

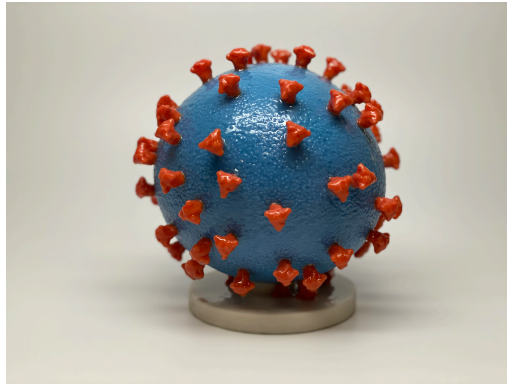


# **The Tale of the Virus and Sample: Considerations from Expert Groups**

**Anna Laurén, on behalf of the EBF**

**13<sup>th</sup> EBF Open Symposium**

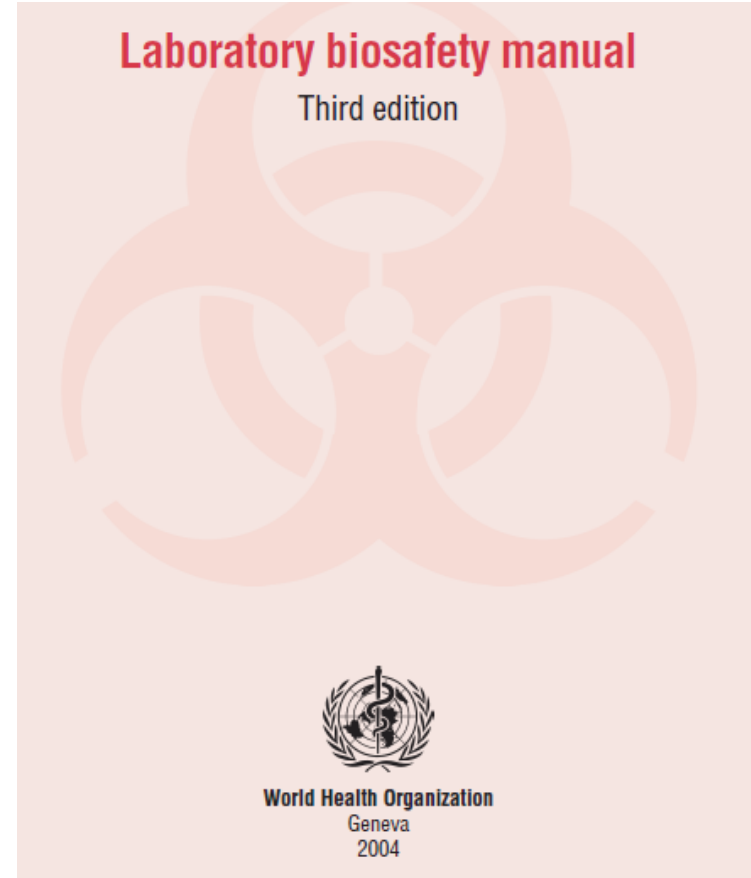
- Have the COVID-19 outbreak established a need for new routines in our laboratories?
- What can history, experts and literature tell us?
- How do we ensure a safe working environment for our laboratories?



*Modell of Coronavirus SARS-CoV-2  
Picture from NIAID*

# Literature

- DIRECTIVE 2000/54/EC: on the protection of workers from risks related to exposure to biological agents at work
- WHO Laboratory biosafety manual (LBM) Third Edition 2004
- National regulations
- Scientific publications



# What about more Recent updates?

WHO have plans to update the third edition for Laboratory Biosafety Manual:

- Publication in Science April 2018
- Risk-based reboot for global lab biosafety
- New WHO guidance shall focus on access to lab facilities
- Authors from: WHO; Health and Safety Laboratory, UK; Institute of Virology and Immunology, Switzerland; Public Health England, UK; Public Health Agency of Canada, Canada; Mahidol Oxford Tropical Medicine Research Unit, Thailand; Centre for Tropical Medicine and Global Health, UK; Centers for Disease Control and Prevention, Washington, USA.



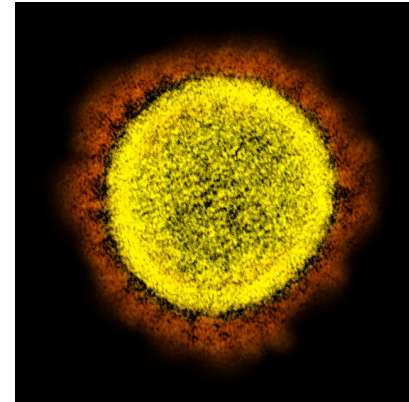
BIOSAFETY AND BIOSECURITY

## ***Risk-based reboot for global lab biosafety***

New WHO guidance could expand access to lab facilities



## Then there was the virus



*SARS-CoV-2  
EM Picture from NIAID*

## Laboratory biosafety guidance related to coronavirus disease (COVID-19)

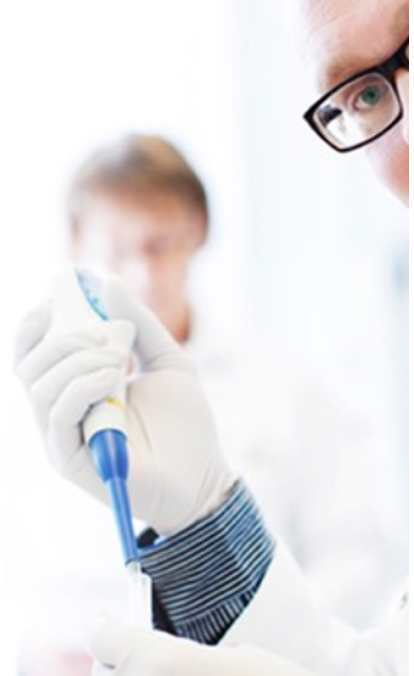
Interim guidance

13 May 2020



# Biosafety in the lab: A Risk based approach

- A shift in focus to a risk-based, technology-neutral, and cost-effective approach to biosafety
- Laboratory facilities, safety equipment, and work practices shall be locally relevant, proportionate, and sustainable
- This shall:
  - Allow flexibility in laboratory design
  - Reduce focus on pathogen risk groups and biosafety levels
  - **Place emphasis on human factors and worker training**



*Kojima et al Science Mag (2018)*

# Risk based approach

- Why the update?
  - The first publication of the LBM coincided with the year (1983) during which PCR was invented and HIV was isolated from AIDS patients
  - In the 80'ies and 90'ies pathogen diagnostic and research involved propagation of infectious agents
  - Since then diagnostic and research technologies have evolved but the LBM has not been fully aligned
- Risk shall be focused on how we work and not how infectious the pathogen
- Pathogen risk groups (RGs, or hazard groups) and biosafety levels (BSLs) should not be assumed to be the same

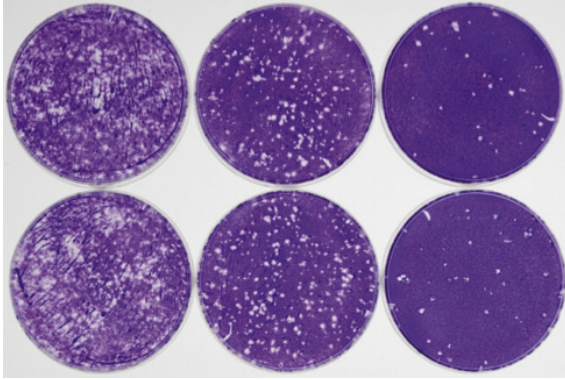
RG2 pathogens  $\neq$  BSL2 laboratory

RG3 pathogens  $\neq$  BSL3 laboratory

RG4 pathogens  $\neq$  BSL4 laboratory

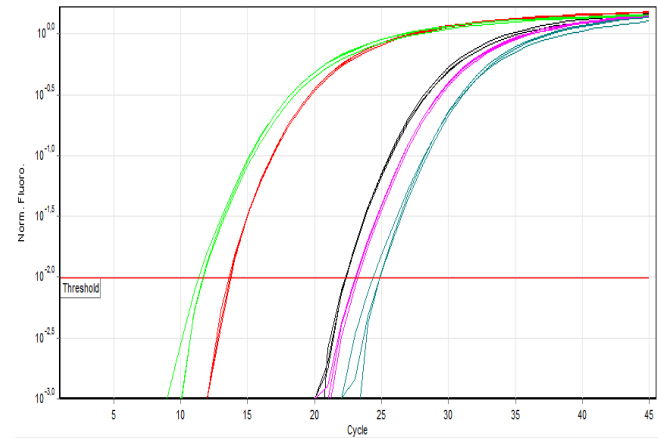
# Technology driven Likelihood for transmission

80-90'ies: Traditional diagnostic by culture of pathogens and test for infectivity



Likelihood for transmission  
HIGH

Today's labs: No propagation of pathogen



Likelihood for transmission  
LOW

# Cause of laboratory acquired infections

- Majority of laboratory-acquired infections was caused by human factors such as:
  - improper use of personal protective equipment
  - disregard for or inadequate risk assessments
  - lack of standard operating procedures
  - properly trained staff
- Proper equipment and facilities were less important

*Wurtz et al Eur J Clin Microbiol Infect Dis (2016)*

The best designed and most engineered laboratory  
is only as good as its least competent worker

*Kojima et al Science Mag (2018)*

# WHO LBM 2004: Biosafety levels, practices and equipment

BIOSAFETY LEVEL	LABORATORY TYPE	LABORATORY PRACTICES	SAFETY EQUIPMENT	
Basic – Biosafety Level 1	Basic teaching, research work	Good microbiological practice and procedure (GMPP)	None; open bench	
Basic – Biosafety Level 2	Primary health services; diagnostic service; research	GMPP plus protective clothing and biohazard sign	Open bench plus biological safety cabinet (BSC) for potential aerosols	Labs working with unknown biological samples – study samples
Containment – Biosafety Level 3	Special diagnostic services, research	As Level 2 plus special clothing, controlled access, directional airflow	BSC and/or other primary devices for all activities	
Maximum containment – Biosafety Level 4	Dangerous pathogen units	As Level 3 plus airlock entry, shower exit, special waste disposal	Class III BSC or positive pressure suits in conjunction with BSC II BSCs, double needed autoclave	



# Work with samples related to COVID-19

- Patient specimens from suspected or confirmed cases should be transported as UN3373, “Biological Substance Category B”
- Laboratories should be labelled for work with biohazard
- Initial processing (before inactivation) of specimens should take place in a validated BSC or primary containment device
- Non-propagative diagnostic laboratory work should be conducted at a facility using procedures equivalent to Biosafety Level 2 (BSL-2) on an open bench
- Propagative work (for example virus culture or neutralization assays) should be conducted in a containment laboratory with inward directional airflow (BSL-3).

## Shipment label



BIOLOGICAL SUBSTANCE  
CATEGORY B

## Laboratory label



# Why is the recommendations for lab not a higher biosafety level for SARS-CoV-2?

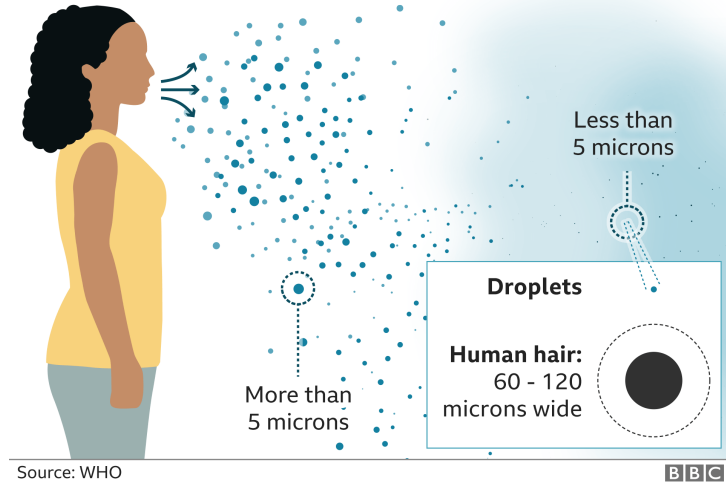
## The difference between droplet and airborne transmission

### Droplet transmission

Coughs and sneezes can spread droplets of saliva and mucus

### Airborne transmission

Tiny particles, possibly produced by talking, are suspended in the air for longer and travel further



- SARS-CoV-2 RNA genome has been detected in: nasopharyngeal swabs, sputum, bronchoalveolar lavage fluid, fibrobronchoscope brush biopsy, stool, ocular fluid, and blood
- SARS-CoV-2 is transmitted from infected persons through respiratory droplets and possible airborne
- Contagion can occur by direct contact of the mucosae or conjunctiva with infected surfaces, like the skin or objects that have been exposed to infected droplets, sputum or sneeze
- SARS-CoV-2 RNA can be detected in the plasma or serum of 15% of the infected subjects but transmission by blood transfusion remains unproven
- Controversies over when, and for how long the virus is contagious are listed in the overview

# Laboratory infections and COVID-19

- A retrospective study nullified potential infection by contaminated surfaces or transmission from samples in a COVID-19 outbreak Israel's central virology laboratory (ICVL) facilities
  - Phylogenetic analysis clarified transmission events, confirming one source subject as having infected at least three other staff members plus staff member's infected spouse

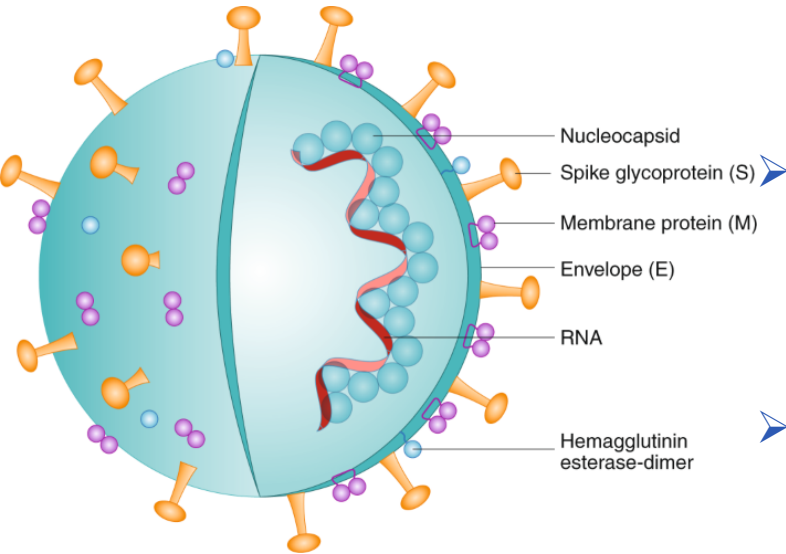
*Ref: Zuckerman et al. Viruses August 2020*

- Laboratory-acquired infection has not been reported for SARS-CoV-2.
  - Laboratory-acquired infections with the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) have been reported previously but only in laboratories performing virus propagation

*Ref: Public Health England, July 2020. COVID-19: safe handling and processing for samples in laboratories*

**The person delivering the samples is a potentially higher risk than the actual samples**

# Coronaviruses and replication



*Florindo et al July 2020.  
Nature Nanotechnology*

- **The virus do not survive outside droplets**
  - Corona is a family of enveloped virus: the outer membrane of the virus is derived from the infected cells
- **Virus needs an intact membrane with spike glycoprotein for the capsid to enter cells**
  - The spikes of the virus are used to bind to ACE2 receptor followed by endocytosis and entry of the virus nucleocapsid/RNA into the cell
- **Virus RNA alone is not infectious**
  - The nucleocapsid consists of 16 nonstructural proteins, including proteases, RNA-dependent RNA polymerase, and others, that form the viral replicase complex, a platform to propagate viral mRNAs

# WHO Laboratory biosafety guidance related to coronavirus disease (COVID-19) 2020

- Interim guidance on laboratory biosafety related to COVID-19
- All procedures must be performed based on risk assessment
  - Excellent template in *WHO Laboratory biosafety guidance related to coronavirus disease (COVID-19) 2020*
- Staff shall have demonstrated capability, in strict observance of any relevant protocols at all time
- National guidelines on laboratory biosafety should be followed in all circumstances



*SARS-CoV-2 erupting from  
infected cells  
EM Picture from NIAID*

# Personal protection for BSL2

- Apply standard safety considerations for all lab work
- Staff shall use personal protective equipment(PPE) such as gloves, labcoats, glasses, goggles, protection screens (when applicable)
- Sharp objects should not be used
- Wash hands after laboratory work
- In the present COVID-19 context, a local risk assessment should be conducted to determine whether the use of respiratory protection is needed for example at risk of aerosols





# Good microbiological practice and procedure (GMPP)

- All technical procedures should be performed in a way that minimizes the generation of aerosols and droplets
- All handling that may cause splashes, droplets, or aerosols of infectious materials should be performed in appropriately maintained and validated BSCs or primary containment devices
- Use appropriate disinfectants with proven activity against enveloped viruses
  - recommended contact time
  - correct dilution
  - within the expiry date of the working solution
- Do not work when fatigue
- Keep good distance
- Do not eat or drink in the laboratory

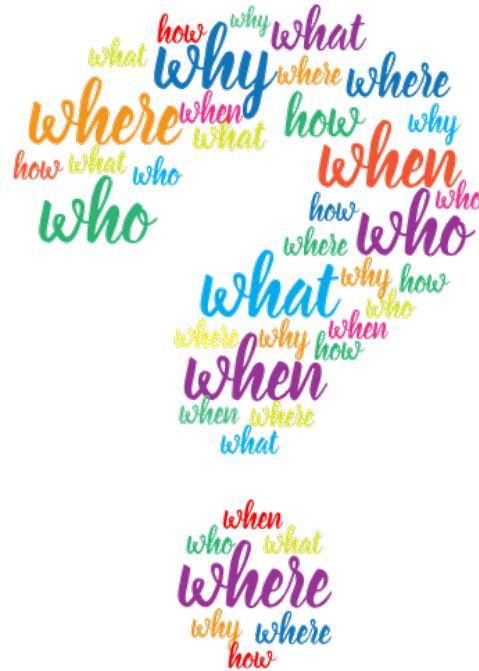
## Summary

- Work with unknown samples is associated with a risk
- A risk assessment shall always be performed and documented
- General work with blood related to the testing of specimens of COVID-19 patients is similar to standard diagnostic work practices
- SARS-CoV-2 RNA can be detected in the plasma or serum of 15% of the infected subjects but transmission by blood transfusion remains unproven
- Virus RNA in itself is not infectious
- The person delivering the samples is a potentially a higher risk than the actual samples

# Acknowledgment

- EBF community
- EBF Open Symposium Organising committee

## Thank you and time for questions



# Contact Information

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