 facility to establish an Institutional Biosafety Committee (IBC) which includes at least biosafety coordinator, microbiologist, facility maintenance personnel and representative from senior

**Table 2**

Summary of approvals and permits required to handle biological agents under the BATA.

Approval/Permit Requirement	Schedule of BA					
	1(I)	1 (II)	2	3	4	5
Approval to possess	Yes	Yes	Yes	No	No	Yes
Approval to produce (Large scale)	Yes	Yes	Prohibited	Yes	No	NA
Special Approval to handle	NA	NA	Yes	NA	NA	NA
Import permit	Yes	Yes	Yes	Yes	Yes	Yes
Notify Failure of Receipt of Import	No	Yes	Yes	No	No	Yes
Transshipment permit	Yes	Yes	Yes	No	No	Yes
Transfer Notification in Singapore	Yes	Yes	Yes	No	No	Yes
Notify Failure of Receipt of Transfer	Yes	Yes	Yes	No	No	Yes
Certified BSL3 Facility	Yes*	Yes*	Yes	No	No	No
Protected Place	No	Yes	Yes	No	No	Yes

NA = Not applicable

\* = Uncertified facility may appeal for exemption

management. The IBC is responsible to formulate and review biosafety policies and programs including training of staff, conducting risk assessment and approving the research projects. All activities involving schedule 1, schedule 2 and schedule 3 (large-scale production) biological agents and schedule 5 toxins must be endorsed by the IBC before submitting the applications for approvals and permits or reporting to the MOH.

Every facility appoints a biosafety coordinator who participates in a recognized biosafety course conducted by the MOH-approved training provider (ATP) and passes the competency test administered by the MOH. Training for BSL-3 staff is mandated under the BATA. Such training for personnel working in a BSL-3 facility can be conducted in-house or by experienced external trainers. The BATA has given a six-month transitional period from the date of commencement of the BATA to BSL-3 facilities in Singapore for necessary arrangements and preparations to meet the BATA requirements.

### Activities Exempted from the BATA

The act will not apply in relation to the use of biological agents and toxins for certain purposes which include disposing of any biological agent by a hazardous waste contractor; the handling of any agent in the course of carrying out a diagnosis and an autopsy; and collecting of food samples or samples from the environment for the purpose of carrying out laboratory analysis to determine or identify for public health purpose the nature of any biological agent that is present in such samples. Exemptions are also given to the use or possession by any person lawfully manufacturing, supplying, selling or dispensing the finished cosmetic or medicinal product; any registered practitioner using the finished cosmetic or medicinal product in the course of treating another person; and, any person using those product for cosmetic or medical purpose for which it is intended.

### Conclusions

The regional and global spread of emerging infectious diseases has driven Singapore to put emphasis on research in life sciences and to develop comprehensive system of control for potentially hazardous biological agents. The strict rules have been introduced to protect people from being exposed to the potentially hazardous biological agents and also to prevent terrorists from turning research samples into biological weapons. The laboratory operating environment needs to be defined in terms of biosafety and biosecurity capabilities. Where threats of bioterrorism and biological attacks are of global concern, the measures used to secure a facility storing high-risk agents are of the utmost importance. If biological agents and toxins fall into the wrong hands, the destruction and

dangers posed will be indescribable. A good regulatory framework will strengthen Singapore's standing as a bio-medical hub and help it to attract world-class researchers. The laws have to strike a good balance between keeping research safe and being too restrictive. The requirements should not result in unnecessary cost increases, research being hampered, and scientists being discouraged from working to prevent disease outbreaks. There is a fine is of up to \$1 million Singapore dollars and life imprisonment if charges involve a deliberate attempt to use biological agents and toxins for biological warfare or any non-peaceful purpose. Such severe penalties for convicted offenders reflect Singapore's serious commitment to biosafety and biosecurity.

### References

- AVA. (2005). *Requirements for the Import and Transshipment of Pathogens*. Circular IED 2/1. Agri-food & Veterinary Authority of Singapore.
- Disease Control Branch. (2004). *Guidelines on the import, transport, transfer, handling and disposal of human pathogens for diagnosis, scientific research and industrial uses in Singapore*. MOH Singapore.
- Ministry of Health (MOH). (7 December 2005). Commencement of Biological Agents and Toxins Act. MOH Circular, 70(13/15-0026), Singapore.
- MOH Biosafety. (2006). *Public Information*. Singapore. Available at [www.biosafety.moh.gov.sg/bioe/index.do](http://www.biosafety.moh.gov.sg/bioe/index.do)
- Singapore Statutes Online. (2006). *Biological Agents and Toxins Act 2005, Act 36 of 2005*. Available at <http://statutes.agc.gov.sg/>
- Singapore Customs. (2006). *Tradenet-the one-stop e-platform for Trade Declaration*. Available at [www.tradenet.gov.sg/trdnet/index\\_home.jsp](http://www.tradenet.gov.sg/trdnet/index_home.jsp)
- The Strait Time. (19 October 2005). *New Law to Regulate Use of Bio-Agents*. H5/Home. Singapore.
- Tun, T., Sadler, K., & Tam, J. P. (2006). Implementation of a Biosafety Level 3 (BSL-3) Facility in Singapore: Requirements, Work Practices, and Procedures. *Applied Biosafety: Journal of the American Biological Safety Association*, 11(1), 15-23.
- World Health Organization. (2004). *Laboratory Biosafety Manual* (3rd ed.). Geneva. Available at [www.who.int/csr/resources/publications/biosafety/WHO\\_CDS\\_CSR-LYO-2004\\_11/en/](http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR-LYO-2004_11/en/)