

NATIONAL BIOSAFETY SYSTEMS

Case studies to analyze current biosafety approaches and regulations for Brazil, China, India, Israel, Pakistan, Kenya, Russia, Singapore, the United Kingdom, and the United States

*UPMC
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UPMC Center for Health Security Project Team

Gigi Kwik Gronvall, PhD, Senior Associate, ggronvall@upmc.edu

Matthew P Shearer, MPH, Analyst, shearerm@upmc.edu

Hannah Collins, Research Assistant, collinshl@upmc.edu

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Introduction

This document summarizes the governmental policies and regulations for biosafety in research laboratories in the nations of Brazil, China, India, Israel, Pakistan, Kenya, Russia, Singapore, the United Kingdom, and the United States. In previous research, we found that there is a lack of international norms governing biosafety precautions for dangerous or especially contagious¹; by describing a variety of biosafety governance approaches in these nations, we hoped to find areas of commonality which could be further developed into international norms.

Online database searches for government documents, websites, media reports, and biosafety reviews were used to identify existing biosafety guidelines for each assessed nation and identify regulatory agencies, laboratory staff training programs, and incident response and reporting requirements. Additionally, information was collected regarding current notable research priorities, research and development investments, and global biotechnology rankings to provide a well-rounded overview of each nation's biological research capacity and interest and their existing investments in biosafety. It should be noted that this research **does not** address the success of implementing the relevant legislation and regulations.

In comparing the biosafety policies of the ten nations, we identified the following important trends:

- **Biosafety regulation exists in all ten nations.** All nations were found to have national biosafety guidelines and regulatory bodies responsible for oversight and compliance.
- **Information availability was extremely variable, making comparisons difficult.** The quantity and quality of information available varied widely between countries, which may be due to differences in scope or transparency of the biosafety programs or due to differences in priorities for biosafety regulation.
- **The incentives behind biosafety regulation are varied, ranging from agricultural development to infectious disease control to biotechnology investments.** National-level research priorities contributed significantly to the emphasis placed on developing biosafety legislation and oversight. It is therefore possible that there are resulting gaps in regulation for non-priority areas.
- **Advanced or synthetic biology is not consistently addressed by national-level biosafety policy.** Some nations have very strict regulatory policies for advanced or synthetic biology, and others only address it in a limited capacity or from a very specific perspective (e.g., genetically modified crops).
- **Funding information for biosafety was generally unavailable.** The lack of information about funding may be a function of transparency, but it also could be that biosafety is incorporated into larger budgets and not “called out” as a separate item. Additionally, the biosafety funding may be spread across a number of governmental agencies rather than being a single budget item.

Moving forward, these biosafety case studies will provide a foundation for identifying national-level biosafety norms and enable initial assessment of biosafety priorities necessary for developing effective national biosafety regulation and oversight. In the long term, developing international norms for biosafety will help to build confidence between nations that scientific work in research laboratories—particularly work with high consequence, contagious pathogens—is being carried out safely.

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Brazil

Biosafety Oversight Summary

There is a long history of biosafety oversight and training in Brazil, evolving with biotechnology capabilities.² Biosafety in Brazil is largely focused on the oversight of genetically modified organisms (GMOs), but there is a pathogen select agent list and pathogen categorization similar to the US. Biosafety oversight largely derives from Law 11.105, called the “Biosafety Law,” which delineates major government responsibilities and regulations for biosafety, with responsibilities in the Ministries of Health and Agriculture. Additionally, the Biosafety Law establishes a National Technical Biosafety Commission (CTNBio) under the Ministry of Science & Technology, which is responsible for the oversight of all laboratories conducting GMO research.³ Brazil has a National Association of Biosafety (AnBio) that promotes national biosafety training and outreach.⁴ There is currently no oversight for university labs that do not conduct GMO research.²

Pathogen Characterization

Brazil uses the same biosafety level designations for infectious agents as the US (BSL-1 to BSL-4). Also similar to the US, Brazil established a select agent list in 2008 to classify and regulate pathogens. The Brazilian list is largely identical to the US list, but it includes several pathogens not on the US list as well as some specialized dual-use equipment.^{2,5} Brazil regulates GMOs, categorizing them into four risk classes, from Risk Class I (Low individual/low community risk) to Risk Class IV (high individual/high community risk), and designates biosafety levels for GMOs, from NB-1 (low containment) to NB-4 (high containment). GMO work that requires production of GMOs “in great scale” is subject to additional biosafety regulations and containment measures.⁶

Relevant Regulations and Legislation

The major law governing biosafety is Law 11.105 (2005), the “Biosafety Law,” which delineates safety and inspection/approval for GMOs and their derivatives and establishes Brazil’s National Biosafety Policy. The Biosafety Law creates a National Biosafety Council (CNBS) to analyze requests for approval and/or the commercial use of GMOs and their derivatives.⁷ In addition to GMO regulation, the Ministry of Labor & Employment’s Normative Resolution 32 (2005) delineates guidelines for protecting health worker safety.⁸ It includes risk classification for non-GMO biological agents as well as standards for infection prevention, waste disposal, environmental cleaning, and other aspects of worker safety with respect to biological risk.⁹ The National Technical Biosafety Commission’s (CTNBio) Normative Resolution 2 categorizes GMOs into four risk classes and corresponding biosafety containment levels.⁶ CTNBio also issued Normative Instructions 8, regulating genetic manipulation in humans and human cloning¹⁰, and 9, regulating “genetic intervention in human beings.”^{11,12}

Regulatory and Oversight Agencies

The **National Biosafety Council (CNBS)**, created by Law 11.105, was designed to provide the President with assistance regarding “formulation and implementation of the National Policy of Biosafety.”¹³ CNBS is comprised of numerous ministers, including Science & Technology, Agriculture, Justice, Health, Environment, Foreign Affairs, and Defense. Additionally, CNBS is directed to analyze, at the request of CTNBio, requests for approval and/or the commercial use of GMOs and their derivatives.¹³ The **National Technical Biosafety Commission (CTNBio)** is located in the Ministry of Science & Technology (MCT) and is responsible for overseeing all labs conducting GMO research and assessing the risks from GMOs to the environment, agriculture, and human/animal health.^{3,7} The **Ministry of Health (MOH)** is in charge of monitoring public health laboratories, and the **Ministry of Agriculture** is responsible for overseeing agricultural laboratories.² The **Brazilian Health Surveillance Agency (Anvisa)**, created in 1999 by Law

9.782,¹⁴ is charged with health surveillance for laboratories, including “diagnostic and therapeutic services and others of interest for the control of risks to the public health, as well as those involving the incorporation of new technologies.”¹⁵ While Anvisa is associated with MOH, it remains independent and financially autonomous.¹⁴ The **Biosafety Commission in Health (CBS)** was established in MOH for the purpose of “defin[ing] strategies for the assessment and monitoring of actions related to biosafety,” particularly establishing nationally uniform standards.³

The **National Biotechnology Committee** oversees implementation of the national **Biotechnology Development Policy**, in coordination with a range of agencies including CTNBio. The committee is comprised of representatives from a number of ministries, the Office of the Chief of Staff, Anvisa and other entities.¹⁶

Biosafety Associations

Brazil’s National Association of Biosafety (AnBio) was founded in 1999 as a non-profit “nongovernmental multidisciplinary organization promot[ing] biosafety as a field of knowledge.”³ AnBio is affiliated with the American Biological Safety Association (ABSA International) and the European Biosafety Association (EBSA),³ and they conduct training on a range of topics relevant to biosafety.⁴ In 2011, designated as the Year of Biosafety in Brazil, AnBio established the Seal of Biosafety (Bioselo) to improve biosafety and infection control standards at healthcare facilities,¹⁷ including clinical laboratories and research facilities.¹⁸

Biosafety officers and Institutional Biosafety Committees

Each entity conducting work with GMOs is required to have a Biosafety Internal Commission (CIBio) under Law 11.105,⁷ specifically for the purpose of “monitoring and surveillance of activities with GMO and their derivatives...and for the fulfillment of bio-safety norms.”¹⁹ The CIBio is responsible for submitting requests to conduct GMO work to CTNBio, conducting risk assessments and annual facility inspections, implementing biosafety training and inspection programs, and investigating accidents. Each project must be assigned a Main Technician responsible for ensuring adherence to biosafety regulations imposed by CTNBio and the institution’s CIBio, obtaining authorization to commence GMO research, ensuring proper biosafety training of technical and support staff, reporting accidents to the CIBio, and ensuring proper equipment and biosafety infrastructure maintenance.¹⁹

Accident and Incident reporting

Hospital laboratories have a formal notification system for accidents.² The CIBio and CTNBio at each institution working with GMOs have the authority and responsibility to investigate laboratory accidents resulting from GMO research, as delineated in Law 11.105.^{2,7} Article 7 of Law 11.105 and CTNBio’s Normative Resolution 1 mandate that accidents involving genetic engineering research be investigated immediately and reported within 5 days to “the competent authority.”^{7,19} Additionally, these regulations also require notifying CTNBio and applicable “public health, agricultural, environmental and defense authorities of any accident that may cause dissemination of GMO and GMO derivatives.”⁷ The Main Technician is responsible for immediately reporting accidents involving GMOs to the institution’s CIBio.^{7,19}

Synthetic/Advanced Biology

Brazil has embraced synthetic biology, particularly as a way to develop sustainable agriculture.²⁰ Biotechnology is a priority research area in Brazil. The University of Sao Paulo operates the Biomass Systems and Synthetic Biology Center (BSSB or SynBio Center) to support synthetic biology research across genetics, biomedical engineering, biology, chemistry, and other fields.²¹ As one of the world

leaders in sugarcane-based ethanol, Brazil is well-placed to be a growing factor in biofuel development and biomass production.²² Crucially, the Sao Paulo Research Foundation (FAPESP) has identified bioenergy as one of its four primary research programs.²³

Training

Brazil has a long history of biosafety training, with programs going back to at least the 1980s.³ In 2000, the National Health Foundation (FUNASA; in MOH), the FIOCRUZ Biosafety Nucleus (NUBio), and the US Centers for Disease Control and Prevention (CDC) established a biosafety mentorship program to develop biosafety educational programs in high school and undergraduate institutions, establish biosafety equipment and procedural norms, and build and improve BSL-3 facilities. The program trained approximately 4,000 biosafety professionals in its first five years.³ AnBio has focused largely on developing biosafety programs and training researchers and other professionals.² Due in large part to AN Bio's efforts, a number of Brazilian academic institutions offer biosafety and biosecurity courses at the undergraduate and graduate levels.^{2,8} In collaboration with the US Biosecurity Engagement Program (BEP), Brazilian Ministry of Education, and FIOCRUZ, AnBio recently developed a post-graduate course in biosafety and biosecurity,² and they also host a number of biosafety seminars and symposia as well as the biennial Brazilian Biosafety Congress.²⁴

Laboratory numbers

A 2012 report indicated that Brazil operates 12 BSL-3 laboratories;² however, an earlier report in 2010 stated that 13 BSL-3 laboratories were operational at that time.²⁵ Several reports state explicitly that there are no BSL-4 laboratories in Brazil.^{2,25}

Research Status

Brazil ranked 46th on Scientific American Worldview's 2015 Biotechnology Scorecard. Brazil's greatest strengths were listed as "talent retention" (scored 5.15 out of 10), biotechnology patents (compared to all patents filed; scored 5/10) and "patent strength" (scored 4.18/10). Weaknesses included "brain gain" (i.e., global students studying in Brazil) and infrastructure quality.²⁶ In 2014, industry giants (including BASF, BP, Dow, and DuPont) partnered to establish the Brazilian Industrial Biotech Association (ABBI) to "promote dialogue with stakeholders and policymakers to improve Brazil's biotechnology regulations and update current legislation."²⁷ In 2009, Brazil invested 1.2% of its Gross Domestic Product (GDP) in research and development (the most of any Latin American country, but only half the Organisation for Economic Co-operation and Development [OECD] average).²⁶ One of Brazil's major research and development funding sources is the Sao Paulo Research Foundation (FAPESP). FAPESP receives, by law, 1% of state taxes in Sao Paulo, and in 2013, they invested approximately \$500 million (US) in various research endeavors, including a major investment in biofuels.²³ After a decade of economic growth in Brazil that contributed significantly to a booming research sector, a stagnating economy in 2015 resulted in considerable cuts to research funding across scientific fields, including biology.²⁸

Funding for Biosafety

One 2011 report indicates that there is no long-term program direction and no dedicated budget for biosafety and biosecurity.²

China

Biosafety Oversight Summary

China's biosafety policies were consolidated and made more comprehensive after SARS, specifically after a laboratory-acquired SARS infection in 2003.^{29,31} Biosafety oversight is the responsibility of a number of governmental agencies, with considerable overlap in responsibility.^{29,31} Still, China has been observed to have a "shortage of officials, experts, and scientists who specialize in laboratory biosafety," increasing the challenge of implementing the new regulatory measures since 2004.³⁰

Pathogen Categorization

Infectious agents are classified into four grades (Class I: most harmful; Class IV: least harmful).²⁹ Laboratories are also categorized into four levels (BSL-1: lowest containment; BSL-4: highest containment),^{29,31} and requirements for each level are determined by national standards.²⁹ Animal laboratories are designated as ABSL-1 through ABSL-4, similar to the US.²⁹ While initially based on US and European laboratories, biosafety standards for BSL-3 laboratories in China lie somewhere between those for BSL-3 and BSL-4 laboratories in the US and Europe.³⁰ The "BSL" convention is sometimes referred to as "P" in China, as it is sometimes referred to in the US, though rarely.³²

Relevant Regulations and Legislation

In 2004, China's State Council issued the **Regulation on the Biosafety Management of Pathogenic Microbiology Laboratories**, China's primary biosafety document, providing an "overarching framework for laboratory biosafety."²⁹ The regulation also addresses the "collection, packaging, transportation, storage, and destruction" of infectious/pathogenic organisms; infection control; and treatment for laboratory accidents.²⁹ Additionally, the Principal Group on Biosafety of Pathogenic Microorganism Laboratories (affiliated with the State Environmental Protection Administration) formed the Experts' Committee in 2005 to "conduct biosafety assessments and technical consultation" regarding laboratory operations.³¹ The following regulations also govern biosafety in China.

Transportation and shipment of pathogens are regulated by two different policies. The **Packaging Criterion on Transportation of Highly Pathogenic Animal Microbial Strains or Samples** (Ministry of Agriculture; 2005), based on the International Air Transportation Association's (IATA) Dangerous Goods Regulations, focuses on packaging and shipping pathogenic organisms.²⁹ The **Regulations on Transportation Management of Highly Pathogenic Microbial Strains or Samples of Microorganisms Contagious to Humans** (MOPH; 2005) require "prior approval by the veterinary or public health authority at the provincial or national level" to ship Risk Group 1 or 2 agents.²⁹ Transport of these pathogens between entities requires two escorts at all times to ensure safety and security.^{29,31}

China has also developed regulations governing genetic research and production. The **Safety Administration Regulation on Genetic Engineering** (State S&T Commission; 1993) applies to "all genetic engineering work" in China, including research, manufacture, and use of GMO products.²⁹ Additionally, the **Safety Administration Regulations for Agricultural GMOs** (State Council, 2001) establish biosafety measures for commercial GMO products. As of 2007, there were more than 30 additional supplements to regulate GMO testing in China.²⁹ In 2002, China implemented export controls for dual-use "biological agents, equipment, and technologies" based on the Australia Group lists (updated in 2006).^{31,33} The **Self-Disciplinary Guidelines for the Scientific Ethics of Academicians** (Chinese Academy of Science, 2001) require adherence to scientific ethics and betterment of mankind, in part to put focus on reducing the threat of nefarious employment of dual-use research.³¹

Regulatory and Oversight Agencies

A number of governmental agencies have biosafety responsibilities in China, particularly for laboratories. The **Ministry of Health** oversees human health research, laboratory approval, experiment approval, and biosafety oversight. In 2002, they published the **General Biosafety Standard for Microbiology and Biomedical Laboratories**. The **Ministry of Agriculture** is responsible for “[a]nimal research and health,” laboratory approval, experiment approval, and biosafety oversight. They published the **Veterinary Laboratory Biosafety Guidelines** in 2003. Laboratory planning, construction, and certification is governed by numerous bodies, including the **National Development and Reform Committee** (laboratory planning), the **General Bureau of Environmental Protection** (environmental impact certification), and the **Ministry of Construction** (construction standards, certification, and inspection).²⁹ Additional authority for laboratory inspections lie with the **National Accreditation Board for Laboratories** (equipment and management)²⁹ and the **National Accreditation Service for Conformity** (biosafety regulations and BSL-3 facilities).³⁰ The **State Food and Drug Administration** and **Ministry of Construction** regulate biological safety cabinets, and the **State Council, MOH, and Environmental Protection Agency** regulate medical waste.²⁹

The **State Science & Technology Commission** oversees policy for biosafety for genetic engineering research, production, and use in China. They established the **National Genetic Engineering Biosafety Council** to act in an operational capacity to regulate genetic engineering biosafety.²⁹ The public health and science & technology departments at the State Council regulate human genetic engineering work and “jointly established the **Human Genetic Resources Administration**” to handle operational oversight.²⁹ “Under the State Council, the **Health Department** and the **Veterinary Department** are responsible for managing all biosafety matters associated with activities in laboratories that deal with human and animal health, respectively.”³¹ [emphasis added]

Biosafety Associations

The Asia-Pacific Biosafety Association (A-PBA) offers biosafety training throughout the region, including biosafety principles, practices, and program management. The A-PBA sponsors biosafety and biosecurity training and conferences, forms national biosafety working groups, and initiates technical collaboration activities.³⁴

Biosafety Officers and Institutional Biosafety Committees

China uses a “three-tier system for biosafety management” at BSL-3 laboratories.³⁰ There is an Institutional Biosafety Committee (IBC), responsible for “establishing biosafety policies, procedures, and regulations;” reviewing, approving, and overseeing work on organisms that have not been assigned to a Risk Group; ensuring that the “institution’s Biosafety Office makes biosafety information services, training programs, and emergency assistance available;” and “supervis[ing] and assist[ing] the institution’s Biosafety Officer.”³⁰ The laboratory director is responsible for “review[ing] and renew[ing] certificates for the proper operation of laboratory safety equipment, facilities, and personnel training;” and overseeing laboratory surveillance.³⁰ The IBC and laboratory director share “primary responsibility for laboratory biological safety.”³⁰ Finally, the Principal Investigator (PI) oversees laboratory biosafety and registers for institutional and national oversight for any work with recombinant DNA, infectious agents, human blood or “potentially infectious materials,” or animal/plant pathogens.³⁰

Accident and Incident Reporting

Legal responsibility for accidents resides with the department overseeing the failed infrastructure or procedure.²⁹ Accident and incident reporting is required if a GMO is involved, and “punishments include a warning notice, dismissal from work, stopping of funds for the improper work, and confiscation of

income gained through the illegal activity.”²⁹ If a highly pathogenic organism is “stolen or diverted,” it must be “reported to the competent authorities within two hours.”³¹ Laboratory accidents or non-compliance must be reported to the institution and appropriate national authorities, as necessary. If there is a resulting laboratory-acquired infection, the laboratory is closed during the investigation and required to be “recertified to work at the appropriate biosafety level prior to resuming operations.”³⁰ China’s biosafety regulations recommend criminal investigations for lab managers that do not follow biosafety protocols.³⁵

Synthetic/Advanced Biology

The Chinese Academy of Sciences listed synthetic biology as one of 22 strategic areas for science and technology research in the 2009 report *Science & Technology in China: A Roadmap to 2050*.³⁶ Synthetic biology is a key component of China’s efforts to “address public health, nutrition, and resource needs.” As of 2013, China contributed approximately 10% of the world’s scientific papers on synthetic biology, ranking China 7th in citations globally. Of the approximately \$100 billion (US) total annual investment in research (1.8% of their GDP, compared to 2.7% in the US), China dedicates approximately \$33 million (US) to synthetic biology. China’s synthetic biology research is conducted primarily by “the Chinese Academy of Science [CAS]..., the Chinese Academy of Engineering,...the China Academy of Machinery Science and Technology, and medical universities.”³⁷ Funding sources include “the National Natural Science Foundation of China, state-level labs, and the CAS Knowledge Innovation Program.”³⁷ There does not, however, appear to be a national-level, cohesive discussion of the “ethical, legal, equity, and societal implications of synthetic biology.”³⁸ Among the high-profile research being conducted in China, researchers at Sun Yat-sen University in Guangzhou successfully utilized CRISPR/Cas9 to edit a human embryo in 2015.³⁹

China has established a series of advanced biology goals and projections for the next 5, 10, and 20 years, to include the following:¹⁴

- 5 years: Database of standardized parts and computational competency for designing parts and devices, module design and production of chemicals and biomaterials, and validated design of devices to increase plant tolerance of drought and salinity
- 10 years: Expanded database of standardized parts and devices and computational competency for design of bio-systems, commercial production of selected chemicals and biomaterials, and validated design of synthetic devices for nitrogen fixation
- 20 years: Integrated platforms for design, modeling, and validation of bio-systems; commercial production of a range of natural compounds, drugs, chemicals, and biofuels; clinical application of devices and bio-systems for detecting, controlling, or treating major diseases; and creation of artificial microbial life

Established in 1983 in the Ministry of Science & Technology, the China National Center for Biotechnology Development functions as the “national biotechnology and industrial management and coordination center, a research center of biotechnology policy, science and technology project management center of biotechnology, the biotechnology industry consulting and service center, a focal point for international cooperation in biotechnology, bio-technology management talent training center, [and the] communication center [for] international biotech industry information.” [translated to English]⁴⁰

Training

China does not appear to have a comprehensive biosafety training program for highly pathogenic agents.^{29,31} Individual institutions with BSL-3 laboratories are responsible for providing “initial and

annual training to laboratory personnel to ensure their mastery of the standardized laboratory technology, operational procedures, and biosafety precautions, knowledge, and operational and technical know-how.”³⁰

Laboratory Numbers

China, in partnership with France, opened its first BSL-4 facility in February 2015 at the Wuhan Institute of Virology.³² According to the China National Accreditation Service for Conformity Assessment, China currently has 61 BSL-3/ABSL-3 laboratories.⁴¹

Research Status

As discussed previously, the state government in China is the largest source of support for scientific research. Since 1986, China has included biotechnology as a priority in its Five Year Plan⁴², and total annual funding for research and development has increased fourfold since 2005, reaching \$191 billion (US) in 2013. Two high-profile, state-run programs, The National High Technology Research and Development Program (863 Program)⁴³ and the National Basic Research Program (973 Program)⁴⁴, provide significant funding for basic science and for product development and commercialization for a broad spectrum of scientific disciplines, including biology.⁴⁵ China’s 12th Five-Year Plan (2011-2015) identifies biotechnology as the focus for research and development growth, highlighting pharmaceuticals and biomedical engineering as priorities.⁴⁶ The details of China’s 13th Five Year Plan will not likely be revealed until spring of 2016;⁴⁷ however, experts anticipate that biotechnology will remain a priority.⁴⁸

The government focus and support for biotechnology in China has boosted private and international support as well. For example, BGI (formerly the Beijing Genomics Institute), “the world’s largest genomics organization,”⁴⁹ operates the “world’s largest rapid gene sequencing center” (as of 2013) in Shenzhen, China.^{50,51} Another Shenzhen company, SiBiono GeneTech, licensed the “world’s first gene therapy drug” in 2004.⁵¹⁻⁵³ Novartis operates a Novartis Institute for BioMedical Research facility in Shanghai’s Zhangjian Hi-Tech Park, investing more than \$1 billion to make the facility the top research center in China. The first stage of Novartis’ “state-of-the-art drug discovery campus” was scheduled to be complete in 2015.⁵⁴ Merck also moved to establish a research and development facility in China, reportedly investing \$1.5 billion for a facility in Beijing that was slated to open in 2014.³⁷

A significant portion of China’s scientific research and development, including life sciences, occur in research clusters across the country. The majority of these clusters receive initial funding from government sources at the national, provincial, and/or local levels as well as state-owned enterprises, and a number of them are owned entirely by the government. These clusters incorporate state-owned, private, and academic institutions and offer a number of benefits, including tax incentives, integrated infrastructure, and collaboration opportunities to foster research and production success. Prominent clusters are located in Chengdu (Sichuan Province) as well as major cities such as Beijing, Shanghai, Shenzhen, and Hong Kong.⁴²

In addition to state-owned enterprises and private ventures, Chinese academia contributes significantly to biology and biotechnology research. The Chinese Academy of Agricultural Sciences operates the Biotechnology Research Institute (BRI) in Beijing. “It is the only non-profit research institute focusing on frontier basic and applied agro-biotechnology in China,” including, plant, environmental microbial, and agro-microbial genetic engineering and GMO biosafety. BRI collaborates with the Hong Kong University of Science & Technology (HKUST) to conduct research on neuro-proteins, plant biotechnology and protein engineering and design as well as development of biopharmaceutical products.^{55,56} The Chinese University of Hong Kong operated the Centre for Plant and Agricultural Biotechnology from 2000

through 2011, with funding of more than \$63 million (HK). This center addressed issues related to population growth and agriculture as well as using biotechnology to increase crop yield and improve food quality.⁵⁷ Zhejiang University is home to the James D. Watson Institute of Genome Sciences (postgraduate training and research)³⁸ and the Zhejiang University Center for Genetic and Genomic Medicine, which offers academic research programs, clinical genomics services, and technical as well as ethical education and training opportunities.⁴¹

China ranks 42nd (out of 50 ranked countries; separately, Hong Kong is 11th and Taiwan is 25th) on Scientific American Worldview's list of biotechnology countries and has dropped from 25th since 2009. The low ranking was driven by a lack of public biotechnology companies, biotechnology patents filed, and talent retention. China had comparatively higher scores in intellectual property protection and capital/venture capital availability.²⁶ China's biotechnology and biopharmaceutical industry grew 30% annually between 2000 and 2005 to reach \$3 billion; however, the majority of the biotechnology market (90%) was directed at developing biogeneric pharmaceuticals rather than novel products.⁵⁸ Recent reports indicate that the fragmented regulatory and approval processes for pharmaceuticals are resulting in multi-year delays in bringing new drugs to the market in China, owing largely to the sheer number of agencies and policies that cover biological research.⁵⁹

Funding for Biosafety

No information found.

India

Biosafety Oversight Summary

Biosafety in India is primarily focused on genetically modified (GM) agricultural research and ensuring environmental safety. This is evidenced by the Indian definition of biosafety as “the need to protect the environment including human and animal health from the possible adverse effects of the Genetically Modified Organisms (GMOs) and products thereof derived from the use of modern biotechnology.”⁶⁰ The Environment Protection Act (EPA) of 1986 created room for the development of India’s first biosafety regulations,⁶¹ the 1989 *Rules for the Manufacture/Use/Import/Export and Storage of Hazardous Microorganisms, Genetically Engineered Organisms or Cells*. Since the publishing of the “Rules 1989,” several other key guidelines have been released to provide revised legislation and guidance for studies involving recombinant DNA^{62,63} and transgenic plants.^{3862,64} Each research institution working with rDNA or GMOs is required to have an Institutional Biosafety Committee (IBSC)^{62,65,66} that reports to the Ministry of Environment, Forests, and Climate Control (MoEFCC) and Department of Biotechnology (DBT), who together provide oversight for biological research institutions.⁶²

Pathogen Characterization

According to *the Recombinant DNA Safety Guidelines, 1990*, microorganisms are categorized in to four risk groups based upon pathogenicity, transmissibility, host range, the availability of preventative or curative treatment, prevalence in the country, and its ability to cause disease in humans, animals and plants.³⁶ Risk Group IV contains agents of the greatest risk to human safety, and Risk Group I contains those who pose the smallest risk. India uses the same BSL 1-4 containment facility categorization as the WHO and the United States.^{63,67}

Relevant Regulations and Legislation

Listed below are important biosafety guidelines and legislation in chronological order:

- The **Environment Protection Act (EPA) of 1986**⁶¹ provides regulations for the manufacturing, use, export, import, and storage of GMOs, GMO products, and hazardous agents.^{62,68} This piece of legislation provided the foundations for the development of the “Rules 1989” and India’s biosafety regulating framework.⁶¹
- **Drugs and Cosmetics Rules, 1988** (8th Amendment) designates the Ministry of Health and Family Welfare (DoH) as the regulatory body overseeing the import or manufacturing of biological and biotechnological products.⁶⁸
- **Rules for the Manufacture/Use/Import/Export and Storage of Hazardous Microorganisms, Genetically Engineered Organisms or Cells**, commonly referred to as “Rules 1989,” is India’s official biosafety document.⁶² This document provides guidelines for the use, handling, transport, and production of microorganisms as well as GMOS, genetically engineered crops, and products made with engineered crops.^{61,62,69} Notified under the Environment Protection Act of 1986, this document establishes regulatory agencies and categorizes pathogens.⁷⁰
- The **Revised Guidelines for Research in Transgenic Plants & Guidelines for Toxicity and Allergenicity Evaluation of Transgenic Seeds, Plants and Plant Parts** (1998) provides rules for recombinant DNA research on plants including molecular analysis and field evaluation. These guidelines also address importing and exporting of GM plants for research use.^{62,64}
- The **Recombinant DNA Safety Guidelines** (1990, 1994) includes agent classification and risk categorization, facility specifications, and laboratory protocol for working with recombinant DNA.^{37,3968}

- The **Guidelines for Generating Preclinical and Clinical Data for rDNA Vaccines, Diagnostics and Other Biologicals** (1999) cover preclinical and clinical testing of rDNA vaccines, diagnostics and other biologicals. The guidelines are specific to ensuring the safety, quality, potency and effectiveness of the product.⁶²
- The **Guidelines and Handbook for Institutional Biosafety Committees** (2011) provides details on the necessary composition of the biosafety committees and each member's role, procedures for registration, the role of IBSCs in project approval, training requirements and committee meeting specifics, among other details.⁷¹
- The **Biotechnology Regulatory Authority of India Act (BRAI Act)** (2013) mandates the establishment of the Biotechnology Regulatory Authority of India to "regulate the research, transport, import, manufacture and use of organisms and products of modern biotechnology and for matters connected therewith or incidental thereto."⁷² It was initially prepared by the Department of Biotechnology (DBT) in 2008, the bill went through several revisions before it was passed in 2013.^{72,73}

Regulatory and Oversight Agencies

The Ministry of Environment, Forests, and Climate Change (MoEFCC) along with the Ministry of Science & Technology's Department of Biotechnology are responsible for enforcing the policies of the 1986 Environmental Protection Act. The Genetic Engineering Approval Committee (GEAC), the Review Committee on Genetic Manipulation, and Institutional Biosafety Committees (IBSCs) review and approve research projects. Both the State Biotechnology Coordination Committee (SBCC) and the District Level committee (DLC) monitor ongoing studies. The recombinants DNA Advisory Committee (RCAC) advises committees and government agencies when necessary.⁶²

Biosafety Officers and Institutional Biosafety Committees

The *Guidelines and Handbook for Institutional Biosafety Committees* identifies the need for a Biosafety Officer (BSO) "...if research is conducted on organisms that require special containment conditions (Biosafety Level 3 or 4)...or if large-scale rDNA research is conducted."⁷¹ According to these guidelines, the BSO must "also a member of the IBSC and act as a technical liaison between researchers and the IBSC. The Biosafety Officer should be adequately trained and be able to offer advice on specialized containment requirements."⁷¹ Specifics about the level of training are not provided, but the BSO must know enough to ensure that rDNA safety guidelines and good laboratory practices are followed.⁷¹

Institutional Biosafety Committees (IBSC) are required for every facility working with rDNA and GMOs.^{62,65,66} These committees are authorized to approve laboratory studies, excluding field trials and hazardous genetic experiments or methods.⁶⁵ Each committee is comprised of academics and researchers from the institute, including the head of the institution and a medical expert, plus a member of the DBT.^{61,65} There are currently about 500 IBSCs within India.⁶²

Accident and Incident reporting

The *1990 Recombinant DNA Safety Guidelines* specify that an emergency plan should be in place in every facility for incidents such as breakage and spillage; accidental exposure to a chemical, toxin or agent; and natural disasters. Specific instructions are given for cleanup, sharps containers and disposal of contaminated materials.⁶³ The *Guidelines and Handbook for Institutional Biosafety Committees* states that all accidents, illnesses, or breaches in protocol must be reported to the Principle Investigator (PI) who then must report the incident to the IBSC Chairperson within 24 hours and to the RCGM within 48 hours of the incident.⁷¹ In anticipation of an accidental GMO release, the PI of a study is required to have

emergency protocol in place and distributed to appropriate regulatory committees, as is outlined in the “Rules, 1989.”⁷¹

Synthetic/Advanced Biology

To date, there are a limited number of institutions and research centers, and a handful of industrial or commercial companies engaged in research or work with synthetic biology.⁷⁴ India’s DBT is actively pushing to increase national interest and engagement in synthetic biology.⁷⁵ The nation’s 12th Five-Year Plan (2012-2017), with a budget of approximately EUR 277 million, has taken recommendations from the Task Force on Synthetic and Systems Biology Resource Network to boost interest in synthetic biology research.^{74,76,77} As the DPT pushes for greater investment in synthetic biology, the need for guidelines to accommodate these new endeavors has been expressed by many academics.⁷⁴

Training

The *Guidelines and Handbook for Institutional Biosafety Committees* state that biosafety training is required “for all individuals conducting research with GMOs/LMOs/rDNA materials.”⁷¹ The training can be conducted by the research institution itself as long as the IBSC has documentation that all staff are trained or have appropriate experience in biosafety protocol and standard operating procedures. All staff must have “knowledge in handling and management of incidents/accidents in the facility and information on when and how to report laboratory incidents.” Additionally, lab staff working in BSL 3 and BSL 4 facilities must have more detailed training, but the specifics of the training or who is to provide the training is not provided.⁷¹

Laboratory numbers

In 2008, it was reported that India had 14 BSL-3 facilities with 6 planned for construction and 1 BSL-4 facility with 2 planned for construction.⁷⁸ In conflict with this report are several 2013 sources which reported that in March of 2013, India’s first BSL-4 facility was completed at the National Institute of Virology (NIV) in Pune. At this time, the NIV had already constructed a BSL-3 facility at its Microbial Containment Complex campus. The new BSL-4 facility allows for extended research capabilities with agents like pandemic influenza, SARS, Nipah virus and Crimean-Congo hemorrhagic fever virus.⁷⁹

Research Status

India was listed 51st on the 2015 Scientific American Worldview Overall Scores for biotechnology innovation. Its highest scores were in productivity and intensity, and its lowest scores were in IP protection and enterprise support.²⁶ India’s Department of Biotechnology has dedicated significant effort increasing the nation’s global contribution to biotechnology and scientific research. In the past few years, the DBT has worked to create an “Open Access Policy,” developing a database where funded researchers can share and learn from each other’s work.^{80,81} Much of Indian investment and effort in biotechnology is directed towards genetically modified agriculture. India’s first transgenic crop, Bt cotton, was introduced in 2002.⁶² Now, India produces 11.6 million hectares of Bt cotton and is the 4th highest producer of biotech crops in the world.⁸² Currently, India has developed 23 biotech crops with 67 biotech traits in different stages of development. These crops are developed by both the public and private sectors (39 public sector, 20 private, 8 autonomous institutes).⁸⁰

Biopharmaceuticals, bioinformatics, and bioservices are also major parts of India’s biotechnology industry. India’s biopharmaceutical industry accounts for 62% of the total biotechnology sector, with bioservices at 18%. The Bioservices sector continues to grow in capacity for contract research, clinical trials, and manufacturing engagements.⁸³

Funding for Biosafety
No information found.

Israel

Biosafety Oversight Summary

Israel has a fairly comprehensive set of biosafety legislation. This legislation addresses biosafety from a worker protection and safety perspective, so the majority of oversight is the responsibility of the Ministry of Industry, Trade, & Labor (MITL). A number of worker safety policies contain measures that address biosafety specifically, including laboratory accreditation. Increasing demands of Israel's major sources of international research support, including the US National Institutes of Health and Department of Defense, have resulted in significant improvements in Israeli biosafety regulation and oversight.⁸⁴

Pathogen Characterization

Israel categorizes “workers exposed to contagious biologic agents” into four risk groups (Risk Group 1: “little or no risk of infection;” Risk Group 4: “may cause a grave disease, disability, death, and the outbreak of epidemics”). Israel also outlines general requirements for personnel and supervisor experience level and physical containment requirements (e.g., hoods, suits, rooms) required to handle agents in each risk group.^{84,85} In 2008, Israel implemented the Research into Biological Disease Agents Act, which included a list of “Disease Agents”—including bacteria, viruses, and toxins—analogueous to the US Select Agent List. Special accreditation from MOH is required to store or conduct research on Disease Agents..^{84,85}

Relevant Regulations and Legislation

Israel approaches biosafety largely from the worker and occupational safety perspective. As such, most of the identified biosafety regulations fall under the purview of the Ministry of Industry, Trade, & Labor (MITL). The Work Safety Regulations (Occupational Safety and Hygiene in the Handling of Dangerous Agents in Medical, Chemical and Biological Laboratories), published in 2001, define pathogen risk groups and differentiates types of laboratories (e.g., biological, chemical; medical, research, teaching, quality control). They also delineate responsibilities of the laboratory holder and workers and specify occupational safety measures for laboratories, worker training requirements, and notification of intent to work with “dangerous agents.” (NOTE: these regulations precede the official Dangerous Agents list and presumably refer to “dangerous agents” in the general sense). Additionally, these regulations cover the general experience level for workers and supervisors, physical containment requirements, and personal protective equipment (PPE) for each risk group of biological agents.⁸⁶

The Work Organization and Supervision Law (1954⁸⁴) outlines governmental inspection authority for laboratories under MITL oversight, establishes the Institute of Safety and Hygiene, and institutes requirements for institutional safety committees, trustees, and officers. The Work Safety Ordinance (New Version), published in 1970^{84,87}, establishes oversight and regulatory authority for biological, chemical, and medical laboratories. The Work Supervision Organization Regulations (Environmental Monitoring and Biological Monitoring of Persons Handling Dangerous Agents), published in 1990, “impose environmental monitoring at an enterprise or workplace engaged in work with certain harmful agents,” specifically “harmful chemical and physical agents located in the workplace to which the workers are exposed in the course of work.” These regulations also establish exposure limits for biological agents and identify “biological markers of occupational exposure.”^{84,87} Law ISRA 1997⁸⁶ established the MITL Laboratory Accreditation Authority. MITL's **Safety Oversight Order for Medical, Biological, and Chemical Laboratories** (2001) mandates that MITL and MOH are responsible for ensuring laboratory safety within their respective research facilities.^{88,89}

The **Regulation of Research into Biological Disease Agents Act** (Disease Agents Act; 2008) was developed in response to a report by the Steering Committee on Issues in Biotechnology Research in an Age of Terrorism. The Disease Agents Act created a list of biological agents with bioweapons potential and identified specific types of dual-use research of concern (DURC). Additionally, the act established the Council for Dangerous Biological Agents to “regulate institutions that store or conduct research with Disease Agents.”⁸⁸ The responsibility of implementing the Disease Agents Act falls on the Israeli Minister of Health and the MOH Director General, and the act provides oversight and regulation for all labs working on Disease Agents, including government laboratories as well as public and private entities from academia and industry.⁸⁸

Biosafety Associations

The **Israel Biological Safety Association (IBSA)** was founded in 2007 to promote professional safety in the biological sciences. IBSA is a non-profit professional organization and does not collect membership fees. Principle objectives include promoting biosafety awareness and developing “professional standards in the field of biological safety as well as providing a forum to represent the “needs and interest[s]” of biological professionals and for the exchange of biosafety knowledge. The IBSA holds meetings every two months, and Association Chairman elections are held biennially. Israel’s Workplace Safety & Health biosafety website also provides information and links for the European Biological Safety Association (EBSA), American Biological Safety Association (ABSA International), and International Federation of Biosafety Associations (IFBA).⁹⁰

Regulatory and oversight Agencies

Biosafety authority is shared across a number of federal agencies in Israel. MITL has the “primary legislated responsibility for worker and workplace safety, and hence laboratory biosafety.”⁸⁴ MITL’s **Laboratory Accreditation Authority (LAA)** provides biosafety regulations for non-MoH research facilities.⁸⁹ Lab accreditation through LAA is not required for all sectors in Israel, although laboratories can voluntarily seek accreditation. “For example, the MOH’s water and food laboratories must be accredited, but the same ministry’s medical laboratories are exempt.” A 2009 report indicated that the extent to which MITL oversees commercial biological laboratories was unclear and recommended further investigation in this area.⁸⁴

MOH is responsible for overseeing medical laboratories. Again, the application of their authority is unclear across this sector. “Laboratories in state-owned hospitals are under full MOH supervision;” however, MOH has only limited oversight of those run by private health plans or HMOs. MOH must approve these laboratories and personnel, but they do not regulate any research. Only recently has MOH entered into the realm of tracking biological agents or conducting inspections. Laboratories in medical schools are under the responsibility of institutional safety committees, not MOH.⁸⁹ The Minister of Health and the Director General of MOH are responsible for implementing the Disease Agents Act for all institutions and laboratories possessing or conducting research on specified biological agents.^{88,89} The MOH Plant Safety Committee is responsible for implementing the laboratory safety program.⁹¹ The **Ministry of Agriculture and Rural Development** operates several laboratories that “engage in biological and biotechnological research: the Volcani Center, the Veterinary Institute and the Institute of Plant Protection.”⁸⁴ The Veterinary Institute researches a wide range of pathogens, including several that could potentially be used as bioweapons. These facilities operate under “well-defined entry and security procedures for access to sensitive storage facilities; and inspection and tracking procedures are regulated and enforced.”⁸⁴

Biosafety officers and Institutional Biosafety Committees

Private research institutions and universities experience considerable independence from government regulation in their research endeavors.⁸⁹ They are held accountable to biosafety policy by institution-specific committees for safety, biosafety, bioethics, and animal safety which review their work annually.^{89,92} Each facility is required to have a full-time safety officer tasked with overseeing research with pathogenic agents, toxic materials, recombinant DNA, and human tissue samples.^{88,89,92}

In Israel, the “laboratory holder” is defined as the employer, enterprise owner, workplace owner, workplace manager, or corporation manager.⁸⁴ Under the Work Safety Regulations, the laboratory holder is responsible for, among other things, ensuring proper waste disposal, implementing biosafety measures against emergencies (e.g., fire), conducting semiannual training and drills for emergencies, and performing periodic environmental testing. Additionally, the holder is charged with ensuring that the personnel working on dangerous pathogens have the proper experience and supervision and that physical containment measures are in place (e.g., hoods, suits, rooms). Additional “safety and hygiene measures” for laboratory holders are outlined in the Public Health Regulations (Medical Laboratories). The laboratory manager is responsible for compiling an annual list of “dangerous agents in use in the laboratory” and biosafety procedures and practices for submission to the district work inspector for approval. The laboratory manager is also responsible for installing and maintaining “biological and chemical hoods” for worker safety.⁸⁴

Laboratories also employ safety committees, trustees, and officers to promote and ensure biosafety measures in laboratories. Enterprises with at least 25 employees are required to have a safety committee comprised of both management and workers. Workers serving on the safety committee will serve as safety trustees in the workplace. The Minister of Labor may also require the appointment of a safety officer, someone for whom safety is their primary focus. Additionally, “[a]ll academic research institutions have safety units, a fulltime safety director, and safety committees.”⁸⁴

Accident and Incident reporting

Israel has in place a number of measures to monitor biosafety status and report laboratory incidents. Under the Work Safety Regulations (Occupational Safety and Hygiene in the Handling of Dangerous Agents in Medical, Chemical and Biological Laboratories), laboratory managers are required to “report in writing to the district work inspector for every instance of accident involving sprays, spills and general contamination involving exposure to a contagious biologic agent.” (NOTE: this is quoted in the cited reference, but it is unclear whether the language is taken directly from the legislation). Local work supervisors (i.e., government inspectors) have the right to inspect work and safety conditions; however, this right is limited with respect to “dangerous agents” (NOTE: the cited reference pre-dates development of the formal Disease Agent list and presumably refers to this “dangerous agents” in a general sense) for safety reasons.⁸⁴ If the work supervisors have the authority to “ban the use of a facility [or] equipment” if they identify an issue that “endangers the human welfare or health,” until the issue has been resolved. Laboratory holders are required to submit a work plan to the district work supervisor that includes protocols to address “work accident cases.”⁸⁴

Synthetic/Advanced Biology

Israel’s long history with advanced biology even predates its own existence. Before being elected as Israel’s first President, Chaim Weizmann, developed a process to use *Clostridium* bacteria to produce acetone for Great Britain in World War I.⁹³ Several academic institutes represent Israel’s modern leaders in synthetic and advanced biology. Several laboratory groups at the Weizmann Institute of Science, located in Rehovot, conduct advanced biology and synthetic biology research, including biofuels.⁹⁴ The Weizmann Institute of Science is home to the National Bioinformatics Center—also supported by the

Israel Academy of Sciences and Humanities (Israel Academy)—that conducts genomic research. The Israel Academy was an early supporter of the Human Genome Project and also supports genomic research the National Laboratory for the Genetics of Populations at the Tel Aviv University.⁹⁵ The first Pearl Seiden International Meeting in the Life Sciences was held at the Technion Institute of Technology in December 2015, focusing on synthetic biology.⁹⁶ The iGEM team from Ben-Gurion University was awarded Best Health and Medicine Project for their synthetic biology cancer therapy in 2015.⁹⁷

The Disease Agents Act expressly prohibits gain-of-function (GOF) research on Disease Agents.⁸⁸

Training

MOH requires that laboratory personnel go through training laboratory equipment before beginning work. Additionally, every employee must receive safety training on building evacuation, PPE, and biosafety policy. Biosafety officers specific to each facility are responsible for ensuring that their respective staffs receive annual biological and chemical training.^{84,98} Under the Work Safety Regulations (Occupational Safety and Hygiene in the Handling of Dangerous Agents in Medical, Chemical and Biological Laboratories), laboratory holders are responsible for conducting semiannual training for laboratory personnel for responding to emergencies. Additionally, the laboratory holder is required to conduct personnel training when they start working and yearly thereafter “on matters related to safety, hygiene and health risks arising from work with dangerous agents as related to the various methods for the prevention of such risks.”⁹⁵ Safety trustees (i.e., employees serving on the safety committee) are legally responsible for training other employees on “safety and hygiene” measures.⁹⁵

The Disease Agents Act requires that the Council for Biological Disease Agent Research “institute public information campaigns...as well as in-service training courses” for Disease Agent research; however, the legislation does not specify any requirements for such training. The Council can allow individual institutions to develop their own education and training programs, but the Council has authority to ensure these programs are adhered to.⁹⁹

Laboratory numbers

Israel has not declared the existence of BSL-3 or BSL-4 facilities.¹⁰⁰

Research Status

The majority of medical and life science research in Israel is conducted in the academic sector.^{84,88,89} The Ben-Gurion University is part of a public-private partnership to sponsor the Advanced Technologies Park in southern Israel, home to the National Institute for Biotechnology in the Negev among other centers of excellence.^{101,102} The Weizmann Institute, in addition to the National Bioinformatics Center, conducts research in the fields of agriculture and plant genetics; biotechnology, pharmaceuticals, and diagnostics;^{103,104} molecular genetics; and biological regulation, among other advanced sciences. In 2009, a Weizmann Institute professor, Ada Yonath, was awarded the Nobel Prize in chemistry for her research on the structure of ribosomes.¹⁰⁵ Tel Aviv University offers a microbiology and biotechnology graduate program, and faculty research interests include biofuels, antibody engineering, tissue engineering, and “experimental evolution of RNA viruses.”¹⁰⁶ The Technion Institute offers undergraduate, graduate, and postgraduate programs in a range of biology fields, including a dual program in biotechnology and food engineering.¹⁰⁷⁻¹⁰⁹ The Technion Institute also partners with the Massachusetts Institute of Technology for a postdoctoral program in engineering, physics, and chemistry.¹¹⁰

In the private sector, Genome Compiler, based in the US and Israel, specializes in “computer aided design and collaboration platforms for synthetic biology.”¹¹¹ Genome Compiler recently announced a partnership with Amyris to provide custom online design and production for “DNA and other biological

products.”¹¹² Johnson & Johnson partnered with Israel’s Office of the Chief Scientist to establish a “biotechnology incubator” near the Weizmann Science Park, a hub of scientific research and industry, including biotechnology.¹¹³ Several other similar science parks are located across the country as well. Teva, an Israeli pharmaceutical company, is the largest generic pharmaceutical provider in the world and is ranked among the world’s top 15 pharmaceutical organizations.^{100,114}

In 2010, Thompson Reuters ranked Israel in the top 20 nations worldwide in “biology, biochemistry, molecular biology, genetics, neuroscience, and clinical medicine, with an overall standard comparable with Austria, Belgium, and China.”¹⁰⁰ Israel’s rank on the Scientific American Worldview Scorecard fell from 5th in 2009 to 22nd in 2014 before rebounding to 18th in 2015.¹¹⁵ Israel also has an extensive biotechnology industry;¹⁰⁰ it is Europe’s second largest private producer of biotechnology per capita.¹¹⁶ “Biotechnology, biomedical, and clinical research account for over half of [Israel’s] scientific publications.”¹¹⁷ According to a 2009 report, Israel invested an impressive 4.53% of its GDP in research and development⁹⁵ (compared to 2.7% in the US).

Funding for Biosafety

No information found.

Kenya

Biosafety Oversight Summary

Kenya, a leader in African biological and agricultural research, first developed biosafety policy in the late 1990s.¹¹⁸ Kenya's most significant biosafety policy is the National Biosafety Act, which was passed in 2010 after signing the United Nations Cartagena Protocol in 2009. The Act mandated the establishment of the National Biosafety Authority (NBA) in 2010, under The National Commission for Science and Technology (now NACOSTI) and the Ministry of Science and Technology. The NBA approves and regulates the development, transport, and use of GM products.^{118,119} Research facilities use the Laboratory Biosafety and Biosecurity Policy Guidelines to develop their specific biosafety protocol and establish Institutional Biosafety Committees (IBCs) to enforce biosafety policy.¹²⁰

Pathogen Characterization

The NBA categorizes microorganisms and toxins by Risk Groups 1-4, Risk Group 4 having the highest individual and community risk. Laboratories are categorized based on their design, operational procedure and equipment. Biosafety facilities are ranked BSL 1-4 (equivalent to the WHO norm), with increased biosafety standards as pathogen Risk Group increases.¹²⁰

Relevant Regulations and Legislation

The **Regulations and Guidelines for Biosafety in Biotechnology, 1998** was produced by the National Council for Science and Technology (now NACOSTI) as Kenya's first biosafety policy.¹²¹ The **National Biosafety Act of 2009**, modeled after the Cartagena Protocol's policies, regulates all research, transfers, handling and use of GMOs. The Biosafety Act was updated in 2011-12 to include updated policies for contained use, transfer, labeling and environmental release of GMOs.^{122,123} Finally, the **Laboratory Biosafety and Biosecurity Policy Guidelines** is a template for individual laboratories at all biosafety levels to use in developing their laboratory biosafety protocol. The document complies with guidelines established by the WHO's biosafety guidelines, the Environmental Management and Coordination Act (EMCA), the Occupational Safety and Health Act (OSHA) regulation, as well as the National Infection Prevention and Control Guidelines for Health Care Services in Kenya.¹²⁰

Biosafety Agencies

The National Commission for Science, Technology and Innovation (NACOSTI) oversees the quality of technology and science innovation within Kenya and directly advises the government on funding these innovations.⁷³ The **Kenyan National Biosafety Authority** (NBA) under the Ministry of Science and Technology is the central body for biosafety and GMO research regulation within the country.^{124,125} The NBA, as specified in the Biosafety Act, collaborates with several government agencies to enforce biosafety law.¹²³ The National Biosafety Committee (NBC), comprised of a diverse group of academics and ministry representatives, reviews research applications submitted to the NBA.¹²⁶ Lastly, the **Kenya Plant Health and Inspectorate Service** (KEPHIS) works with the NBA as a regulatory agency to enforce biosafety guidelines for agricultural GM research.¹²⁷

Biosafety Associations

Kenya is a member of several African biosafety organizations including the International Centre for Genetic Engineering and Biotechnology (ICGEB), the Program for Biosafety System (PBS), the African Biosafety Network of Expertise/New Partnership for Africa's Development (ABNE/NEPAD) and Forum for Agriculture Research in Africa (FARA).¹¹⁸

Biosafety officers and Institutional Biosafety Committees

Institutional Biosafety Committees (IBCs) are regulated by the Kenya Agricultural Research Institute (KARI) and the International Center for Insect Physiology and Ecology (ICIPE) to review the research within these organizations.¹²⁶

The *Biosafety Act* stipulates that biosafety officers are tasked with monitoring compliance with the Biosafety Act and performing inspections among other functions.¹²⁸ Specifics about the organization through which these biosafety officers are hired and trained is unclear.

Accident and Incident Reporting

The *Biosafety Act* stipulates that all occupational incidents must to be reported and investigated, although the timeframe is unspecified. Upon receiving an incident report, an investigation must be carried out by a biosafety committee and/or Infection Prevention and Control Committee (IPCC). *The Kenyan Biosafety and Biosecurity Guidelines* require that post-exposure prophylaxis (PEP) be available to lab staff at all times as a precaution.¹²²

Synthetic/Advanced Biology

Kenya's primary use for synthetic biology is in GMO agriculture development. Thus most of Kenya's biosafety policy pertains to GMO research. Over the past few years, Kenyan scientists have pushed to end the government's ban on genetically modified (GM) foods. Prior to the ban, Kenya had conducted significant research into GM cassava, sweet potato, cotton, maize, and sorghum.¹²⁹ The Kenyan government, after considerable debate, committed to lifting the ban by the end of 2015.¹³⁰

Training

Procedures outlined in the Kenyan Biosafety and Biosecurity Guidelines recommend that all new and transferred staff should be trained within 30 days of employment. This training includes laboratory safety guidelines, risk assessment of the work place to make the employee aware of hazards, and training on specific procedures. Additionally, there are also recommendations for occupational health training, regular medical tests, and a health surveillance program.¹²² Specifications about the type of training and experience required for work in a biosafety lab are not provided.

Laboratory Numbers

Kenya is home to five BSL-3 labs and two BSL-2 labs as of 2013. These facilities are a joint collaboration between and Nagasaki University's Institute of Tropical Medicine (NUITM) and the Kenya Medical Research Institute (KEMRI). The Institute of Tropical Medicine Kenya research station and the Center for Microbiology Research (CMR) are both key BSL-3 facilities, completed in 2005 and 2007, respectively.¹³¹

Research Status

Kenyan investment in biotechnology and research is steadily increasing, and there are commitments to keep up the momentum through the Vision 2030 Medium Term Plan II.¹³² Government spending on agriculture R&D increased by 10 percent between 2008 and 2011. Over half of this funding comes from the national government and the second highest funding comes from donors and development banks.¹³³ In 2013, under the Science and Technology Innovation Act, Kenya established The National Research Fund which will receive 0.5 percent of the country's Gross Domestic Product (GDP) for research funding. The Kenyan government hopes to invest a total of 2% of its GDP to research projects by 2015.¹³⁴

Biotechnology is a growing field within Kenya. KARI is the leading biotechnology institute in the nation, with a center dedicated solely to biotechnology. As of 2013, all public Kenya universities offer biotechnology and biosafety courses, and several have impressive facilities dedicated to biotechnology

research. The University of Nairobi, for example, has the Center for Biotechnology and Bioinformatics and Kenyatta University has a biosafety level II green house with a plant transformation facility. ¹¹⁸

Though government suspension of GM research has temporarily slowed progress¹²⁹, there are several GM crops in development to meet needs for insect and disease resistant crops. ¹¹⁸

Funding for Biosafety

No information found.

Pakistan

Biosafety Oversight Summary

Pakistan has two fundamental biosafety documents, known as the Pakistan Biosafety Rules and the National Biosafety Guidelines established under the Pakistan Environmental Protection Act, 1997.^{58,135} The Pakistan Biosafety Rules provides broad regulations on the storage, manufacturing, and import of specified agents and GMOs as well as the regulatory which enforce biosafety policy.^{136,137} Separately, the National Biosafety Guidelines provides biosafety protocols for use within research facilities.¹³⁵ The Pakistani government has three key regulatory bodies, the National Biosafety Committee, the Technical Advisory Committee, and Institutional Biosafety Committees, which approve research projects and ensure that biosafety protocols and standards are up to par.¹³⁷

Pathogen Characterization

According to the National Biosafety Guidelines, Pakistan's laboratory research is classified as "minimal risk," "low risk," and "considerable level of risk" (Risk Categories 1-3), with biosafety regulations becoming increasingly strict for higher-risk research. Research conducted at a Risk Category 1 level does not need to be performed in a containment facility. Research of Risk Category level 2 must be performed in a facility of containment level C1 or higher. This level of risk is typically associated with recombinant DNA studies being performed with approved agents, studies performed with non-approved agents, genetic modification of entire plants, or the manipulation of early stage reproduction. Studies done with agents that pose substantial risk to laboratory personnel are classified as Risk Category 3 and require facilities of higher levels of containment.¹³⁵ Specifics on biosafety facility requirements are taken from WHO guidelines, the United States CDC's BMBL and the ABSA-Canada, depending on the institution.¹³⁸

Relevant Regulations and Legislation

The **Pakistan Environmental Protection Act, 1997** provides the legislation for Pakistan's existing regulatory framework including the production of the Pakistan Biosafety Rules and the National Biosafety Guidelines.^{58,139} With consideration for the Cartagena Protocol, the **Pakistan Biosafety Rules** (2005) provides regulations for the storage, manufacturing, and import of microorganisms, GMOs, and Living Modified Organisms (LMO)s.^{136,137,140} The rules outline the composition and functions of the National Biosafety Committee (NBC), Technical Advisory Committee (TAC), and Institutional Biosafety Committees (IBC)s and delineates Biosafety Officer expectations.¹³⁷ The **National Biosafety Guidelines** (2005) are the official Pakistani guidelines on biosafety practices and protocols for research and are prepared by the NBC.^{135,141} The guidelines are intended for research with recombinant DNA, transgenic organisms, GMO production, vaccine production, and any field trial or intentional environmental release.¹³⁵

Regulatory Agencies

- The **National Biosafety Committee (NBC)**(2005)^{138,142} as outlined in the Pakistan Biosafety Rules, works under the Ministry of Environment and is chaired by the Secretary of the Ministry of Environment.^{135,136} It serves as the executive body over both the TAC and the IBCs and is responsible for broad-scale risk management and assessment, laboratory regulation, and regulation of the release of GMOs, LMOS, and other research products.^{135,136} The NBC and IBC jointly approve and regulate high-level research facilities and Risk Category 3 projects.¹³⁵
- As stipulated in the Pakistan Biosafety Rules, the **Technical Advisory Committee (TAC)**, directed by the EPA Director General, functions as an intermediary between the IBCs and the NBC. It advises the National Biosafety Committee on which projects to approve, reviewing safety

protocol and research methodologies. Additionally, the TAC handles the regulation of large-scale GMO projects and their field trials.^{135,136,143}

- **National Biosafety Center** (2006) is regulated by the Pakistan Environmental Protection Agency (PAK-EPA) and the Ministry of Environment in compliance with the Cartagena Protocol on Biosafety. It serves to regulate GMO production and use by supporting the NBC, TAC, and IBCs.¹⁴¹

Biosafety Associations

- The **Biological Safety Association of Pakistan (BSAP)** organizes monthly and semiannual meetings with speakers on relevant biosafety topics and facilitates local forums to increase the sharing biological safety information. Additionally, BSAP hosts conferences held in conjunction with the American Biological Safety Association (ABSA), among others.¹⁴⁴
- The **Pakistan Agricultural Research Council (PARC)** is a national organization established in 1981 to foster agricultural research, establish research institutions, circulate research information, and aid in training agricultural researchers. PARC has four research divisions: plant sciences, animal sciences, social sciences, natural resources.¹⁴⁵
- The **Pakistan Biotechnology Information Center (PABIC)** was established under the National Commission on Biotechnology and the International Services for Acquisition of Agri-Biotech Application (ISAAA) to provide a place to exchange research information for greater coordination between research facilities.¹⁴⁶
- The **Organization of the Islamic Conference (OIC) Committee on Scientific and Technological Cooperation (COMSTech) (2008)**. COMSTech is a cooperation among members of the OIC, established to strengthen research in science and technology for enhanced socio-economic growth in member states.¹⁴⁷

Biosafety officers and Institutional Biosafety Committees

According to the Pakistan Biosafety Rules, Biosafety Officers (BSOs) are specific to each institution, performing research and serving as a liaison between the institution and their Biosafety Committee. The Biosafety officer is to review laboratory protocols and facility records regularly and make biosafety recommendations.¹³⁶ They also participate in regular instruction and training of the staff. To hold this position, BSOs must have training in biosafety and emergency countermeasures procedures.¹³⁵

Institutional Biosafety Committees (IBCs) are specific to each institution and report to the NBC through the TAC. As specified in the National Biosafety Guidelines, IBCs receive research application proposals from their institution, review the biosafety protocol, and then performs facility inspections and regulates project activity. IBCs have special oversight over Risk Category 1 research.¹³⁵

Accident and Incident Reporting

The details of a response to an incident and the reporting of the incident are specific to each institution, their BSO, and their IBC. If an incident is deemed by the IBC to require repercussions, the chair of the IBC is required to present the incident to the NBC for review. The NBC will then determine the next steps and if discipline is necessary.¹³⁵

Synthetic/Advanced Biology

The National Biosafety Guidelines provide guidance on research with GMOs, particularly pertaining to GM agriculture, with regulation from the NBC, TAC, and IBC.¹³⁵

Training

The IBC and the BSO are responsible for ensuring that laboratory staff are competent and current in their training. Supplemental training for staff in emergency preparedness, equipment operations, and specific test protocol is regulated by the BSO. The IBC, BSO, and the research project manager are permitted to administer random tests to ensure that all staff is competent.¹³⁵ Pakistan has participated in a number of biosafety training workshops and conferences hosted both domestically and internationally over the past ten years.^{138,148} Specifications about the type of training and experience required for work in a biosafety lab are not provided.

Laboratory Numbers

In Pakistan, many research facilities are limited to BSL-1 and BSL-2 capabilities, but work is being done to extend Pakistan's research abilities. The National Institute of Health, Islamabad has a BSL-2+ facility with a BSL-3 lab under construction and both Aga Kahn University and Indus Hospital Karachi now have BSL-3 facilities.¹³⁸

Research Status

According to the International Service for the Acquisition of Agri-biotech Applications (ISAAA), Pakistan has 41 organizations involved in biotechnology development. Pakistan's biggest biotechnology accomplishments are in GM agriculture,¹⁴⁹ ranking 9th in the world in 2014 in GM crop production.¹⁵⁰ Pakistan's primary crop is Bt cotton, of which farmers grew 2.9 million hectares in 2014, this was a 4% growth increase from the previous year.¹⁴⁹ However, despite producing such a large amount of GM crops, no other GM crops have been developed or released within Pakistan.¹⁵⁰

Aside from agri-biotech, Pakistan is pushing to increase its authority in research. Notably, Pakistan is one of few countries to have sequenced the human genome. The Panjwani Center for Molecular Medicine and Drug Research (PCMD), in collaboration with Beijing Genomics Institute (BGI), sequenced the genome of the President of the Pakistan Academy of Sciences, Dr. Ata-ur-Rehman.¹⁵¹

Funding for Biosafety

No information found.

Russia

Biosafety Oversight Summary

The Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing (Rospotrebnadzor) oversees Russian research institutes as well as hygiene and epidemiology centers, anti-plague institutes, and sanitary services.¹⁵² It awards permissive documents, certifications, licensing, and registration related to research and sanitation and communicates directly with the federal government and relevant agencies on matters of biosafety.¹⁵³ The Russian's *Regulations on Handling Microorganisms in Pathogenicity Groups 3, 4*, written in 2008, is a key biosafety guidelines document, providing detail on standard operating procedure and laboratory best practices. Under these regulations, safety oversight in daily operations is the responsibility of the facilities' laboratory manager while the Rospotrebnadzor and public health offices provide oversight at a national level.¹⁵⁴

Pathogen Categorization

The State Sanitary-Epidemiological Inspection Committee classifies pathogens into Hazard Groups 1-4, comparable to the reverse order of the WHO's risk group 1-4 (i.e., Russian Hazard Group 1 is equivalent to a WHO Risk Group 4). This translates to BSL facilities as well, where a BSL-1 facility in Russia contains the most hazardous pathogen group.¹⁵⁵ Russia classifies some agents as a lower risk than the US and some other nations do; for example, work done with Crimean-Congo hemorrhagic fever virus, Omsk hemorrhagic fever virus, and tick-borne encephalitis virus are all typically performed in BSL-4 labs in the U.S. but are performed in a BSL-3 equivalent facility in Russia.¹⁵⁶

Relevant Regulations and Legislation

The national **Sanitary Regulations (SR)** in 1993 were Russia's first published policy on biosafety practices. This document has been updated since its original publication and includes facility biosafety categorizations, accountability to biosafety policy, and a standard for biosafety training.¹⁵⁷ Guidelines for working specifically with the most pathogenic agents are found in the 2008 **Regulations on Handling Microorganisms in Pathogenicity Groups 3,4**, which was extensively revised in 2009 and is intended to provide biosafety guidelines for both federal and private facilities.¹⁵⁴ Another influential biosafety document is the **English-Russian Harmonized Dictionary in Biosafety and Biosecurity (2010)** which is a resource for biosafety and biosecurity terminology along with information about organizations involved in biosafety.¹⁵⁷

Regulatory Agencies

The Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing (Rospotrebnadzor) was created in 2004.¹⁵⁷ This organization oversees Russian research institutes as well as hygiene and epidemiology centers, anti-plague institutes, and sanitary services.¹⁵² The Rospotrebnadzor awards permissive documents, certifications, licensing, and registration related to research and sanitation. It communicates directly with the federal government and coordinates with the Ministry of Defense, Ministry of Internal Affairs, Federal Security Service for epidemic preparation and response.¹⁵³

Biosafety Associations

Global Partnership Against the Spread of Weapons and Materials of Mass Destruction. Through this partnership, Canada provided Russia assistance in improving biosafety and biosecurity standards. Canada has translated biosafety training programs and documents into Russian for more widespread use.^{158,159}

Biosafety Officers and Institutional Biosafety Committees

Every facility working with Russian groups 1 and 2 pathogenic biological agents is required to write specific procedures for lab safety, for “safe operation under the specific conditions with consideration for the nature of the work, features of the process, properties of the microorganism, and the products of its vital functions.” The drafted procedures have to be approved by a designated committee created for biosafety accountability at the specific facility. The daily oversight of safety regulations is tasked to the laboratory manager or an individual assigned that task. The Rospotrebnadzor, along with unnamed federal authority agents, and public health offices are tasked with regulation compliance.¹⁵⁴

Accident and Incident Reporting

Section 3.3 of the *Regulations on Handling Microorganisms in Pathogenicity Groups 3, 4* provides procedures for several different categories of laboratory incidents. These incidents include agent dissemination, agent release in a localized area, an agent passing the skin barrier, and a centrifuge accident. In all of these cases, an accident alarm is to be activated, and facility manager notified. The lab manager must then report the incident to their committee for monitoring compliance with biological safety requirements and to the organization's head. The facility manager and the chairman of the committee for monitoring compliance must then determine the necessary steps for response after assessing the issue. After the incident is over, the facility manager must submit a formal report to both the organization head and the committee for monitoring compliance for review. These two parties will then analyze the incident and determine what needs to be changed to prevent a similar accident.¹⁵⁴ Any employee who starts to display symptoms consistent with that caused by an agent used in their facility is required to immediately notify their superior. No further details are specified.¹⁵⁴

Synthetic /Advanced Biology

One of Russia's largest synthetic biology initiatives is SynBio, a project for the innovation of new medicine, called Biobetters, contributed to by several pharmaceutical companies and collaborators in England, Germany and Russia. The largest shareholder, Russian organization Human Stem Cells Institute (HSCI), uses gene-therapy, stem cell research, and post-genome technologies for medicine development.¹⁶⁰ SynBio receives funding from Rusano, a Russian government co-investor for nanotechnology development.³⁹ The project has developed and produced nine medications which are currently on the market.³⁷

In September of 2015, the Russian government banned the production of genetically modified agriculture, excluding research, within Russian borders. Concern about the safety of GM products led to a ban on importing GMOs in 2014 and now the ban on production.¹⁶¹

Training

The Sanitary Regulations outline requirements for hired personnel. To work with Hazard Groups 1-4 pathogen, a lab employee must meet the following requirements: advanced education, experience in medicine, biology, or veterinary science, and specific permission from the director of the institution, which must be renewed every two years.¹⁵⁵ Employees working with agents of Russian Hazard Groups 1-2 must meet the above requirements and additionally be at least 18 years of age and have completed the appropriate courses of specialization in addition to their secondary education. Staff training must occur annually to ensure competency with biological protocol. Supplementary research staff, such as technicians, engineers, cleaning staff, and assistants, working in facilities with Hazard Groups 1-2 must also undergo periodic training. Prior to starting work, they are required to participate in an introductory

course and then must complete refresher courses periodically afterwards.¹⁵⁴ Specifications about the type of training and experience required for work in a biosafety lab are not provided.

In 2008, Russia received assistance from the Canadian Association for Biological Safety to train instructors for biosafety programs.¹⁵⁷ WHO and US biosafety documents were translated and used for training purposes.¹⁵⁹ With assistance, Moscow Medical Academy and several other Russian universities and institutes added new biosafety and biotechnology courses to their repertoires.^{157,162} In fact, the Saratov Anti-Plague Institute has developed several very specialized biosafety training programs including programs for epidemic control for counter-bioterrorism purposes.¹⁵⁷

Laboratory Numbers

According to Rospotrebnadzor, as of 2014 there were 29 scientific research institutes and 12 Plague Control Stations in Russia.¹⁵² Two of Russia's largest research facilities are the State Research Center of Virology and Biotechnology VECTOR, located in Novosibirsk, and the Defense Ministry's Microbiology Research Institute at Sergiev Posad. These centers perform research with some of the world's most pathogenic agents. Significantly, the Russian Federation's VECTOR facility is one of two labs in the world to host samples of live smallpox virus.¹⁶³

Research Status

Though Russia has made significant contributions global IT and nanotechnology research, its biotech industry has room for growth.¹⁶⁸ Through the BIO2020 plan, the Russian Federation is committed to investing \$39 billion for bio-tech industry between 2012 and 2020.^{164,165} Russia is hoping that by 2020 the bioeconomy will be valued at 1 percent of Russia's GDP and 3 percent by 2030.¹⁶⁶ To foster bioeconomic growth, the government plans to build 10 factories for biogenerics production.¹⁶⁸ It has also initiated public-private partnerships with biotech organizations like *SynBio*, and has invested in private organizations like *BIND Biosciences*, *BiOptix Diagnostics*, and *Selecta Biosciences*.¹⁶⁷

Funding for Biosafety

No information found.

Singapore

Biosafety Oversight Summary

Singapore's biosafety focus sharpened after a 2003 laboratory-acquired SARS infection. Recommendations from a formal nationwide review of BSL-3 biosafety practices led to national legislation for biosafety standards (Biological Agents and Toxins Act or BATA), formalized certification for laboratory structure, and tightened operational procedures.¹⁴⁵ The Biosafety Branch in the Ministry of Health (established in 2005) is responsible for nationwide biosafety policies.⁹³

Pathogen Categorization

Singapore categorizes biological agents by "schedules." First Schedule agents include bacteria, fungi, and viruses that can cause severe disease in humans. First Schedule agents are broken into two parts; agents in Part II are capable of being weaponized. Second Schedule agents include other highly dangerous viruses, including Ebola virus, Nipah virus, and smallpox. The Third and Fourth Schedules are comprised of Bordetella pertussis, Legionella bacteria, Hepatitis B virus, and all other infectious biological agents not included in the First and Second Schedules. Fifth Schedule agents are harmful toxins such as botulinum toxins and shiga toxins. Under the BATA, possessing First or Second Schedule biological agents requires the facility be designated as a "protected place" and that personnel be vetted by the Ministry of Home Affairs. Additionally, the facility must be certified by a Director of Medical Services (DMS)-approved certifier. Alternately, the DMS can approve work with First Schedule agents if he/she is confident that work will be conducted in a "safe and proper manner."¹⁴⁷ Certification criteria are based on the WHO Laboratory Biosafety Manual checklist.¹²⁰ Singapore uses the same BSL rating system as the WHO, but they require additional safety measures for labs working with GMOs (GM-BSL2 through GM-BSL4).¹⁶⁹

Relevant Regulations and Legislation

Based on recommendations from the National Biosafety Committee (comprised of representatives from a wide range of agencies, organizations and companies), Singapore enacted the Biological Agents and Toxins Act (BATA) in 2006.^{120,147} The BATA "prohibit[s] or otherwise regulate[s] the possession, use, import, transshipment, transfer and transportation of biological agents, inactivated biological agents and toxins" and supports safe handling of dangerous biological agents. The BATA also classifies biological agents and toxins into schedules, as discussed above. The BATA covers "companies and institutions (including educational institutions) involved in biomedical and life sciences work or research with biological agents and toxins listed in the Schedules of the BATA."¹⁷⁰ The Protected Areas and Protected Places Act provides authority to limit authorized access to designated areas and facilities, such as those working with First or Second Schedule biological agents.¹⁷¹

In 2013, the Genetic Modification Advisory Committee (GMAC) published The Singapore Biosafety Guidelines for Research on Genetically Modified Organisms to address "safe containment, handling and transport" of GMOs and implement an "assessment and notification" framework for GMO research.¹⁶⁹ These guidelines are not legally binding, but GMAC partners with several federal agencies, including the MOH, to implement them nationwide.¹⁷²

Regulatory and Oversight Agencies

The Biosafety Branch, established in 2005 under MOH, is primarily responsible for Singapore's nationwide biosafety policy and implementation of BATA. It also serves as the "secretariat for the National Biosafety Committee, and the three Technical Working Committees, namely, Select Agents List, Biosafety Training and Biosafety Standards."⁹³ They conduct audits and inspections required under the

BATA, investigating laboratory accidents and developing procedures for “biosafety emergencies and response.”⁹³

The Genetic Modification Advisory Committee (GMAC; under Ministry of Trade) oversees “research and development, production, release, use and handling of genetically modified organisms (GMOs).” GMAC has subcommittees for the release of agriculture-related GMOs, research on GMOs, labeling of GMOs, and public awareness.¹⁷³ The Subcommittee for Research on GMOs developed and released the Singapore Biosafety Guidelines for Research on GMOs in 2006, and they have research oversight over all GM/GMO research.¹⁷⁴ The guidelines were designed to “ensure the safe containment, handling and transport of GMOs...and provide a common framework for assessment and notification of research on GMOs.”^{175,176} Facilities doing GMO research are required to have an Institutional Biosafety Committee to oversee the work, and “GMAC should be notified or consulted for medium to high risk projects.”¹⁷⁵ GMAC has also published supplemental guidance regarding the importation and release of GMOs.¹⁷⁷

Biosafety Associations

The Biorisk Association of Singapore (BAS; founded in 2010 by Dr. Ai Ee Ling) is a non-profit, multidisciplinary association promoting biosafety in Singapore with the aim of fostering the development and recognition of biorisk management as a profession, promoting safe management of biological materials, providing a key platform for knowledge-sharing in biorisk management, facilitating collaboration within the local and international biorisk management groups/associations, promoting education in biorisk management, and promoting applied biorisk research. BAS is affiliated with the American Biosafety Association (ABSA International) and the Asia-Pacific Biosafety Association (APBA).¹⁷⁸ APBA offers biosafety training throughout the region, including principles and practices, biosafety management, and Certified Biosafety Coordinator for Singapore.^{34,179}

Biosafety officers

The BATA requires that each facility has a biosafety committee and a biosafety coordinator. It also requires Institutional Biosafety Committees (IBCs) to oversee biological research, facilities, and personnel. IBCs must be comprised of a biosafety coordinator, microbiologist, maintenance officer, and a senior management representative. They are required to conduct risk assessments, manage the risks that may arise from the proposed activity, formulate other policies as may be necessary for the proposed activity to be carried out safely, and provide appropriate training for staff. They review all measures, policies, programs, and codes of practice every 2 years. The biosafety coordinator is responsible for implementing “measures, policies, programmes and codes of practice as devised or formulated by the biosafety committee” as well as implementing changes determined by the biosafety committee during reviews of the program.¹⁴⁷

Accident and Incident Reporting

Under the BATA, notification is required for failure of receipt for First Schedule Part II, Second Schedule, and Fifth Schedule agents and toxins within 24 hours of the expected delivery. In the event of an actual or suspected incident involving a biological agent/toxin which is an imminent threat to public health, threat to national security, or contrary to the public interest, the DMS has the authority to order the immediate stoppage of all work with biological agents and toxins, the destruction of any agent or toxin, facility decontamination, facility closure, and/or medical examination and/or quarantine for exposed individuals. Unauthorized possession, import, and transfer of biological agents or other biosafety violations involving biological agents carry severe penalties in Singapore. Violations involving First Schedule Part I, Third Schedule, or Fourth Schedule agents are punishable by up to \$10,000 and 12

months in prison. Violations involving First Schedule Part II, Second Schedule, or Fifth Schedule agents carry a penalty of up to \$100,000 and 10 years in prison.¹⁴⁷

Synthetic/Advanced Biology

The field of synthetic biology is growing rapidly in Singapore, and considerable efforts are being made in both the public and private sectors to facilitate synthetic biology progress. Since 1999, GMAC has provided science-based guidance for the growing field of genetic modification in Singapore. GMAC generates recommendations regarding the “research and development, production, use and handling of GMOs” and conducts public education and awareness efforts regarding GMOs.¹⁷³ Biopolis opened in 2003, providing Singapore a concentrated research and development hub to facilitate public, private and academic collaboration in a wide range of biological research field, including biotechnology and synthetic biology. It is located in close proximity to several universities with advanced biology programs, including the National University of Singapore. As of 2013, the total investment in Biopolis development and construction is estimated at \$700 million (SG) (approximately \$500 USD).¹⁸⁰

The academic sector is also actively involved in advanced biology research. In 2015, the National University of Singapore—with partnerships at the University of California Berkeley, Lawrence Berkeley National Laboratory, Imperial College London and the University of Edinburgh—established the Synthetic Biology for Clinical and Technological Innovation (SynCTI) research initiative at a cost of \$25 million (SG). SynCTI aims to “train 30 post-graduate students each year, and more than 90 synthetic biologists over the next three years.”¹⁸¹ Nanyang Technological University has also established a synthetic biology program and is building international collaborative relationships.¹⁸²

The Singapore Agency for Science, Technology and Research (A*STAR) established the Genome Institute of Singapore in 2000 (then called the Singapore Genomics Programme) to conduct a wide range of genetic research, including synthetic biology and genetic engineering.¹⁸³ In January 2016, Singapore hosted the International Conference on Biomolecular Engineering, including plenary sessions on metabolic engineering, biomaterials design and assembly and synthetic biology.⁴⁵ While synthetic biology research is abundant in Singapore, industrial synthetic biology presence is limited. Without significant industry investment, funding for synthetic biology is relatively limited. Government agencies such as A*STAR, the National Medical Research Council, and the National Environment Agency provide the majority of funding in this area.¹⁸⁴

Training

In 2015, the APBA, BAS, MOH, Singapore Workforce Development Agency and Temasek Life Sciences Laboratory jointly developed a “biosafety training structure” and “biosafety passport.” The initial effort targeted 9,000 personnel across “more than 50 companies, local universities, and 30 public-sector institutes.” The program consists of the Biosafety Induction Programme (orientation for all lab personnel), Biosafety Professional Programme (experienced lab personnel who want to be Biosafety Coordinators or Biosafety Officers), and Professional Certification for Continued Education (professional workshops, conferences and courses conducted by APBA and BAS to address emerging trends and the future of the biological industry). The biosafety passport documents training completed to allow personnel to transfer between companies/organizations without needing to repeat training and allowing them to get to work sooner. Additionally, the WDA coordinates with universities to incorporate the biosafety passport into the curriculum, and the WDA can conduct training at facilities that do not have an in-house training staff.¹⁸⁵

Biosafety coordinators must undergo training as designated by the DMS.¹⁴⁷ Biosafety coordinators in a certified facility are required to take a training course and pass an exam provided by a MOH-approved

trainer. Training for staff working in a certified BSL-3 laboratory is required under the BATA; it can be conducted by in-house or external trainers. Staff and Biosafety coordinators at non-certified facilities are not required under the BATA to attend any specific training—training is recommended, however.¹⁷⁰ Biosafety coordinators at non-certified facilities approved to work with First Schedule agents may be subject to additional training as determined by MOH.¹⁸⁶ MOH maintains a database of approved training providers that have “relevant and suitable resources to conduct courses for Biosafety Coordinators working in BSL-3 facilities.”¹⁸⁷

Laboratory numbers

After the 2003 SARS laboratory incident, Singapore ordered a review of its national BSL-3 laboratories. The report provided detailed information and recommendations for four BSL-3 laboratories: Environmental Health Institute, Singapore General Hospital, National University Singapore and the Defence Science Organization.¹⁴⁵ Explicitly addressing these laboratories implies that these were the only BSL-3 labs in existence at the time. In 2009, WHO reported that Singapore had increased its laboratory capacity to ten BSL-3 laboratories;¹⁸⁸ however, a report about the opening of a BSL-3 lab at the National University of Singapore in 2015 indicated that there were only 7 such facilities in the country at that time.¹¹¹ The Phase 4/5 expansion of the Biopolis biotechnology research complex (completed in 2013) put the campus at a total of 13 buildings and more than 4.0 million square feet of space.¹⁸⁹ Part of the impetus for the 2003 post-SARS biosafety review was Singapore’s desire to have formal biosafety regulation and training policies in place to support anticipated BSL-3 laboratories at Biopolis, at the time estimated at 16 laboratories.¹⁴⁵

There are several uncited accounts reporting that the Singapore Defense Science Organization operates a BSL-4 facility.¹⁹⁰⁻¹⁹³ A 2009 WHO report, supported by other sources, indicates that Singapore operates a mobile BSL-4 autopsy suite.^{188,192,193}

Research Status

Scientific American Worldview ranked Singapore 5th for biotechnology research in 2015. Strengths included intellectual property protection; business-friendly environment; and available capital, infrastructure, and political/government landscape (stability, regulation, etc.). Weaknesses included research intensity (patents awarded and contribution to the global field) and education and workforce quality.²⁶ The Biopolis biotechnology research complex—opened in 2003 and expanded in 2006, 2009 and 2013—has been a significant contributor to the growth of biomedical science (BMS) in Singapore. Singapore BMS manufacturing grew from \$6 billion in 2000 to nearly \$30 billion in 2012, and BMS employment grew from 6,000 to 15,700 over that span.¹⁹⁴ Biopolis, alone, houses 38 biomedical companies and 10 research institutes and consortia, employing more than 2,500 researchers from 70 countries.¹⁸⁹

A*STAR oversees public sector research and provides a link between academia and industry. Their Biomedical Research Council (established in 2000) “oversees and coordinates public sector biomedical research and development activities.”¹⁹⁵ A 2008 US Army report indicates that the Singapore scientific output related to high-containment pathogens and genetic manipulation increased 450% between 1997-2001 and 2002-2007. Additionally, Singapore’s investment in science increased more than 8 times faster than its GDP between 2001 and 2006 (US: 1.5; UK: 0.53; China: 2.8; Japan: 20; Russia: 0.014).¹⁹¹

Funding for Biosafety

No information found.

United Kingdom

Biosafety Oversight Summary

After the 2007 laboratory-caused foot-and mouth-disease outbreak in Normandy, the United Kingdom made significant reforms to its biosafety policy and regulatory processes. There is now a singular, unified government agency for biosafety regulation called the Health and Safety Executive (HSE). The HSE is the primary regulator for oversight of pathogens, research, laboratory inspections, and research monitoring. In the UK, pathogens are categorized into hazard groups (HG1-4) and corresponding containment levels (CL1-4). Though there are several biosafety guidelines in use, the most recent and comprehensive document is Genetically Modified Organisms (Contained Use) Regulations, 2014 which encompasses research on human and animal agents and genetic modification.¹⁹⁶

Pathogen Categorization

Under the Control of Substances Hazardous to Health Regulations 2002, Biological agents are defined as any micro-organism, cell culture, prion or human endoparasite which could be hazardous to human health. This includes genetically modified as well as non GM agents. Biological agents are classified into one of four hazard groups (HG1-4) and concordant containment levels (CL1-4) that indicate what kind of containment and control measures should be in place in the laboratory. Regulation is based on the categorization of pathogens into 4 groups, CL1-4 (equivalent to the US norm of Biosafety Level or BSL 1-4, with 4 containing the most hazardous agents).¹⁹⁶

Relevant Regulations and Legislation

- The **Reporting of Injuries, Disease and Dangerous Occurrences Regulations 1995 (RIDDOR) (Updated in 2008, 2013)** HSE guidelines for reporting incidents.¹⁹⁷
- The **Specified Animal Pathogens Order 1998 (SAPO)** (revised in 2008) regulates animal pathogens. SAPO is a licensing system; the license specifies conditions of how the pathogen can be handled following inspection of the laboratory and documentation. Licenses are usually valid for 5 years.¹⁹⁶
- The **Approved List of biological agents (2000)** classifies biological agents as outlined by COSHH.¹⁹⁸
- The **Genetically Modified Organisms (Contained Use) Regulations 2014, (GMO (CU))** is concerns the protection of health from risks associated with the contained use of GMOs. The focus of this legislation is on the environment, as well as the workers. It's now on the 2014 version, and requires notification of all premises to HSE, and requires notification of contained use. Differing from COSHH and SAPO, the GMO(CU) categorizes agents (Class 1-4) according to their risk to both the environment and to lab staff.^{196,199}
- The **Anti-terrorism Crime and Security Act 2001 (ATCSA)** allows the policy to impose security measures on laboratories which handle pathogens of particular concern. Implemented by the National Counter-Terrorism Security Office (NaCTSO).²⁰⁰
- The **Management, design, and operation of microbiological containment laboratories (2001)** ACDP guidelines for general management of BSL 2-3 facilities.¹⁹⁶
- The **Control of Substances Hazardous to Health Regulations 2002 (COSHH)** deals with risk assessment, prevention or control of exposure to biological agents.¹⁷⁷ This also complies with the European Directive 2000/54/EC on protection of workers from risks related to exposure to biological agents at works that requires Member States to classify biological agents. COSHH, together with the Approved Codes of Practice (ACOPs), require employers to assess the risks of

exposure to biological agents and prevent exposure where reasonably practicable, or control it adequately. Work needs to be notified at least 20 days before it begins.¹⁹⁶

- **Biological agents: Managing the risks in laboratories and healthcare premises (2005)** ACDP guidelines for determining the necessary control measures for laboratory research with different agents.¹⁹⁶
- **Biological agents: The principles, design, and operation of Containment Level 4 facilities (2006)** ACDP guidelines for high-containment facilities specifically in regard to human health.¹⁹⁶
- **The Biological Agents and Genetically Modified Organisms (Contained Use) Regulations (2012)**. A singular guideline document encompassing research on human and animal agents and genetic modification which replaced the 2000 GMO(CU) and parts of SAPO and COSHH.¹⁹⁶

Biosafety Agencies

The Health and Safety Executive (HSE) is the central government body for maintaining standards in biosafety. It services as an advisor, regulator, and enforcer of biosafety policy.¹⁹⁶ Within the HSE there are several committees with biosafety functions. The **Advisory Committee on Dangerous Pathogens (ACDP)** gives independent council on biosafety issues of concern to the HSE, Defra, and similar organizations in Scotland, Wales, and Northern Ireland. The ACDP has also produced three documents on biosafety which are published and distributed by the HSE.¹⁹⁶ The **Scientific Advisory Committee on Genetic Modification (SACGM)** is advisory committee to the HSE. It provides noncompulsory regulations on good practice.²⁰¹ Lastly, the **Biological Agents Unit** advises the UK government on matters of biosafety. Outside of the HSE, the **Department of Environment Food and Rural Affairs (Defra)** issues licenses for research with select agents as specified under SAPO.¹⁹⁶

Biosafety Associations

The United Kingdom is a part of several biosafety associations which include the **European Biosafety Association (1996)**, which works to establish and maintain best biosafety practices. Provides a place for biosafety professionals to network and learn from each other.⁸² The UK is also a part of the **International Federation of Biosafety Associations** provides training and certification for biorisk management and biosafety.²⁰²

Biosafety Officers and Institutional Biosafety Committees

Biosafety officers receive accreditation from the Institute of Safety in Technology and Research (ISTR), which is a membership organization in the UK for safety professionals.²⁰³ There are levels of biosafety career accomplishment (Level 1 Practitioner and Level 2 Biosafety Professional). Regulation 6 of the *Management of Health and Safety at Work Regulations 1999* requires every employer to appoint one or more 'competent persons' to assist them in undertaking the measures required to comply with the relevant statutory duties. The majority of requirements listed in the *Genetically Modified Organisms (Contained Use) Regulations 2000* (as amended) need to be delegated to a local level. Where Genetic Modification (GM) work is undertaken, the role of 'competent person' has traditionally been undertaken by a Biological Safety officer (BSO).²⁰⁴ The ACDP highlights the important role of Biological Safety Officers/Advisors (BSOs/BSAs).¹⁹⁶

The GMO(CU) require that a biological safety committee must be formed whenever a risk assessment is performed for a class 3 or 4 facility.²⁰⁵

Accident and Incident Reporting

There are several different biosafety documents which address incident reporting in a research facility. RIDDOR requires that labs report specific accidents or potential incidents involving specific agents to the

HSE. The HSE has the authority to stop research until specific requirements are met by a given facility. It can also revoke, amend, or suspend research licenses if it feels that noncompliance is an issue.

A guide to the reporting of Injuries, Diseases and Dangerous Occurrences Regulation 1995 (2008) contains the guidelines for incident reporting based upon RIDDOR policies. Additionally, GMO(CU) has protocol for incident reporting in GMO studies¹⁹⁶ and COSHH has guidelines pertaining to infections contracted at a biosafety facility. Diseases and any acute illness needing medical treatment must be reported (within 10 days of the incident) whenever there is reasonable evidence suggesting that a work-related exposure was the likely cause of the disease. The doctor may indicate the significance of any work-related factors when communicating their diagnosis. A license holder is required to notify HSE if there is an accident or dangerous occurrence involving any of the animal pathogens listed in schedule 1 of SAPO, or if there is a loss of a specified animal pathogen during its transportation. Such incidents are to be reported by telephone to HSE, and a completed accident notification should be sent within 24 hours in writing.¹²¹

Synthetic/Advanced Biology

Genetically modified agriculture is currently not permitted in the United Kingdom, but GM crops are imported for livestock and some products are used within the region. Public protests have limited GM agriculture endeavors and though there is no legislation prohibiting GMO research, field trials, or use.¹³ The Genetically Modified Organisms (CU) regulations provide a framework for risk assessment and notification of research for work in synthetic biology and also studies on the consumption and use of GM plants and products containing GMOs.¹⁹⁹ Research is classified according to risk groups comparable to containment levels 1-4. Approval from the HSE and Defra is required for working with Class 2-4 agents, and activities in Risk Classes 3 and 4 require written consent from HSE.¹⁹⁶

Training

Some organizations, like the Northern Biosafety Training Centre, use ISTR materials within their curriculum to provide ISTR accreditation.¹⁶ According to *The Biological Agents and Genetically Modified Organisms (Contained Use) Regulations*, staff training within research labs is the responsibility of the laboratory employer. As the risk level of the facility increases, training requirements become more formal and intense. Newly hired staff receive introductory training, followed by periodic refresher courses and assessments.²⁰⁵

Laboratory Numbers

The United Kingdom has about 600 CL3 (basically BSL3) laboratories, and 9 CL4 laboratories.²⁰⁶ Of the 600 CL3 facilities, an estimated 105 are in research institutes, another 150 are in universities, and roughly 75 are privately run facilities. Many of these facilities are run by a small number of institutions. For example, the National Health Service (NHS) owns 170 CL3 laboratories primarily for diagnostic purposes, and two separate universities own 84 CL3 facilities between them. Research with the most pathogenic agents in CL4 facilities is primarily carried out by government agencies.¹⁹⁶

Research Status

The UK Ranked 9th on the 2015 Scientific American Worldview Overall Scores for biotechnology innovation. Its lowest scores were in productivity and intensity and its highest were in Ingress Protection(IP) Production and policy/stability.²⁶ According to the UK Biotech database, there are 1019 biotech organizations in the UK. The most popular areas of Biotech research are Diagnostics and Analytical Services, Contract Research and Manufacturing, and Therapeutics in that order.²⁰⁷

Funding for Biosafety
No information found.

United States of America

Oversight of biosafety (summary)

Biosafety in the United States is regulated by several agencies who work together to ensure comprehensive oversight of ongoing research. The Center for Disease Control and Prevention's (CDC) Federal Select Agent Program (FSAP) regulates the possession, use and transfer of specified biological select agents and toxins. Other government agencies which provide biosafety regulation are the U.S. Department of Health and Human Services (HHS), the National Institutes for Health (NIH), Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA).²⁰⁸ The *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) and the *NIH Guidelines for Research Involving Recombinant or Synthetic nucleic Acid Molecules* (NIH Guidelines) are two biosafety documents which are used across the country work with biological agents and nucleic acids respectively.^{209,210} These guidelines set a standard for biosafety not only within the U.S., but also internationally.²¹¹

Pathogen Categorization

The BMBL gives details on facility biosafety levels based up on pathogen risk levels.²¹¹ Infectious agents are ranked in Risk Groups 1-4, as are the WHO biosafety guidelines and the *NIH Guidelines*.^{210,212} Based lethality to humans, availability of therapeutic interventions, and risk of infection, Risk Group 1 agents pose the smallest risk to humans and Risk Group 4 pose the greatest risk. Biosafety regulation is based on the categorization of pathogens into 4 groups, BSL1-4, in which the agents can be safely handled.^{210,212}

Relevant Regulations

The Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) authored the **Biosafety in Microbiological and Biomedical Laboratories** (BMBL) as a guidance for research laboratories.²⁰⁹ Compliance with the BMBL is considered mandatory for select agent laboratories as a condition of some grants and contracts and in many federal facilities.²¹³ The BMBL is used as a reference internationally and as a standard for international biosafety protocol.^{209,211} The **NIH Guidelines for Research Involving Recombinant or Synthetic nucleic Acid Molecules**, also known as the "NIH Guidelines" provides guidance for safe handling of recombinant or synthetic nucleic acid molecules.¹⁹⁷ According to these guidelines, any nucleic acid experiment must be approved by the NIH or another federal agency with appropriate jurisdiction.²¹⁰ For select agent experiments in which recombinant DNA containing genes from toxins of a specific lethality is used,²¹⁴ the **Restricted Experiment Guidance Document** provides necessary regulations.²¹⁵

Additional biosafety guidelines include **Standard Operating Procedures for Biosafety in the Laboratory**. Released in 2006 and revised in 2011, this is an EPA outline for "required safety measures for working with the microorganisms received and maintained by the OPP Microbiology Laboratory."²¹¹ The **Standard Operating Procedure for OPP Microbiology Laboratory Personnel Training**. "This SOP describes the Microbiology Laboratory Branch (MLB) requirements for education, experience, and training of each employee in order to ensure that testing and other laboratory procedures are performed by qualified individuals."²¹⁶ This protocol was released in 2004 and revised in 2015 and is applicable to all positions within a biosafety laboratory.²¹⁶ Both of these documents refer to the BMBL as a resource for biosafety protocol.

Regulatory and Oversight Agencies & Legislation:

There are several government agencies involved in the regulation of biosafety. When the Antiterrorism and Effective Death Penalty Act of 1996¹⁵⁷ was passed, the **U.S. Department of Health and Human Services** developed a list of biological agents which could threaten national security, regulations for transferring these agents,²¹⁷⁻²¹⁹ and the CDC's **Federal Select Agent Program (FSAP)** to "oversee the possession, use and transfer of biological select agents and toxins."^{217,220} The Select Agent Regulations are established through the following policies:²²¹ the USA PATRIOT Act (determines access to agents),²²² Possession, Use, and Transfer of Select Agents and Toxins²¹⁸ (A Federal Register with the list of Select Agents and Toxins regulated by the HHS and the USDA),²²³ and the Public Health Security and Bioterrorism Preparedness Response Act of 2002 (which inhibits "restricted persons" from sorting, using, and transferring Select Agents and Toxins).²¹³ The FSAP also regulates select agent restricted experiments through its guidance documents.²¹⁴

In addition the CDC's FSAP, **National Institute of Health (NIH)** Office of Biotechnology Activities (OBA) has a biosafety program with "manages and evaluates the current biosafety policies for NIH-supported research at institutions in the US and abroad."²²⁴ The NIH has not only released the previously mentioned "NIH Guidelines" and contributed to the BMBL, but has guidance on Institutional Biosafety Committees (IBCs) and incidence reporting in compliance with the "NIH Guidelines."²²⁴ For issues of biosecurity and dual use research of concern (DURC), the **National Science Advisory Board for Biosecurity (NSABB)** is established under the NIH to advise the U.S. Government on arising issues.^{225,226} Other government agencies involved in biosafety regulation are the FDA's Department of Labor Occupational Safety & Health Administration (OSHA)²²⁷ and the Environmental Protection Agency (EPA).²²⁸ Through the Bloodborne Pathogen and Needle Stick Prevention law (OSHA 29 CFR 1910.1030).

Biosafety Associations

The major biosafety association in the United States is the American Biological Safety Association (ABSA) International. ABSA is a private association for biosafety professionals to share information and needs. The ABSA offers biosafety training, biosafety officer accreditation, and resources on biosafety.⁴⁷ The ABSA is also a member of the International Federation of Biosafety Associations (IFBA).²⁰¹

Biosafety officers

Biosafety officers receive accreditation as a Biological Safety Officer (BSO's) from the American Biological Safety Association (ABSA). To receive accreditation, BSO's must take the ABSA exam through the National Registry of Certified Microbiologists (NRCM). Once they have passed this exam, candidates can then apply to ABSA to be Certified Biological Safety Professionals. (CBSP). Applicants must have met several academic qualifications, including a bachelor's and master's degree with extensive microbiology exposure and professional experience.²²⁹

Accident and Incident Reporting

According to the CDC's Biosafety in Microbiological and Biomedical Laboratories (BMBL), BSL 2-4 labs have protocol mandating that incidences of potential exposure or breach of protocol must be reported immediately to the lab supervisors. Depending on the organization regulating the facility, varying protocols may be in place for reporting an incident. If an agent is released into the environment, stolen, or lost, the Select Agent Program requires that a laboratory immediately make the CDC and/or APHIS aware. After notifying the correct agencies, an APHIS/CDC Form 3 must be completed and submitted within 7 days of the incident.¹⁵⁷

Synthetic/Advanced Biology

Dual Use Research of Concern (DURC) is any research that may be used for negative purposes and threaten US or global security. The benefit of DURC versus the risks is a heavily debated topic within the United States especially concerning the 2014 moratorium called on H5N1, SARS, and MERS virus gain-of-function research.²³⁰ As of September 24 of 2015 all independent and federal institutions are required to follow the *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*.²³¹ This includes the establishment of Institutional Review Entities (IRE) to ensure that institutions doing work with DURC's are doing so responsibly.²³² Additionally, the National Science Advisory Board for Biosecurity (NSABB) advises and provides leadership for dual use life sciences research.²³³

Training

Training requirements depend on the organization under which the laboratory is funded and regulated. OSHA, EPA, NIH guidelines, and the Select Agent Program all require training specialized to the pathogens and protocols with which the employee will be working. High risk lab training commonly includes mentored, within-lab training for new personnel.¹⁵⁷ All lab supervisors are required to ensure that all of their staff show the correct level of proficiency before working with the lab agents.²¹² In the BMBL, BSL 3 and BSL 4 labs are required to advise all personnel of their potential risks and ensure that staff have the correct clearance before entering the lab.²¹² The CDC and the Association of Public Health Laboratories (APHL) released *Guidelines for Biosafety Laboratory Competency* in 2011 which lists capabilities and knowledge that laboratory staff working in BSL facilities 2-4 must have.²³⁴ Additionally, the EPA OPP has published Standard Operating Procedure for laboratory personnel training,²¹⁶ and the ABSA also contains resources for safety training.¹⁵⁷

Laboratory numbers

Since 2001, the number of BSL 3 and BSL 4 facilities has increased significantly.¹⁵⁷ Though it is not the responsibility of a specific agency to know how many biosafety laboratories are in existence within the United States,²³⁵ it is known that there are over 4,000 facilities within the U.S.²³⁶ According to the CDC's Federal Select Agent Program in 2010 there 1,495 laboratories registered through the United States which are primarily BSL 3 labs. As of 2011, there were 8 BSL 4 labs registered through 6 different organizations and there were 6 more planned for construction.¹⁵⁷

Research Status

The United States is a world leader in life sciences research, biotechnology development, and pharmaceutical endeavors. The U.S. was predicted to be the largest investor in R&D in the world at \$465 billion in 2014, which is equal to 2.8% of the U.S. GDP for that year.²³⁷ *Scientific American Worldview* has ranked the US as the best country for biotechnology every year since their biotechnology scorecard began in 2009.²⁶ The U.S. produces the greatest amount of biotech crops in the world, with 73.1 million hectares (40% of the total global hectares produced) in 2014.⁸² Private and public U.S. biotechnology companies generated a combined total of \$100 billion USD in capital in 2014.²⁰³ In the pharmaceutical development world, "...U.S. firms conduct the majority of the world's research and development in pharmaceuticals and hold the intellectual property rights on most new medicines. The biopharmaceutical pipeline also has over 5,000 new medicines currently in development around the world with approximately 3,400 compounds currently being studied in the United States - more than in any other region around the world."²⁰²

The NIH, dedicated to research to "...enhance health, lengthen life, and reduce illness and disability,"²⁰⁴ received over \$30.3 billion USD in FY 2015. Most of this budget "goes to almost 50,000 competitive

grants to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every state and around the world.”²⁰⁴

Funding

No information found.

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