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The 4th ed. of the WHO Laboratory Biosafety Manual

The new risk-based approach to biosafety

Fabio Blaha, January 20th 2021

Intention

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- provide information on
  - the 4th WHO Laboratory Biosafety Manual (LBM4), and
  - its overall approach
- compare the new approach to the previous approach
  - especially regarding the topic of risk assessment, and
  - its integration into a biosafety programme management / biorisk management system

List of references

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1. General outline

What's new?

1. General outline

What's new?

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- The 4th ed. of the WHO Laboratory Biosafety Manual (LBM4) has been published by December 21st 2020.
  - https://www.who.int/publications/i/item/9789240011311
- In addition to the manual itself, there are seven associated monographs on various topics:
  - Biosafety programme management
    - https://apps.who.int/iris/handle/10665/337963
  - Risk assessment
    - https://apps.who.int/iris/handle/10665/337966
  - Biological safety cabinets and other primary containment devices
    - https://apps.who.int/iris/handle/10665/337957
  - Personal protective equipment
    - https://apps.who.int/iris/handle/10665/337961
  - Laboratory design and maintenance
    - https://apps.who.int/iris/handle/10665/337960
  - Decontamination and waste management
    - https://apps.who.int/iris/handle/10665/337958
  - Outbreak preparedness and resilience
    - https://apps.who.int/iris/handle/10665/337959
- Also, there is a new WHO guidance on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories.
  - https://apps.who.int/iris/handle/10665/332244

1. General outline

What's new?

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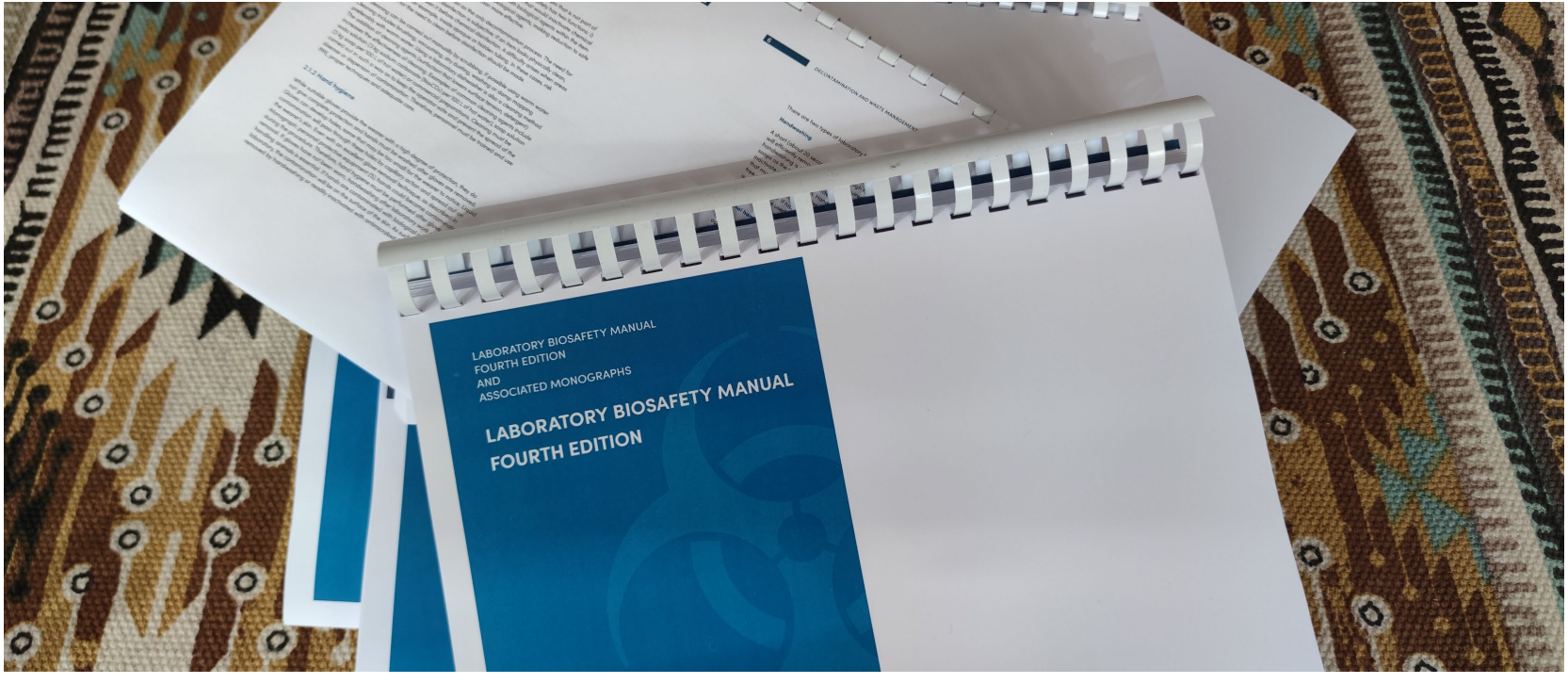

858 pages of information

1. General outline

What's new?

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1. Introduction
2. Risk assessment
3. Core requirements
4. Heightened control measures
5. Maximum containment measures
6. Transfer and transportation
7. Biosafety programme management
8. Laboratory biosecurity
9. National/international biosafety oversight

1. General outline

Target audience

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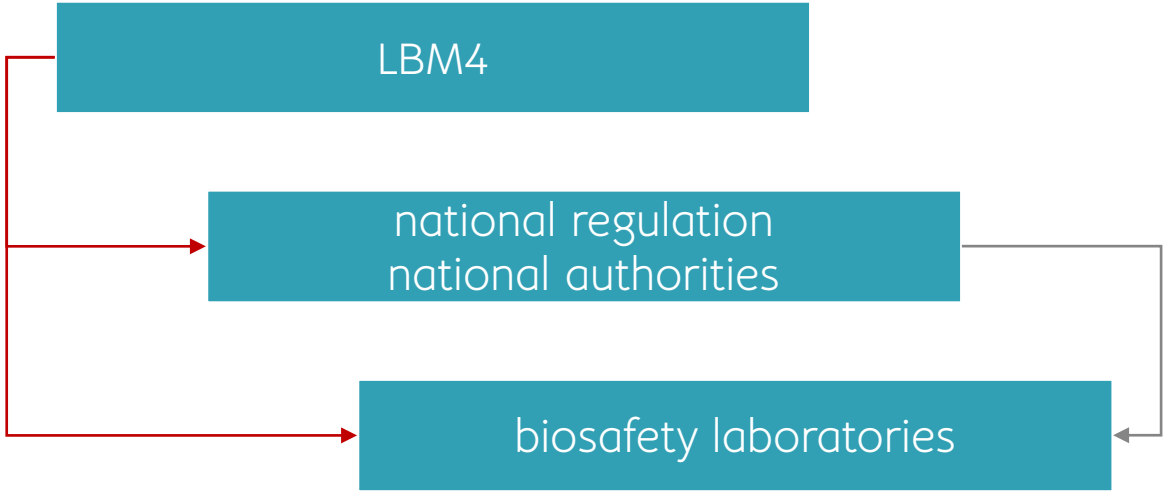

- The LBM4 provides national legislative bodies and authorities with information on biosafety.
- Every biosafety laboratory must adhere to national regulation and authorities, but the LBM4 provides the laboratory with information on how to improve its existing biosafety measures – in addition to national requirements.

1. General outline

Preview: biosafety without risk groups and biosafety levels

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- The approach of the LBM4 works without risk groups (also called hazard groups) and biosafety levels.
- Nevertheless, the LBM4 is open for state-level regulation that uses risk groups and biosafety levels,[1] as well as activity-based, list-based, etc. regulation.
- Thus, the LBM4 uses not a prescriptive approach, but a risk-based approach that is more sensitive to the specific context than previously:
  - with regard to the
    - country, environment in which the laboratory is situated,
    - competence of the prospective laboratory personnel,
    - financial resources, etc.
  - with regard to the
    - biological agent and its pathogenic and epidemic attributes,
    - the activities planned, the technical equipment and methods used, etc.
- Every measure is the result of the assessment of the specific risks that arise from the specific context – with the exception of the core requirements. But they could as well be improved upon by the systematic approach which includes continual improvement.
- The general approach has already been applied to the topic of laboratory biosafety in the WHO Tuberculosis Laboratory Biosafety Manual.[2]

1) Cf. WHO (2020), p. 91.–94.
2) Cf. WHO (2012).

2. The concept of biosafety levels and its limits

2. The concept of biosafety levels and its limits

Its advantages

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- Which advantages does the concept of biosafety levels provide us with?
  - » It does provide us with a general outline of the essential features of the facility. They relate to combinations of laboratory practices and techniques, sets of safety equipment, etc.[1]
  - » It does relate to the function of the facility, such that …
    - "Each combination is specifically appropriate for the operations performed, the documented or suspected routes of transmission of the infectious agents, and the laboratory function or activity."[2]
  - » The preliminary correlation between risk groups and biosafety levels simplifies the approach.[3]

1) Cf. CDC (2009), p. 24.
2) CDC (2009), p. 24.
3) Cf. WHO (2004), p. 1.

2. The concept of biosafety levels and its limits

Its limits

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- Which limits does the concept of biosafety levels have?
  - The preliminary correlation between risk groups and biosafety levels may often be the incentive to not accounting for the specific context of the facility.
  - The practice may sometimes be to make a one-to-one correlation between risk groups and biosafety levels – although there are warnings not to do so:
    - "The BSLs described in this manual should be differentiated from risk groups [...]. Risk groups are the result of a classification of microbiological agents based on their association with, and resulting severity of, disease in humans. The risk group of an agent should be one factor considered in association with mode of transmission, procedural protocols, experience of staff, and other factors in determining the BSL in which the work will be conducted."[1]
  - The risk assessment may necessitate additional safety measures.[2]
  - The categories of the biosafety levels do not capture the actual requirements, in many cases, resulting in designation such as BSL 3+, etc. In such a case, e.g. BSL 3+ has no specific meaning:
    - "Sometimes the appropriate BSL-3 practices determined by the risk assessment may be limited to working in a BSC and restricting sharps in the laboratory. In other situations, multiple BSL-3 practices are selected."[3]

1) CDC (2009), p. 24.
2) Cf. CDC (2009), p. 18.
3) Duane, Elizabeth Gilman (2013), p. 31-32.

3. A short retrospect

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3. A short retrospect

Risk groups

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- Classification of infective microorganisms by risk groups:[1]

  - RG 1: no or low individual and community risk
    - A microorganism that is unlikely to cause human or animal disease.
  - RG 2: moderate individual risk, low community risk
    - A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment.
    - Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
  - RG 3: high individual risk, low community risk
    - A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another.
    - Effective treatment and preventive measures are available.
  - RG 4: high individual and community risk
    - A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly.
    - Effective treatment and preventive measures are not usually available.

1) Cf. WHO (2004), p. 1.

3. A short retrospect

An example from the German TRBA 462

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Pathogen	Risk group
SARS-CoV	3
SARS-CoV-2	3
BEBOV (Ebolavirus Bundibugyo)	4

Biosafety levels

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- Relation of risk groups to biosafety levels, practices and equipment:[1]

Risk group	Biosafety level	Laboratory type	Laboratory practices	Safety equipment
1	1	Basic teaching, research	GMT	Open bench
2	2	Primary health services, diagnostic services, research	GMT, protective clothing, biohazard sign	Open bench, biosafety cabinet
3	3	Special diagnostic services, research	In addition: special clothing, controlled access, directional airflow	Biosafety cabinet, further primary containment equipment
4	4	Dangerous pathogen units	In addition: airlock entry, shower exit, special waste disposal	Class III biosafety cabinet, positive pressure suits in combination with Class II, double ended autoclave, filtered air

1) Cf. WHO (2004), p. 2.

3. A short retrospect

Microbiological risk assessment

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- The risk assessment leans itself on the risk groups. However, additional information is used as well, such as:[1]
  - Pathogenicity of the agent and infectious dose
  - Potential outcome of exposure
  - Natural route of infection
  - Other routes of infection, resulting from laboratory manipulations (parenteral, airborne, ingestion)
  - Stability of the agent in the environment
  - Concentration of the agent and volume of concentrated material to be manipulated
  - Presence of a suitable host (human or animal)
  - Information available from animal studies and reports of laboratory-acquired infections or clinical reports
  - Laboratory activity planned (sonication, aerosolization, centrifugation, etc.)
  - Any genetic manipulation of the organism that may extend the host range of the agent or alter the agent's sensitivity to known, effective treatment regimens
  - Local availability of effective prophylaxis or therapeutic interventions
- Lots of information can be found e.g. in the "Pathogen Safety Data Sheets".[2] Information on the activities planned have to be gathered by the laboratory.

1) Cf. WHO (2004), p. 7.
2) https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment/

3. A short retrospect

Microbiological risk assessment and biosafety level

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4. The risk-based approach

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Risk assessment

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- Since there are no risk groups and biosafety levels in the LBM4, it relies exclusively on the risk assessment itself.[1]

  - **Gather information**: biological agents, procedures, equipment, facility, competency, public perception
  - **Evaluate the risks**: ways of exposure, likelihood of exposure, consequences, tolerance level
  - **Develop a risk strategy**: resources, control strategies, sustainability und achievability of control strategies
  - **Select and implement control measures**: regulations, sustainability and achievability of control measures, efficiency, residual risk, communication to relevant personnel, operational procedures, training of personnel
  - **Review risks and control measures**: changes in activities, new knowledge, lessons learned

1) Cf. WHO (2020), p. 5-9.

4. The risk-based approach

Risk assessment

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4. The risk-based approach

Risk assessment

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Consequences of exposure/release	Severe	Moderate	High	Very High
	Minor to major	Low	Moderate	High
	Negligible	Very low	Low	Moderate
		Unlikely to happen	Possibly could happen	Likely could happen
		Likelihood of exposure/release		

- Kathrin Summermatter will go into detail!

Develop a risk strategy

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- The risk assessment may necessitate action – if the initial risk is unacceptable.
- Any initial risk that is too high must be addressed by a suitable risk strategy:[1]

  - **Elimination:** e.g. inactivation of biological agent
  - **Reduction and substitution:** e.g. substitution of biological agent, reduction of volume, substitution of procedure
  - **Isolation:** e.g. primary containment
  - **Protection:** e.g. PPE, engineering controls, vaccination
  - **Compliance:** e.g. GMPP, SOPs, communication, training, safety culture

1) Cf. WHO (2020), p. 17-18.

4. The risk-based approach

Control measures

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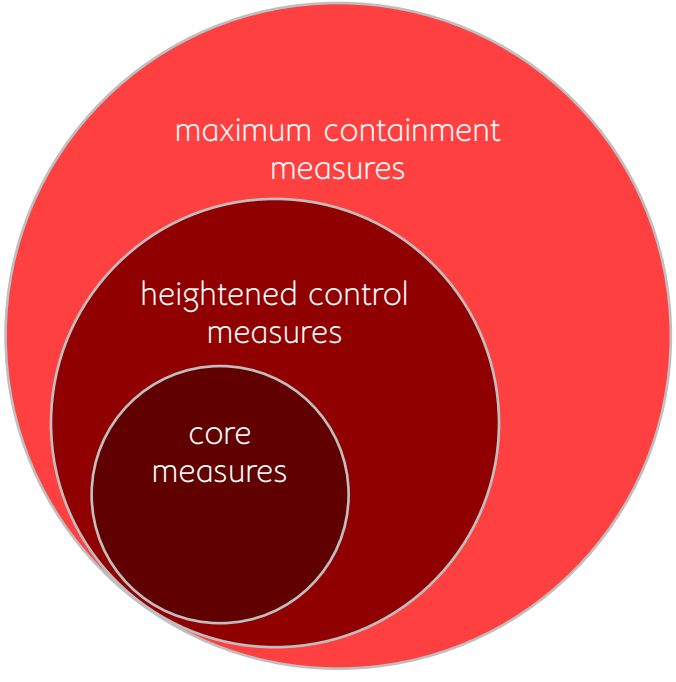
- The selected risk strategy is realized by a set of risk control measures:[1]



1) Cf. WHO (2020), p. 18-25.

Control measures

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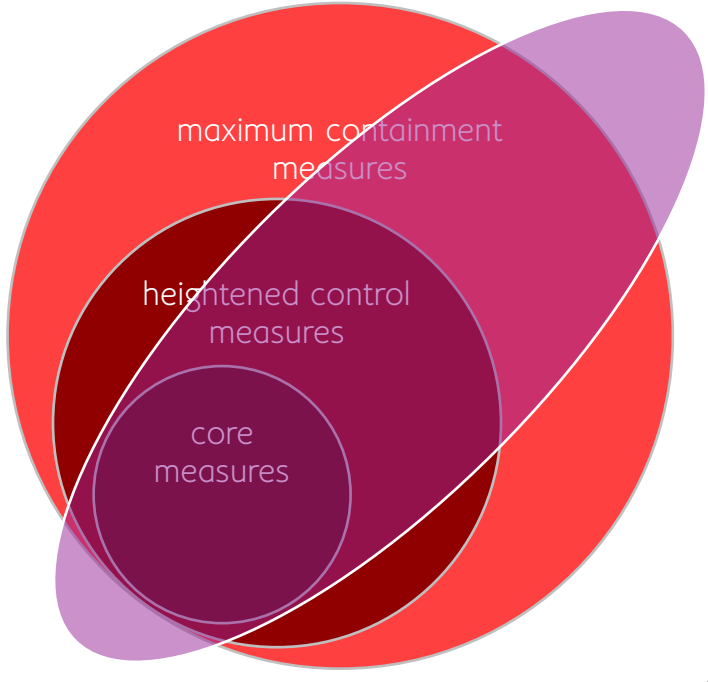
- The core measures define the minimum requirements on biosafety-relevant activities.
- If the risk assessment necessitates it, heightened control measures as well as maximum containment measures must be selected.
- Important factors are the feasibility, affordability, sustainability and suitability of the selected measures.



Biosafety programme management

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- Each laboratory organization may conduct its own risk assessment(s).
  - » “Organization-specific risk assessments can further guide the selection and implementation of appropriate control measures and mitigation strategies that reduce risks to an acceptable level.”[1]
- Such a risk assessment should be embedded and managed by a management system – a biosafety programme management.
  - » The management of this process requires an organization to develop a biosafety programme: a set of tools, information and associated actions that are overseen, and continuously improved upon, by an organization‘s senior management.”[2]
- One could also learn from ISO 35001:2019 “Biorisk management for laboratories”, which has a resembling, but more formal approach.

1) WHO (2020), p. 77.
2) WHO (2020), p. 77.

4. The risk-based approach

Biosafety programme management

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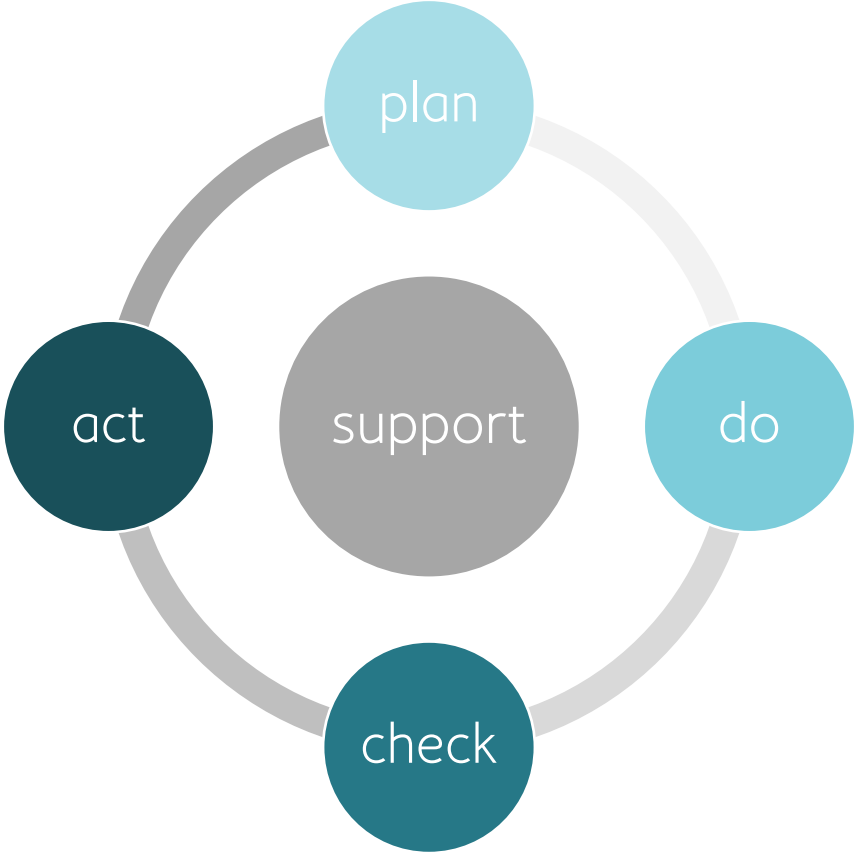

Final thought

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- There are no “stand-alone” or “ad hoc” control measures.
- Safety in biosafety calls for systematic learning – on the international level, national level as well as within the laboratory organization itself.

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Thank you very much!

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