The Biosafety Research Roadmap – building evidence to support risk management

Allan Bennett OBE

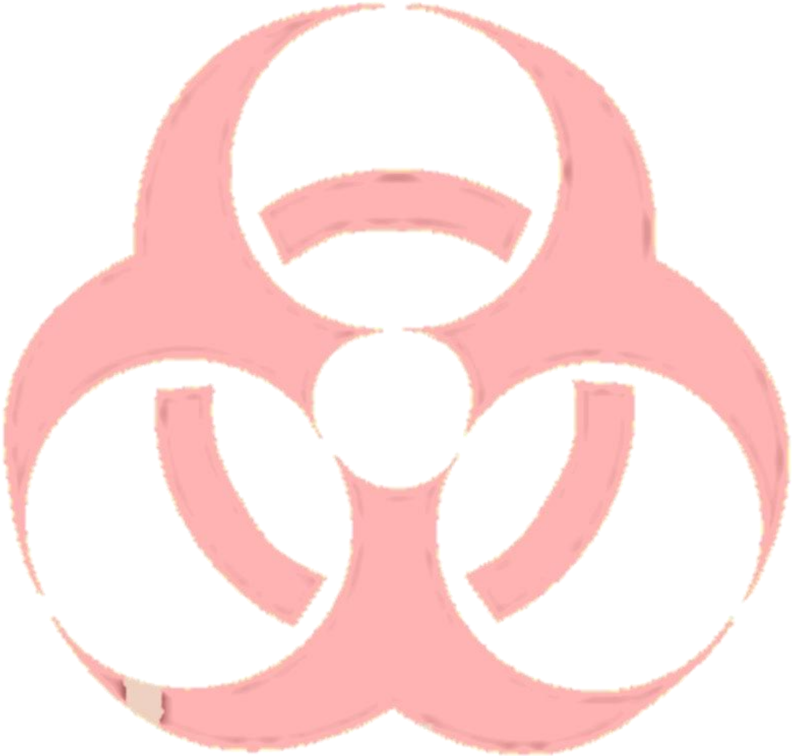
Technical Working Group Member

Introduction

- Biosafety and Microbiology (1980-2025)
- Towards an Evidence and Risk Based Approach
- The Biosafety Research Roadmap
- The Future of Biosafety

What is Biosafety and Biocontainment ?

- The application of knowledge, techniques and equipment to prevent personal, laboratory and environmental exposure to potentially infectious agents or biohazards.
- Defines the containment conditions under which infectious agents can be safely manipulated.
- Confine biohazards to reduce the potential exposure of the laboratory worker, persons outside of the laboratory, and the environment to potentially infectious agents.
- Think of it like insurance – it is an investment in safety and you will be glad to have it if the “worst-case” happens

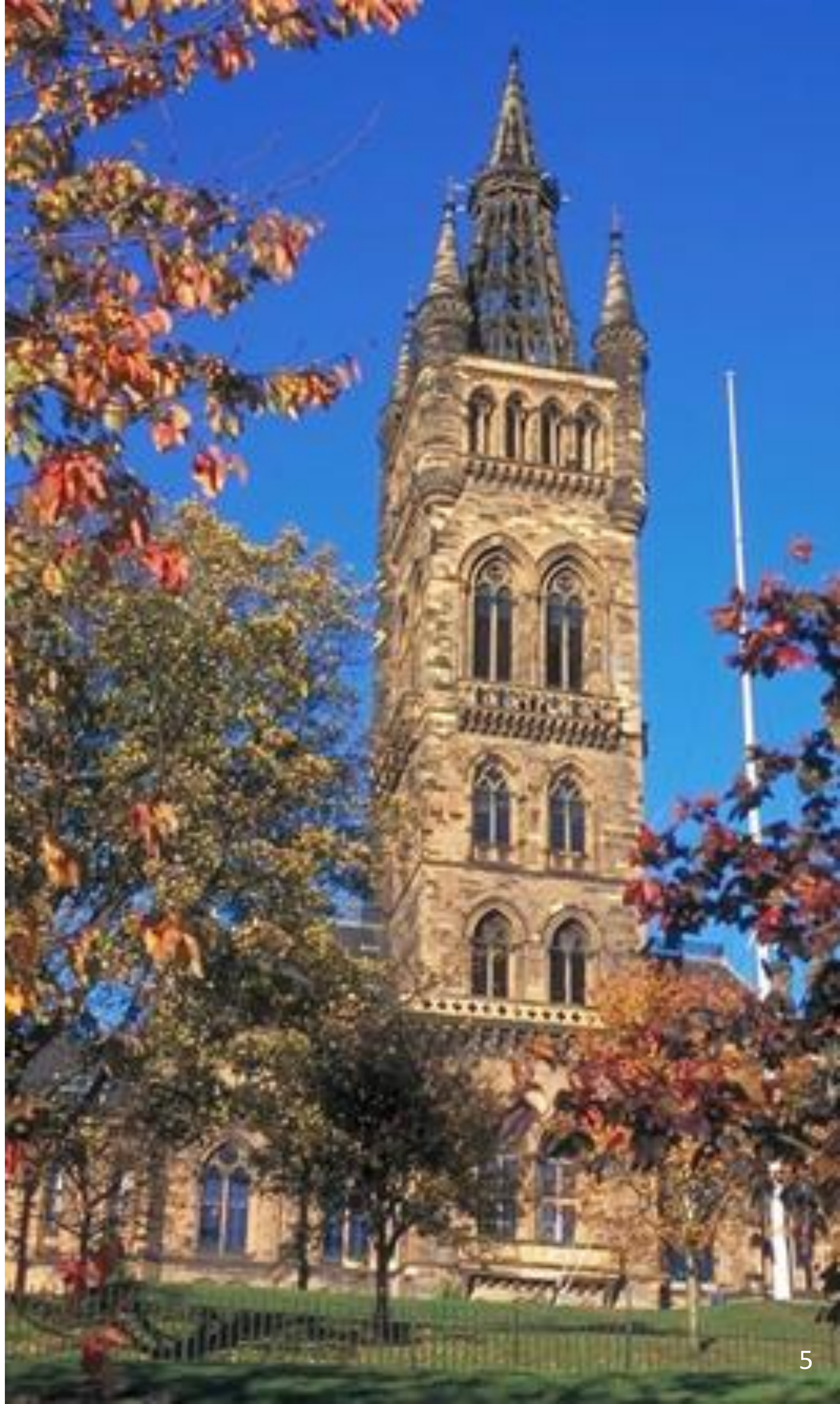


The Development of Biosafety Regulations

- Regulations in biosafety were greatly influences by biosafety experts from the major research institutes of the US and the UK who had developed methods of biocontainment and engineering controls based on the need to contain vaccine development and animal work.
- Classification into 4 risk groups (US,1974, WHO 1979)
- WHO laboratory biosafety manual first edition (1983)
- US BMBL biosafety levels (1980)
- EU biological agent’s directive (1989)
- <u>The basis for present day Biosafety is almost 50 years old</u>

What was a microbiology lab like in 1983? Undergraduate microbiology at Glasgow University

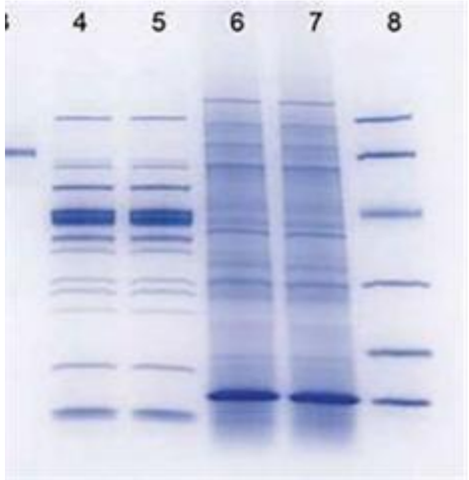
- 10ml glass test-tubes for biochemical tests
- Platinum loops for plating out
- Bench work on wooden benches
- No safety cabinets only laminar flow hoods
- No PCR just culture and immunoassays
- No documented training
- Hazardous chemicals (ethidium bromide, mercaptoethanol)
- TB incidence in lab technicians in UK 59 per 100,000 (4 times normal incidence) Grist & Emslie
- Infected myself with *Strep pyogenes* in the teaching lab
- Animal experiments with tetanus toxin
- Two days laboratory work for final two years



Since the 1980s technology has reduced exposure to pathogens in the laboratory

- Glassware
- Large Volume Assays
- Lab Staff
- Culture
- Gels
- Laboratory assays
- Benchwork
- Inactivated vaccines

- Plasticware
- Microlitres
- Robotics
- PCR
- LFD
- Bed-side assays
- Safety cabinets
- mRNA vaccines



However, the graduate scientist experience is greatly reduced

Towards a Risk and Evidence Based Approach

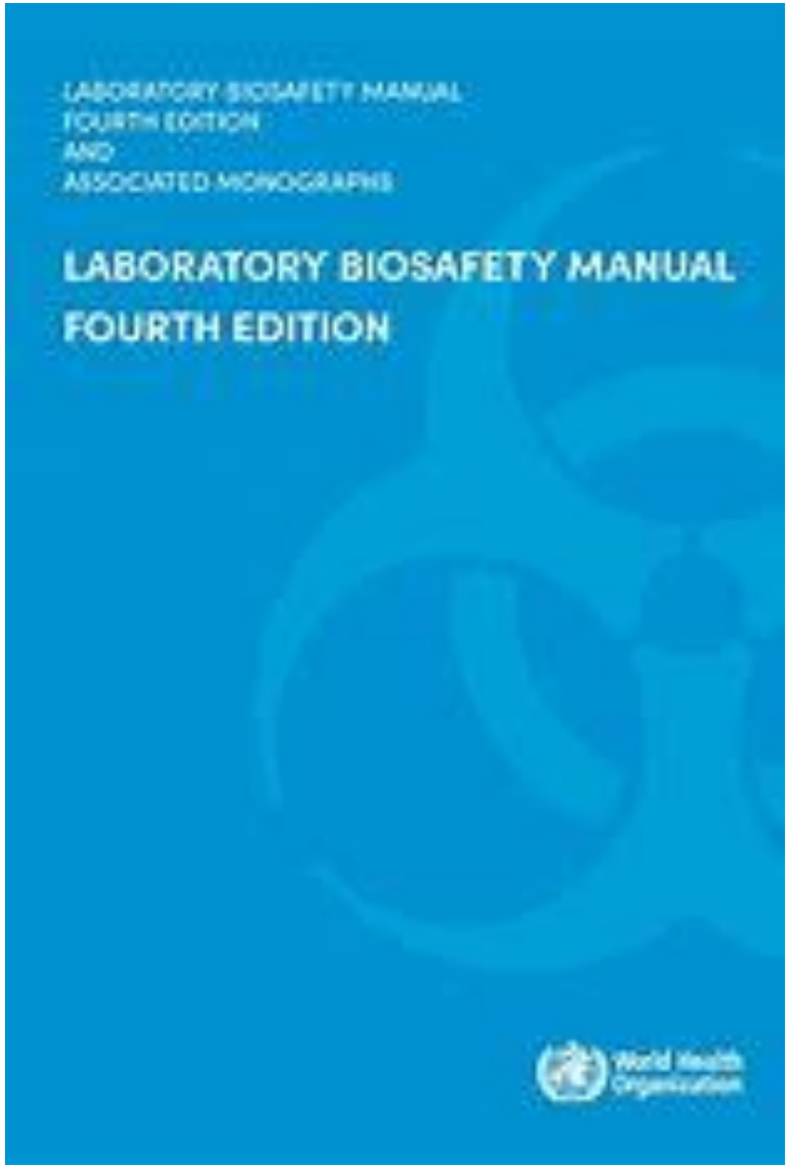
Changing Approach to Global Biosafety

In 2015 WOAH published “Biosafety and biosecurity: Standard for managing biological risk in the veterinary laboratory and animal facilities” as Chapter 1.1.4. of the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.

This chapter proposed moving away from Biosafety levels approach towards and evidence and risk-based approach.

WHO Laboratory Biosafety Manual 4th edition (2022)

- Attempts to provide a scientific evidence-based framework for global biosafety
- Encourages risk assessment based on the process (volumes, titres, aerosol potential) and not the old risk group, containment level approach
- Focuses more on people and less on equipment
- Focuses on sustainability
- However, it relies on qualified risk assessors and will take time to have an impact
- However, much of the evidence base is missing



WHO LBM4 : The Risk-based approach to biosafety

Pathogen
(Hazard)

Process

Risk

[Likelihood + severity of harm]

WOAH biosafety research roadmap

- **A project led by Professor Stuart Blacksell of MORU and supported by WHO, WOAH and Chatham house, and other organisations brought experts together to identify and address biosafety evidence gaps and find funding to address these needs**
- Having a strong and scientifically sound evidence-base on which to base our protocols is essential to sustainable laboratory activities.
- Having a sound evidence-base will reduce waste and increase efficiency of biosafety-related activities
- Having a sound evidence-base will support risk-based biosafety using actual rather than perceived risks.

World Health Organization

World Organisation for Animal Health
Founded as OIE

CHATHAM HOUSE

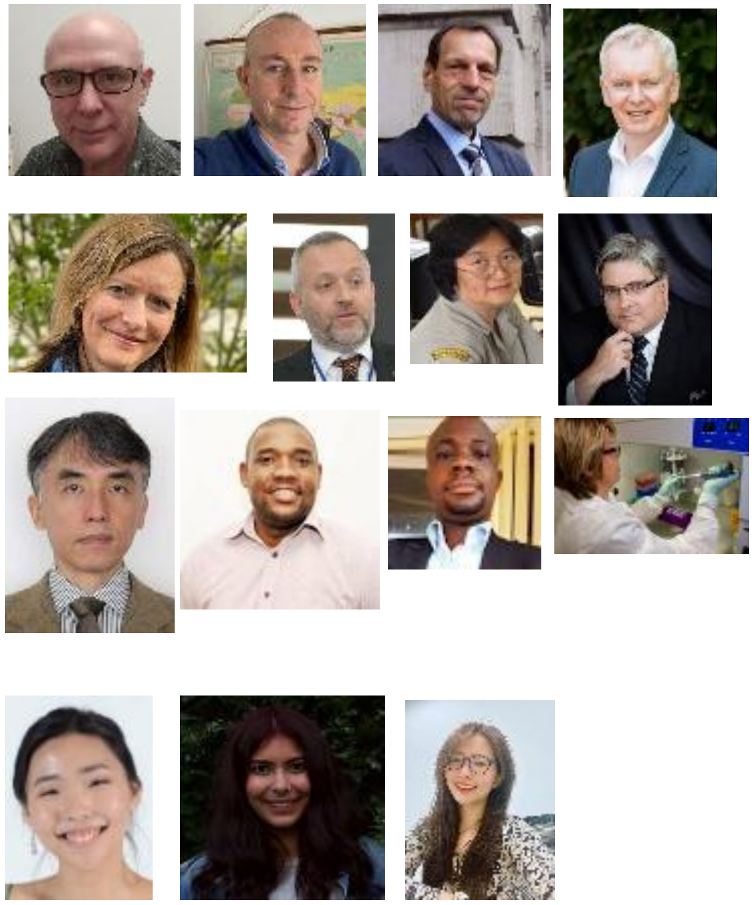
WOAH biosafety roadmap- Aims & Objectives

- Identify research and capability gaps
- Provide recommendations on evidence-based approach for biosafety in low-resource settings
- Application of laboratory biological risk management
- Improve laboratory sustainability using evidence-base
  - Biosafety measures (including engineering)
  - Options for low-resource settings
- Inform strategic decisions on global health security and investments in laboratory systems

Methods

The 16 member TWG met virtually bi-weekly: Research strategy, address knowledge gaps, findings, and key issues:

1. Select pathogens and procedures to test the current evidence
2. Discuss and define a methodology for testing the current evidence base
3. Apply biological risk management to each of the pathogens to identify appropriate biosafety measures
4. Review commonly required risk management measures to evaluate if these are supported by evidence
5. Report on the strengths and weaknesses of the existing evidence base for laboratory biological risk management
6. Make recommendations on research needed to fill gaps in the current evidence base



Priority Pathogens Selected for Further Study

Brucella melitensis	*Bacillus anthracis*	SARS-CoV-2
Crimean Congo haemorrhagic fever	Lassa fever	*Mycobacterium tuberculosis*
Zoonotic avian influenza virus	Foot and mouth disease virus	*Shigella* spp.

Selected general biosafety evidence gaps

1. **Engineering**
    - Why do we test biosafety cabinet annually ?
    - Leak rate measurement/air tightness.
        - Significant variation in international standards
        - Controversy about what constitutes ‘adequate air tightness

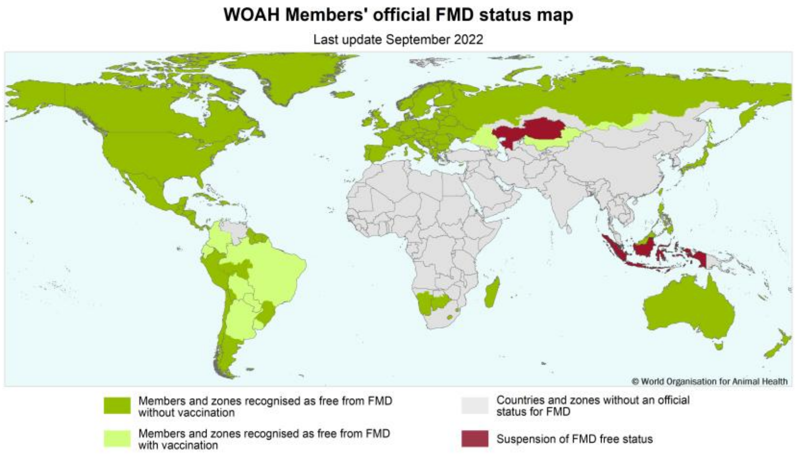
2. **Human factor**
    - What is the best practice for human reliability?
        - Is there a best practice guidelines already?
        - Can you measure human reliability?
    - Can we somehow connect reliability, quality and biosafety –are all interconnected?
    - How to get staff to follow the rules and to change existing practices?
    - What is the best way to determine competency with infectious materials in the laboratory

Source: https://www.antechscientific.com/biological-safety-cabinet-nsf49.html

Source: https://www.science.org/content/article/us-high-containment-biosafety-labs-get-closer-scrutiny

Foot-and-mouth disease 1– Knowledge gaps

- Organizational measures:
  - **3-day quarantine rule** for staff
    - based on studies with **infected large animals** when personnel exposure is greatest
    - Why is this applied in cases of *in vitro* lab work only?
- Risk assessment:
  - Absence of **Standardised risk assessment framework** to determine the risk mitigation measures for animal and lab work.
  - Lack of **proportional risk assessment** for FMD lab facilities
  - Should reflect the **local, regional or national situation** – not “one size fits all”
- Disinfection & decontamination:
  - Lack of standardised methods for **decontamination and decommissioning** of laboratories and engineering facilities

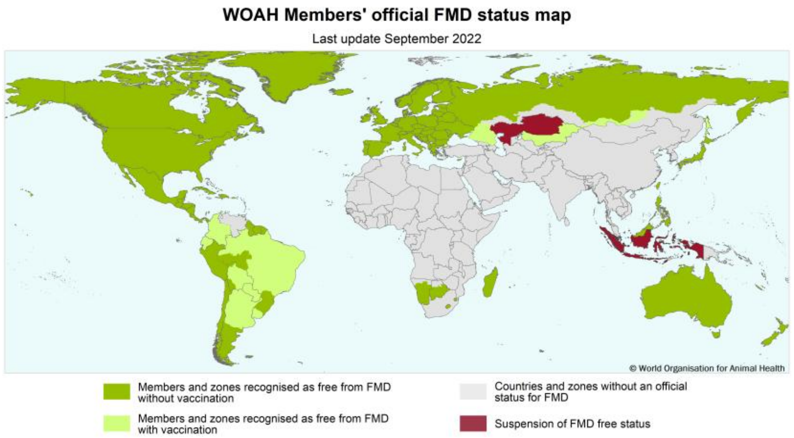


Source: https://www.woah.org/en/disease/foot-and-mouth-disease/

Source: https://www.emergence-msd-animal-health.com/disease/foot-and-mouth-disease-fmd-2

Foot-and-mouth disease 2 – Knowledge gaps

- Engineering control:
  - Little information about the contribution of technical measures to safety
- Requirement for a shower:
  - No scientific data exists which support showering out after ***in vitro* lab work**.
  - No data showing that a shower is necessary in a **vaccine production** facility
- Transmission route under experimental conditions:
  - No data about FMDV transmission to susceptible animals **by staff working in a laboratory**



Source: https://www.woah.org/en/disease/foot-and-mouth-disease/

Source: https://www.emergence-msd-animal-health.com/disease/foot-and-mouth-disease-fmd-2

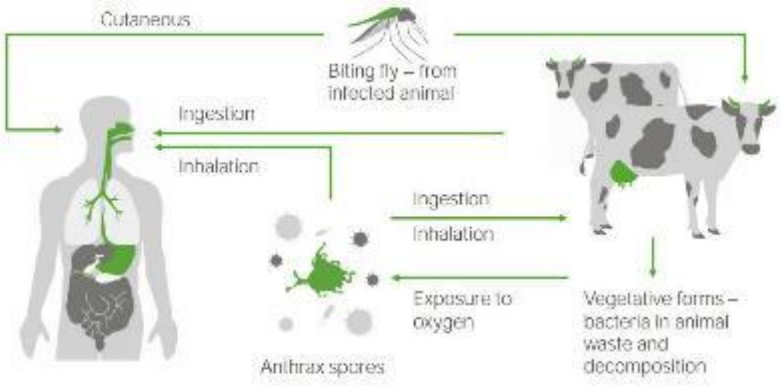
Zoonoses – Knowledge gaps

Bacillus anthracis

- **Infectious dose** for cutaneous and gastrointestinal infections
- Optimal **rapid diagnostic tests** in field in low-resource settings
- **Most appropriate PPE** for performing necropsy of an animal in low-resource settings
- Appropriate method for **disposal of contaminated waste** (incl. carcass) and PPE at completion of animal necropsy in **low-resource settings**

Brucella spp.

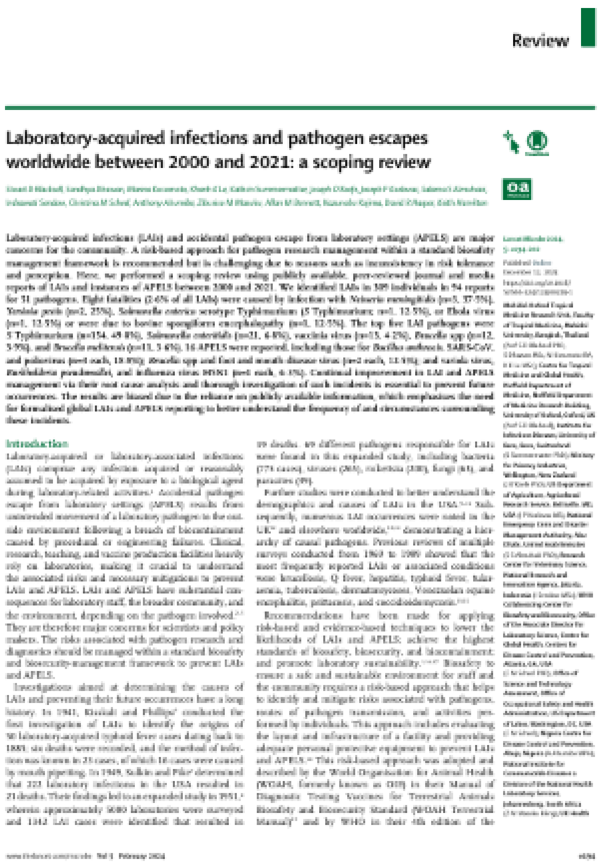
- Optimal **chemical disinfectants** (concentrations and times)
- **Infectious dose** for various Brucella species – impact on LAIs



Source: https://www.lecturio.com/concepts/anthrax/

Source: https://time.com/2976922/cdc-anthrax/

Closing the gap



Review

Laboratory-acquired infections and pathogen escapes worldwide between 2000 and 2021: a scoping review

Applied Biosafety
Volume 00, Number 00, 2023
ABSA International 2023
DOI: 10.1089/apb.2022.0044

The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory—Crimean Congo Haemorrhagic Fever Virus and Lassa Virus

Applied Biosafety
Volume 28, Number 2, 2023
ABSA International 2023
DOI: 10.1089/apb.2022.0046

The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory—*Shigella* spp.

Applied Biosafety
Volume 28, Number 2, 2023
ABSA International 2023
DOI: 10.1089/apb.2022.0040

Open camera or QR reader and scan code to access this article and other resources online.

The Biosafety Research Road Map: The Search for Evidence to Support Practices in Human and Veterinary Laboratories

Stuart D. Blacksell[1,2,*], Sandhya Dhawan[1], Marina Kusumoto[1], Kim Khanh Le[1], Kathrin Summermatter[3], Joseph O'Keefe[4], Joseph Kozlovac[5], Salama Suhail Almuhairi[6,#], Indrawati Sendow[7], Christina M. Scheel[8], Anthony Ahumibe[9], Zibusiso M. Masuku[10], Allan M. Bennett[11], Kazunobu Kojima[12], David R. Harper[13], and Keith Hamilton[14]

Abstract

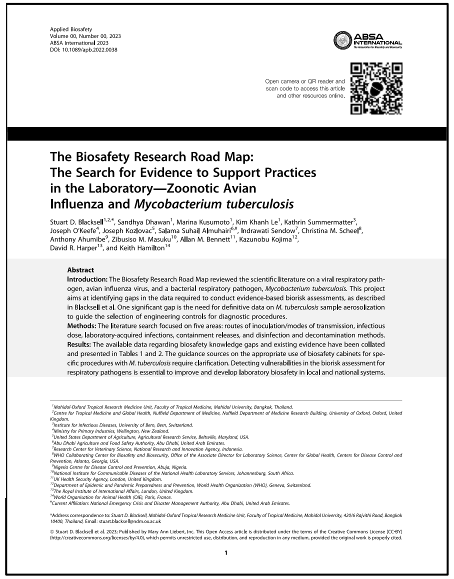
Introduction: Lack of evidence-based information regarding potential biological risks can result in inappropriate or excessive biosafety and biosecurity risk-reduction strategies. This can cause unnecessary damage and loss to the physical facilities, physical and psychological well-being of laboratory staff, and community trust. A technical working group from the World Organization for Animal Health (WOAH, formerly OIE), World Health Organization (WHO), and Chatham House collaborated on the Biosafety Research Roadmap (BRM) project. The goal of the BRM is the sustainable implementation of evidence-based biorisk management of laboratory activities, particularly in low-resource settings, and the identification of gaps in the current biosafety and biosecurity knowledge base.

Methods: A literature search was conducted for the basis of laboratory design and practices for four selected high-priority subgroups of pathogenic agents. Potential gaps in biosafety were focused on five main sections, including the route of inoculation/modes of transmission, infectious dose, laboratory-acquired infections, containment releases, and disinfection and decontamination strategies. Categories representing miscellaneous, respiratory, bioterrorism/zoonotic, and viral hemorrhagic fever pathogens were created within each group were selected for review.

[1]Mahidol-Oxford Tropical Research Medicine Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.
[2]Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, Nuffield Department of Medicine Research Building, University of Oxford, Oxford, United Kingdom.
[3]Institute for Infectious Diseases, University of Bern, Bern, Switzerland.
[4]Ministry for Primary Industries, Wellington, New Zealand.
[5]United States Department of Agriculture, Agricultural Research Service, Beltsville, Maryland, USA.
[6]Abu Dhabi Agriculture and Food Safety Authority, Abu Dhabi, United Arab Emirates.
[7]Research Center for Veterinary Science, National Research and Innovation Agency, Indonesia.
[8]WHO Collaborating Center for Biosafety and Biosecurity, Office of the Associate Director for Laboratory Science, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
[9]Nigeria Centre for Disease Control and Prevention, Abuja, Nigeria.
[10]National Institute for Communicable Diseases of the National Health Laboratory Services, Johannesburg, South Africa.
[11]UK Health Security Agency, Porton Down, Salisbury, United Kingdom.
[12]Department of Epidemic and Pandemic Preparedness and Prevention, World Health Organization (WHO), Geneva, Switzerland.
[13]The Royal Institute of International Affairs, London, United Kingdom.
[14]World Organisation for Animal Health (OIE), Paris, France.
#Current Affiliation: National Emergency Crisis and Disaster Management Authority, Abu Dhabi, United Arab Emirates.

*Address correspondence to: Stuart D. Blacksell, Mahidol-Oxford Tropical Research Medicine Unit, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand, Email: stuart.blacksell@ndm.ox.ac.uk

1



Applied Biosafety
Volume 00, Number 00, 2023
ABSA International 2023
DOI: 10.1089/apb.2022.0038

The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory—Zoonotic Avian Influenza and *Mycobacterium tuberculosis*

Applied Biosafety
Volume 28, Number 2, 2023
ABSA International 2023
DOI: 10.1089/apb.2022.0042

The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory—*Bacillus anthracis* and *Brucella melitensis*

Seven peer reviewed scientific papers published by the task group

The Future of Biosafety

- Having a strong and scientifically sound evidence-base on which to base our protocols is essential to sustainable and safe laboratory activities.
- Having a sound evidence-base will reduce waste and increase efficiency of biosafety-related activities
- Having a sound evidence-base will support risk-based biosafety using actual rather than perceived risks.
- Evidence gaps are still being finalized
- There will need to be a period of consultation following recommendations from the biosafety roadmap group on the prioritization and activities to be completed to fill the knowledge gaps.
- Projects such as Bioprevail are being funded to fill in the evidence gaps and develop best practice in sustainable biosafety.

Acknowledgements

Stuart D Blacksell

Sandhya Dhawan

Marina Kusumoto

Khanh K Le

Kathrin Summermatter

Joseph O'Keefe

Joseph Kozlovac

Salama S Almuhairi

Indrawati Sendow

Christina M Scheel

Anthony Ahumibe

Zibusiso M Masuku

Allan M Bennett

Kazunobu Kojima

David R Harper

Keith Hamilton

Thank you

World Organisation for Animal Health

Allan Bennett OBE

bennettbiosafety@outlook.com

The event is supported by funding from:

In partnership with Canada

Co-funded by the European Union

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

UK Government