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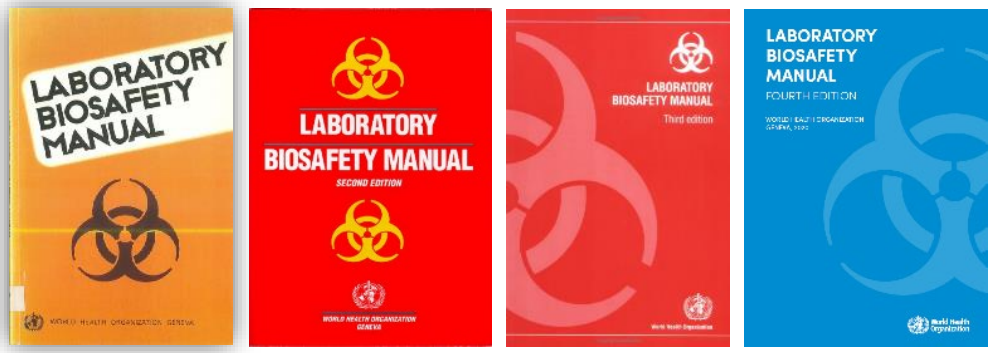
Risk based approach: Practical implications and opportunities

Kathrin Summermatter



Who I am

Kathrin Summermatter
Head of the Biosafety Center ifik,
University of Berne, Switzerland

Scientific contributor to:
LBM, 4th edition
Monograph risk assessment
Monograph decontamination
Monograph PPE

Katharina.summermatter@ifik.unibe.ch

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Where I work

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Institute for Infectious Diseases of the University of Berne

- Clinical microbiology (bacteriology, virology, parasitology, mycology) 24/7/365
- Research and development
- Teaching

- Staff: appr. 180
- BSL1,2 and 3; ABSL1 and 2
- Biosafety Center

Overview - structure

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Introduction

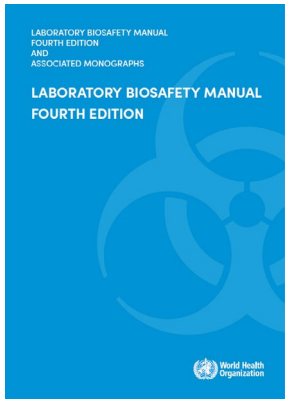
The WHO risk based approach

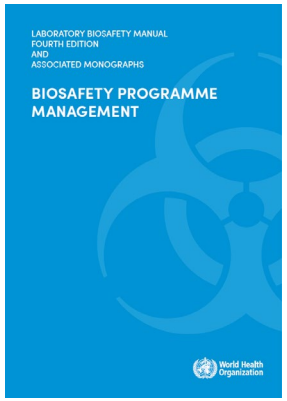
The new laboratory biosafety manual and monographs

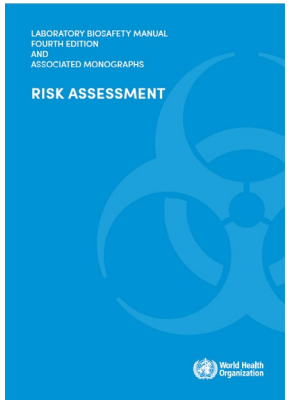
The risk based approach for SARS-CoV-2 diagnostic: an example

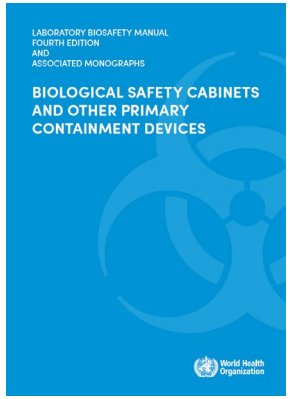
Conclusions

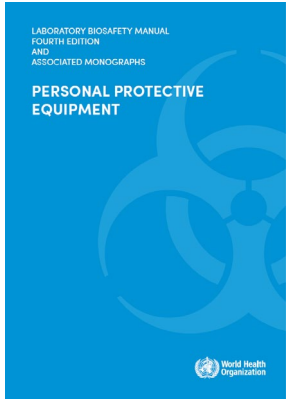
Introduction

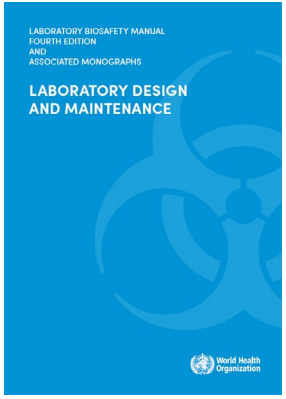


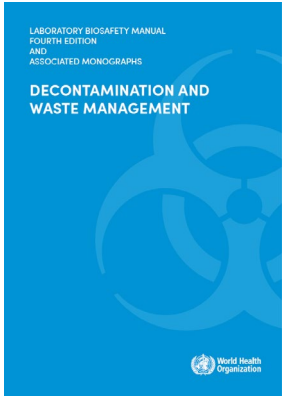


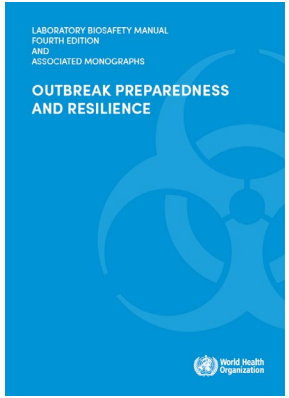


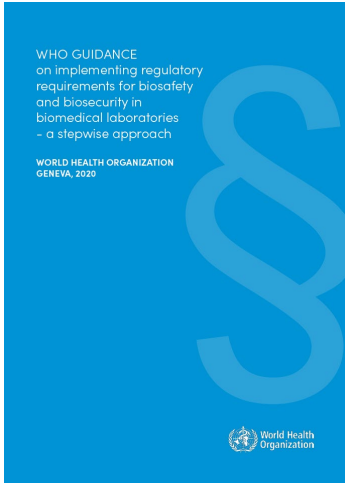












https://www.who.int/publications/i/item/9789240011311

The risk based approach: a new concept and less safety?

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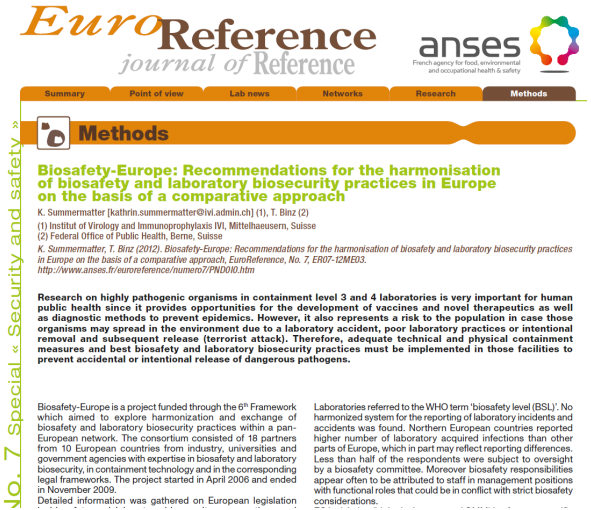
- No!!!
- As biosafety professionals we apply the risk based approach on a daily basis.
- Good example: SARS-CoV-2

- And some do it …..

Findings of Biosafety-Europe, 2012

- Lack of data and pressure of public perception -> unnecessarily complicated and overly expensive physical containment measures
- Cost-effectiveness analyses are not performed routinely in the field of biosafety and laboratory biosecurity
- The collective expertise of the biosafety community should be used to exchange knowledge and best practices
- A discussion on how best to achieve biosafety minimum standards in a cost-efficient way should be encouraged



EuroReference journal of Reference

anses French agency for food, environmental and occupational health & safety

Summary | Point of view | Lab news | Networks | Research | Methods

Methods

Biosafety-Europe: Recommendations for the harmonisation of biosafety and laboratory biosecurity practices in Europe on the basis of a comparative approach

K. Summermatter (kathrin.summermatter@ivi.admin.ch) (1), T. Binz (2)

(1) Institut of Virology and Immunoprophylaxis IVI, Mittelhaeusern, Suisse

(2) Federal Office of Public Health, Berne, Suisse

K. Summermatter, T. Binz (2012). Biosafety-Europe: Recommendations for the harmonisation of biosafety and laboratory biosecurity practices in Europe on the basis of a comparative approach, EuroReference, No. 7, ER07-12ME03. http://www.anses.fr/eurореference/numero7/PND0I0.htm

Research on highly pathogenic organisms in containment level 3 and 4 laboratories is very important for human public health since it provides opportunities for the development of vaccines and novel therapeutics as well as diagnostic methods to prevent epidemics. However, it also represents a risk to the population in case those organisms may spread in the environment due to a laboratory accident, poor laboratory practices or intentional removal and subsequent release (terrorist attack). Therefore, adequate technical and physical containment measures and best biosafety and laboratory biosecurity practices must be implemented in those facilities to prevent accidental or intentional release of dangerous pathogens.

Biosafety-Europe is a project funded through the 6th Framework which aimed to explore harmonization and exchange of biosafety and laboratory biosecurity practices within a pan-European network. The consortium consisted of 18 partners from 10 European countries from industry, universities and government agencies with expertise in biosafety and laboratory biosecurity, in containment technology and in the corresponding legal frameworks. The project started in April 2006 and ended in November 2009.
Detailed information was gathered on European legislation

Laboratories referred to the WHO term 'biosafety level (BSL)'. No harmonized system for the reporting of laboratory incidents and accidents was found. Northern European countries reported higher number of laboratory acquired infections than other parts of Europe, which in part may reflect reporting differences. Less than half of the respondents were subject to oversight by a biosafety committee. Moreover biosafety responsibilities appear often to be attributed to staff in management positions with functional roles that could be in conflict with strict biosafety considerations.

No. 7 Special « Security and safety »

K. Summermatter, T. Binz (2012). Biosafety-Europe: Recommendations for the harmonisation of biosafety and laboratory biosecurity practices in Europe on the basis of a comparative approach, EuroReference, No. 7, ER07-12ME03

Chatham House project (2012)

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Safe and secure biomaterials:

- need for laboratory capacity building
- discrepancy between endemicity and resources
- different standards of biosafety and biosecurity regulations
- **Need to rethink current regulations and practices -> relative risk approach**
- **Safer, more secure and sustainable laboratory capacity building**

Biosafety and Biosecurity: A Relative Risk-Based Framework for Safer, More Secure, and Sustainable Laboratory Capacity Building, P. Dickmann, H. Sheeley, N. Lightfood; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4612646/

Laboratory associated infection

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ClinMicroNet online survey of 2002-2004 (ASM):

- 88 hospital microbio labs and 3 national ref. labs
- 33 % of laboratories reported at least 1 laboratory associated infection
- Most common : shigellosis, brucellosis, salmonellosis
- Highest incidence : Brucella and Neisseria meningitidis

Incidence of infection	General population	Laboratory worker
Brucella species	0.08/100.000	641/100.000
Neisseria meningitidis	0.62/100.000	25.3/100.000

https://academic.oup.com/cid/article/49/1/142/371797

CORRESPONDENCE

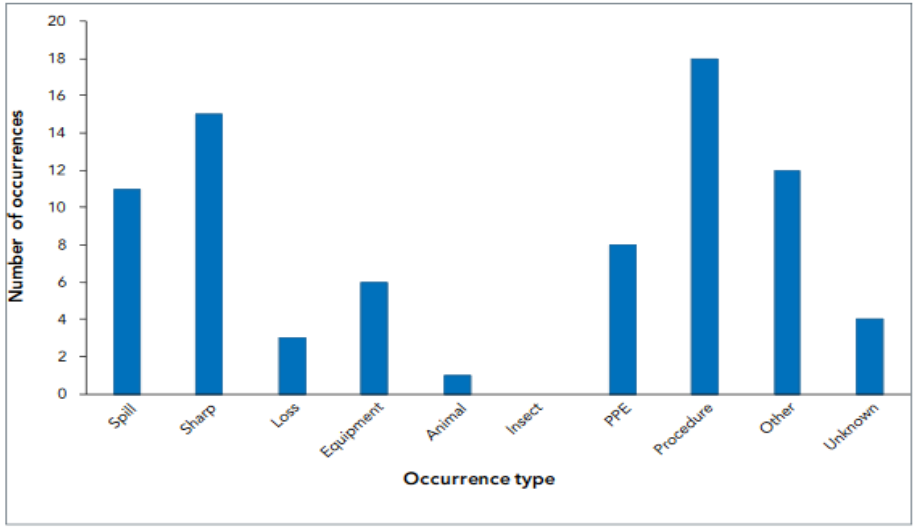
Variant Creutzfeldt–Jakob Disease Diagnosed 7.5 Years after Occupational Exposure

- While she was using forceps to handle the samples, she accidentally stabbed her thumb through a double pair of latex gloves, enough to break the skin and cause bleeding (2010).
- Conclusions: Percutaneous exposure to prion-contaminated material is **plausible in this patient, since the prion strain that she had handled was consistent with the development of variant CJD**. The 7.5-year delay between the laboratory accident and her clinical symptoms is congruent with the incubation period in the transfusion-transmitted form of the disease.

https://www.nejm.org/doi/full/10.1056/NEJMc2000687

Surveillance of laboratory exposures to human pathogens and toxins, Canada 2019

Figure 4: Reported occurrence types involved in reported exposure incidents, Canada 2019 (N=78)



Abbreviation: PPE, personal protective equipment

Table 3: Root causes reported in follow-up reports of exposure incidents, Canada 2019 (N=144) (*continued*)

Root cause	Examples of areas of concern	Citations	
		n	%
Human interaction	A violation (cutting a corner, not follow correct procedure, deviating from standard operating procedure)	35	24
	An error (a mistake, lapse of concentration, or slip of some sort)		
Management and oversight	Supervision needed improvement	20	14
	Lack of auditing of standards, policies, and procedures		
	Risk assessment needed improvement		
Training	Training not in place but should have been in place	17	12
	Training not correct for the task/activity		
	Staff were not qualified or proficient in performing the task		
Standard operating procedure	Documents were followed as written but not correct for activity/task	27	19
	Procedures not in place but should have been in place		
	Documents were not followed correctly		
Other	Not applicable	8	5

Note: Percentages rounded to the nearest whole number

https://www.canada.ca/content/dam/phac-aspc/documents/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2020-46/issue-9-sept-3-2020/ccdrv46i09a07-eng.pdf

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The WHO risk based approach

Are we less safe in the future?

- We still have laboratory acquired infections despite highly sophisticated BSLs
- Risk groups differ in description, name and expression between countries
- Different countries have differents cultures, climates, requirements and resources
- Funding to sustain the labs is not always guaranteed or underestimated

- The one fit all approach does not fit all

- WHO issues guidelines that should be applicable worldwide

https://science.sciencemag.org/content/360/6386/260?rss=1/share

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A researcher dons a protective suit at China's National Biosafety Laboratory in Wuhan, Hubei Province, China.

Facts

Most laboratories:

- BSL1 – BSL2
- Increasing number of BSL3
- Few BSL4

Despite existing regulations:

- Each BSL3 and BSL4 is unique
- Sophisticated enigeering controls
- Cost intensive

Question: What do we really need to perform our activities safely and secure?

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An example: Risk assessment according to Swiss containment ordinance

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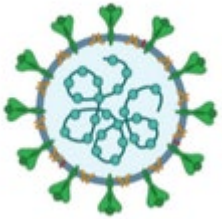
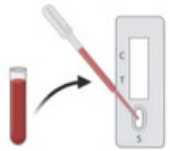
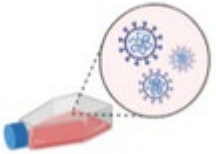


Risk group for organisms





Risk class for activities

Biosafety level for laboratories
Safety equipment
Practices and procedures

Pro's and con's for biosafety professionals

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So far:
Risk group -> biosafety level
National classification systems for organisms
Prescriptive measures not always based on risk
Checklist approach

WHO approach:
Risk assessment for activities (characteristics of agents, activity, facility, local / national circumstances)
Risk based mitigation measures based on available resources

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The new laboratory biosafety manual and monographs

How to use the manual and the monographs

- Existing national regulations are still to be implemented at the national level and will not be undermined by the new WHO manual.
- The manual is intended to serve as a guideline and resource for biosafety professionals:
  - Planning, construction, commissioning and maintenance of laboratories
  - Implementation of a biosafety / biosecurity programme
  - Risk assessment and selection of appropriate risk mitigation measures including PPE
  - Decontamination of waste
  - Outbreak situations
- Templates in the monographs

Laboratory design and maintenance

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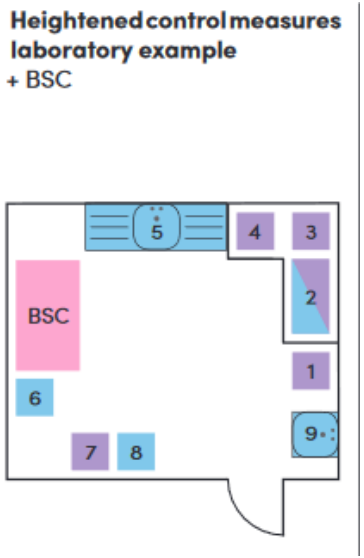
- Detailed information about core requirements, heightened control and maximum containment measures
- Emphasis is put on **good microbiological practices and procedures**
- Framework of a laboratory project:
  Planning – Design – Construction – Operation and maintenance - Decommissioning



Source:
Monograph: Laboratory design and maintenance

Good microbiological practices and procedures

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GMPP are the most essential risk control measures because human error, suboptimal laboratory techniques and improper use of equipment have been found to cause the most laboratory injuries and laboratory-associated infections.

Source:
Monograph: Laboratory design and maintenance

Biosafety programme management

Facilities handling biological agents
-> biosafety programme

Facilities can be of various complexities

Use of low to high consequence pathogens

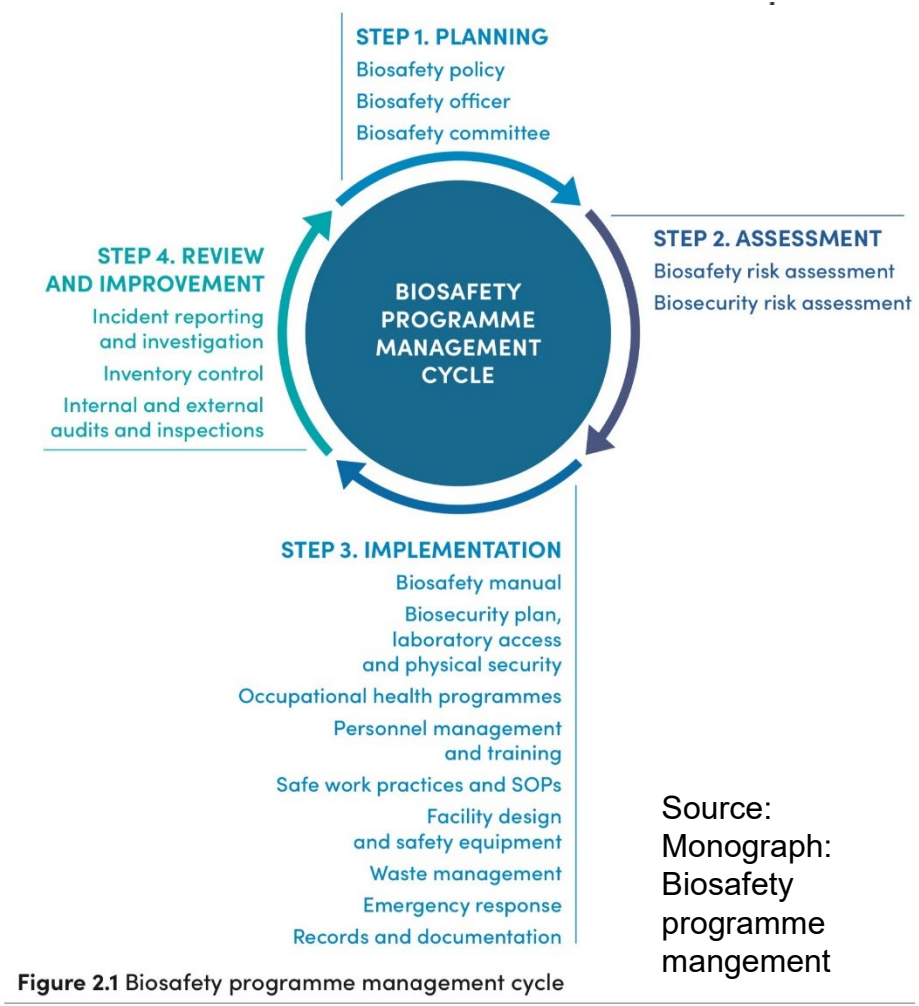

Figure 2.1 Biosafety programme management cycle

Source: Monograph: Biosafety programme mangement

Core element: Risk Assessment

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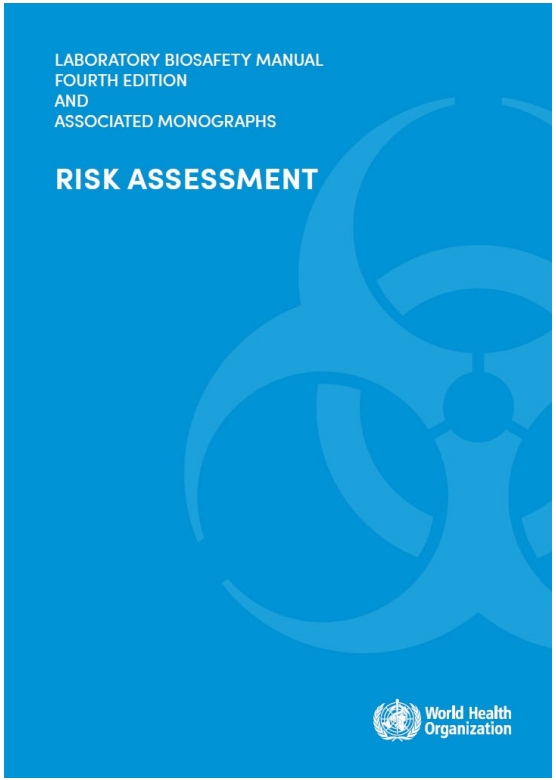
ADORA - principle:

All **D**epend **O**n **R**isk **A**ssessment



Risk

Risk = likelihood x consequence

Likelihood: probability of an incident (exposure / release) occurring in the course of laboratory work

Consequence: Outcome of an incident (exposure / release) of varying severity of harm, occurring in the course of laboratory operations (laboratory associated infections, illness, physical injury, environment contamination, asymptomatic carriage of a biological agent)

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The risk assessment framework

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Standardized and structured way:

- Gather information
- Evaluation of risk
- Development of risk control strategy
- Selection and implementation of controls
- Review

We have to know what we are doing!

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- Biological Material
- Type of laboratory work / procedures
- Type of equipment
- Laboratory facility
- Human factors (e.g. competency)
- Other factors (legal, political, cultural, public perception etc.)

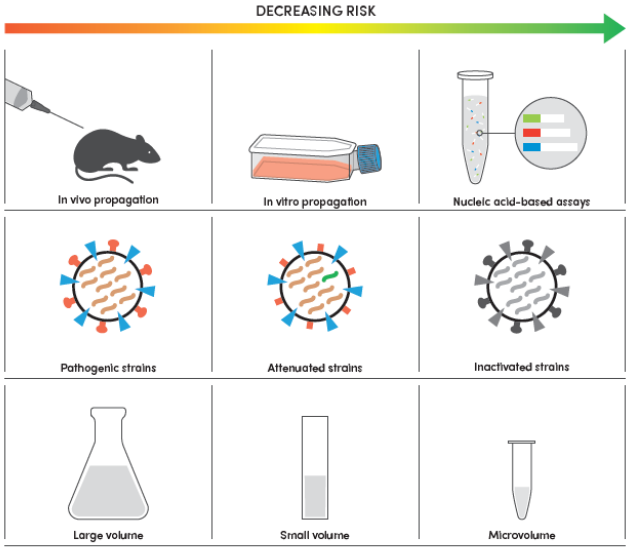

Figure 3.2 Examples of techniques to reduce or eliminate the risks of infection associated with manipulating biological agents. The lower risks reduce the need for risk control measures that would otherwise be required.

Templates to help the user

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Pathogen safety data sheet template

SECTION 1 Biological agent

Pathogen		
Pathogen *(Official taxonomic naming convention)*		
Other names *(for example, former taxonomic name, common name)*		
Agent type	☐ Bacterium ☐ Fungus ☐ Parasite	☐ Virus ☐ Prion ☐ Other (describe)
Taxonomy	Family	
	Genus	
	Species	
	Subspecies/strain/clonal strain	
Characteristics	Appearance	
	Size	
	Shape	
	Genome structure *(for example, RNA/DNA virus, sense/antisense)*	
	Other (describe)	
Properties contributing to risk	Modifications from parental strain	
	Sporulation	
	Toxin production	
	Oxygen requirements	
	Enzymatic activity	
	Life cycle	
	Reproduction	

Laboratory-associated infections		
Are there known exposure incidents within the organization?	☐ No ☐ Unknown	☐ Yes (describe incidents and circumstances)
Are there known exposures external to the organization? *(Evidence from the literature [research, diagnostic, health care] of laboratory-associated infections with the biological agent, including the circumstances)*	☐ No ☐ Unknown	☐ Yes (describe)
Sources/specimens		
List primary biological specimens likely to contain the biological agent *(for example, blood, urine, semen, mucous, faeces, necropsy tissues)*		
Primary hazards		
Indicate primary hazards	☐ Ingestion ☐ Exposure ☐ Auto-inoculation ☐ Inhalation ☐ Fomites	☐ Bites/scratches (from infected animal) ☐ Exposure to animal waste or carcasses ☐ Other (describe)
Special hazards		
Indicate special hazards *(for example, in diagnostic laboratories that receive potentially contaminated testing request forms shipped in the same box as the specimens)*		

Templates for the risk assessment

Institution/Facility name	
Laboratory name	
Laboratory manager/Supervisor	
Project titles/Relevant standard operating procedures (SOPs)	
Date	

If using this template, complete all sections following the instructions in the grey boxes. The instructions and bullet points in the grey boxes can be copied into the text boxes beneath the instructions and used as prompts to gather and record the necessary site-specific information. The grey instruction boxes can then be deleted, and the text remaining will form a risk assessment draft. This draft must be carefully reviewed, edited as necessary and approved by the risk assessment team members.

STEP 1. Gather information (hazard identification)

Instructions: Provide a brief overview of the laboratory work and summarize the laboratory activities to be conducted that are included in the scope of this risk assessment.	
Describe the biological agents and other potential hazards (for example, transmission, infectious dose, treatment/preventive measures, pathogenicity).	
Describe the laboratory procedures to be used (for example, culturing, centrifugation, work with sharps, waste handling, frequency of performing the laboratory activity).	
Describe the types of equipment to be used (personal protective equipment (PPE), centrifuges, autoclaves, biological safety cabinets (BSCs)).	
Describe the type and condition of the facility where work is conducted.	
Describe relevant human factors (for example, competency, training, experience and attitude of personnel).	
Describe any other factors that may affect laboratory operations (for example, legal, cultural, socioeconomic).	

STEP 2. Evaluate the risks

Instructions: Describe how exposure and/or release could occur.	
What potential situations are there in which exposure or release could occur?	
What is the likelihood of an exposure/release occurring (unlikely, possible, likely)?	
What is the severity of the consequences of an exposure/release (negligible, moderate, severe)?	

Instructions: Evaluate the risk and prioritize the implementation of risk control measures. Circle the initial risk of the laboratory activities including risk control measures described in STEP 1 but before any additional risk control measures have been put in place.

Note:

- **When assigning priority, other factors may need to be considered, for example, urgency, feasibility/sustainability of risk control measures, delivery and installation time and training availability.**
- **To estimate the overall risk, take into consideration the risk ratings for the individual laboratory activities/procedures, separately or collectively as appropriate for the laboratory.**

		Likelihood of exposure/release		
		Unlikely	Possible	Likely
Consequences of exposure/release	Severe	Medium	High	Very high
	Moderate	Low	Medium	High
	Negligible	Very low	Low	Medium

Laboratory activity/procedure	**Initial risk (very low, low, medium, high, very high)**	**Is the initial risk acceptable? (yes/no)**	**Priority (high/medium/low)**

Select the overall **initial** risk.	☐ Very low	☐ Low	☐ Medium	☐ High	☐ Very high
Should work proceed without additional risk control measures?	Yes ☐ No ☐				

Templates for the risk assessment for more complex activities

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2.4 Describe the initial risk of the laboratory activities before additional risk control measures have been put in place

Instructions: Circle the initial risk of the laboratory activities before additional risk control measures have been put in place. Based upon your evaluation of the likelihood and consequences of an exposure/release as listed above, assess the initial, or currently existing, risk of the laboratory activity using the table below. Find the likelihood of exposure (top row of the chart) and the consequences (left column of the chart).

		Likelihood of exposure/release				
		Rare	Unlikely	Possible	Likely	Almost certain
Consequences of exposure/ release	Severe	Medium	Medium	High	Very high	Very high
	Major	Medium	Medium	High	High	Very high
	Moderate	Low	Low	Medium	High	High
	Minor	Very low	Low	Low	Medium	Medium
	Negligible	Very low	Very low	Low	Medium	Medium

Instructions: Check the initial risk to determine the appropriate risk control measures required.

Templates for the risk assessment for more complex activities

Assessed initial risk		Potential consequences	Actions
☐	Very low	If an incident occurred, harm would be very unlikely.	Undertake the laboratory activity with the existing risk control measures in place.
☐	Low	If an incident occurred, there would be a small likelihood of harm.	Use risk control measures if needed.
☐	Medium	If an incident occurred, harm would result that would require basic medical treatment and/or simple environmental measures.	Additional risk control measures are advisable.
☐	High	If an incident occurred, harm would result that would require medical treatment and/or substantial environmental measures.	Additional risk control measures need to be implemented before the laboratory activity is undertaken.
☐	Very high	If an incident occurred, a permanent, impairing harm or death and/or extensive environmental effects would be likely.	Consider alternatives to doing the laboratory activity. Comprehensive risk measures will need to be implemented to ensure safety.

Risk tolerance

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*It is important to note that risk can **never be completely eliminated unless the work is not performed** at all.*

X

✓

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The risk based approach for SARS-CoV-2 diagnostic: an example

Activities in a diagnostic setting

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Unpacking, sample splitting, inactivation of samples
PCR of inactivated samples
PCR of non inactivated samples

Activities involving SARS-CoV-2: the traditional approach

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The traditional approach:

- SARS-CoV-2: *Risk group 3*
- Diagnostic of SARS-CoV-2: *biosafety level 2 laboratory* -> need to be notified to the authorities
- Research or activities involving cultivation: *biosafety level 3 laboratory* -> needs a permit

-> Which safety measures for which step?
-> Biosafety level 2, but is this enough?
- > What about the procedures?

Examples

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Activity	Initial risk without measures(L x C)
A. PCR of inactivated SARS-CoV-2 patient samples	Low (unlikely / negligible)
B. Pipetting and vortexing of SARS-CoV-2 patient samples, PCR of non inactivated samples	Medium (likely / moderate)
C. Immunocompromised person: pipetting and vortexing of SARS-CoV-2 patient samples, PCR	High (likely / severe)

Initial risk categorisation

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Consequences of exposure/ release	Severe	Medium	High	C ery high
	Moderate	Low	Medium	B High
	Negligible	Very lo A	Low	Medium
		Unlikely	Possible	Likely
		Likelihood of exposure/release		

Risk categorisation with additional measures

Activity	Initial risk without measures(L x C)	Risk control measures	Residual risk
A. PCR of inactivated SARS-CoV-2 patient samples	Very low (unlikely / negligible)	Core requirements	Very low
B. Pipetting and vortexing of SARS-CoV-2 patient samples, PCR of non inactivated samples	Medium (likely / moderate)	HCM (CR plus BSC)	Low
C. Immunocompromised person: pipetting and vortexing of SARS-CoV-2 patient samples, PCR	High (likely / severe)	HCM (CR plus BSC) **Stop work**	Medium

Risk categorisation with measures

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Consequences of exposure/ release	Severe	Medium **C**	High	Very high
	Moderate	Low **B**	Medium	High
	Negligible	Very low **A**	Low	Medium
		Unlikely	Possible	Likely
		Likelihood of exposure/release		

Some challenges triggering risk assessments

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- Personnel (risk awareness, training, stress, fatigue, rules for social distancing)
- Space (testing equipment, BSC, storage …..)
- Reagents and material inlcuding PPE
- Waste management (solid – liquid)
- How to react to constant changes and to keep the risk assessment up-dated?

Conclusions

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- Intended to prevent **exposure** and **release**
- Risk based approach to be used in a more structed way
- It is more flexible and globally applicable
- Applicable to outbreak situations

Challenges:

- Awareness raising to promote the risk based approach
- Need to share information about biosafety solutions and biosafety best practices
- Need to share lessons learnt

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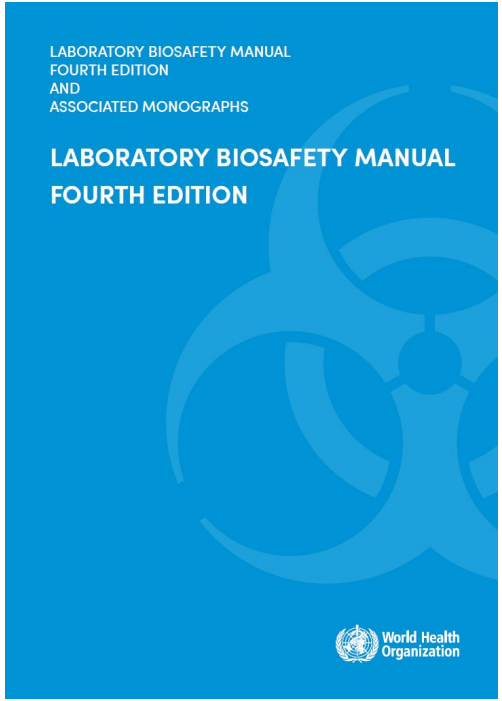
The manual should **complement** any national regulation and oversight mechanisms that may be in place!

It may help countries establishing their own regulations.



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Thank you for your attention!

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Link to WHO website:
Safeguarding biosafety and biosecurity in laboratories

https://www.who.int/activities/safeguarding-biosafety-and-biosecurity-in-laboratories

Contact : katharina.summermatter@ifik.unibe.ch