

# Biorisk Management at a Centre for Clinical and Experimental Infection Research – From concept to practice

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Institut Pasteur du Maroc 07.11.2017

- Head of the Biological Safety Department at Hannover Medical School (MHH), Germany
- Career includes
  - Section leader with the local state authority of Lower Saxony, responsibility for authorization of BSL1 to BSL3 research laboratories and production facilities
  - Responsible for the training of scientists according to the German Genetic Engineering Act and for the student lecture series “Gene Technology, Biosafety and Biosecurity” at MHH
  - Chair of the ABAS subcommittee “New developments – Biosafety and Biosecurity”, Federal Ministry of Labour and Social Affairs, Berlin
  - Chair of the Safety Service Committee (SASEC) at TWINCORE, Hannover



# Hannover Medical School, Germany



Numer of students: 3500

Number of employees: 9100

# TWINCORE - Centre for Experimental and Clinical Infection Research, Hannover



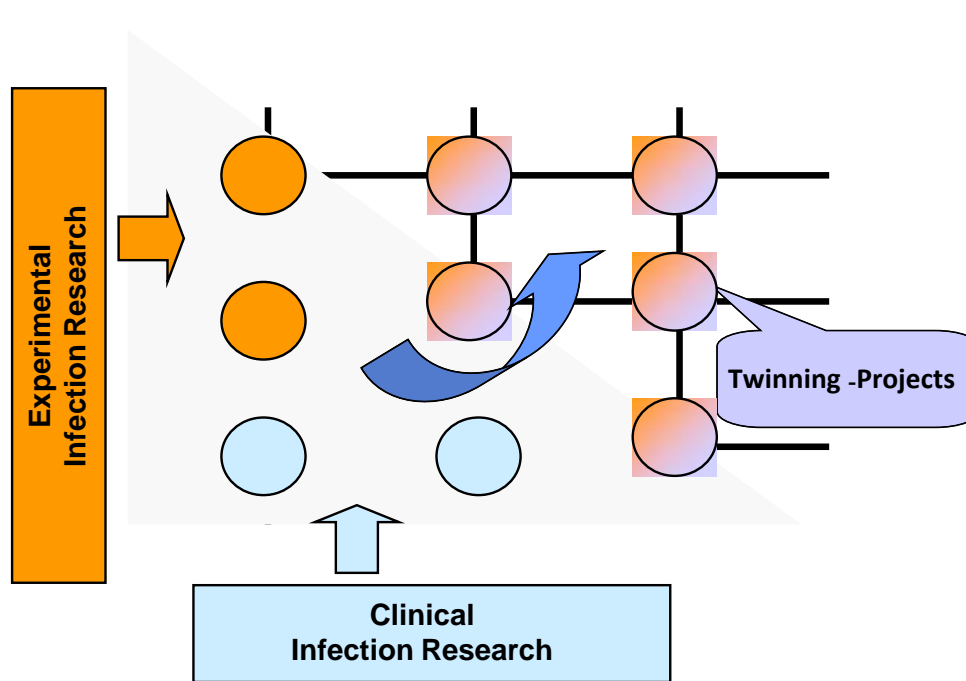
TWINCORE,  
a joint venture between

MHH  
Medizinische Hochschule  
Hannover

HELMHOLTZ  
ZENTRUM FÜR  
INFEKTIONSFORSCHUNG

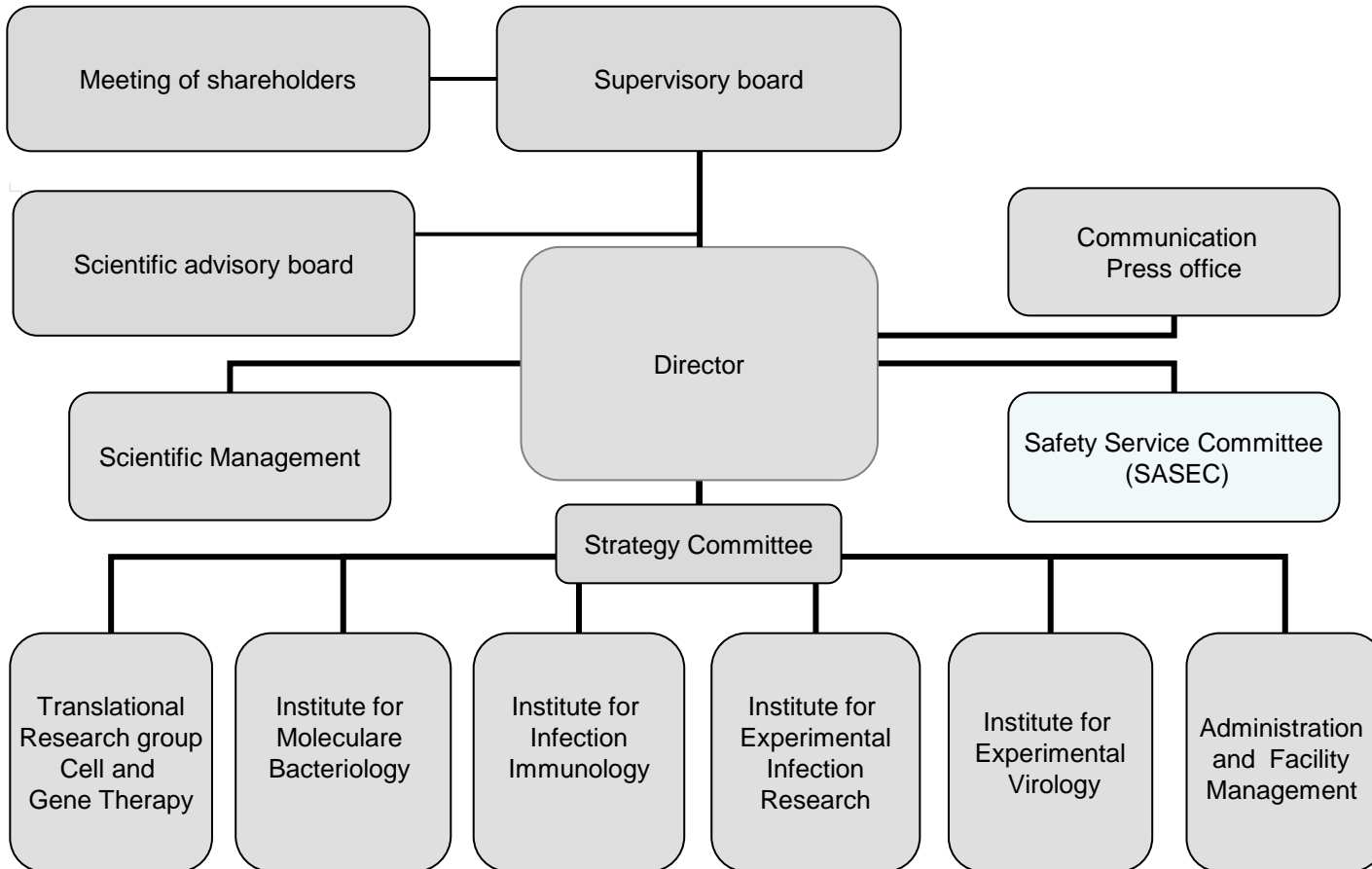
TWINCORE is a translation centre, a collaboration between Helmholtz Centre for Infection Research (HZI) in Braunschweig and Hannover Medical School (MHH).

# TWINCORE - Centre for Experimental and Clinical Infection Research, Hannover

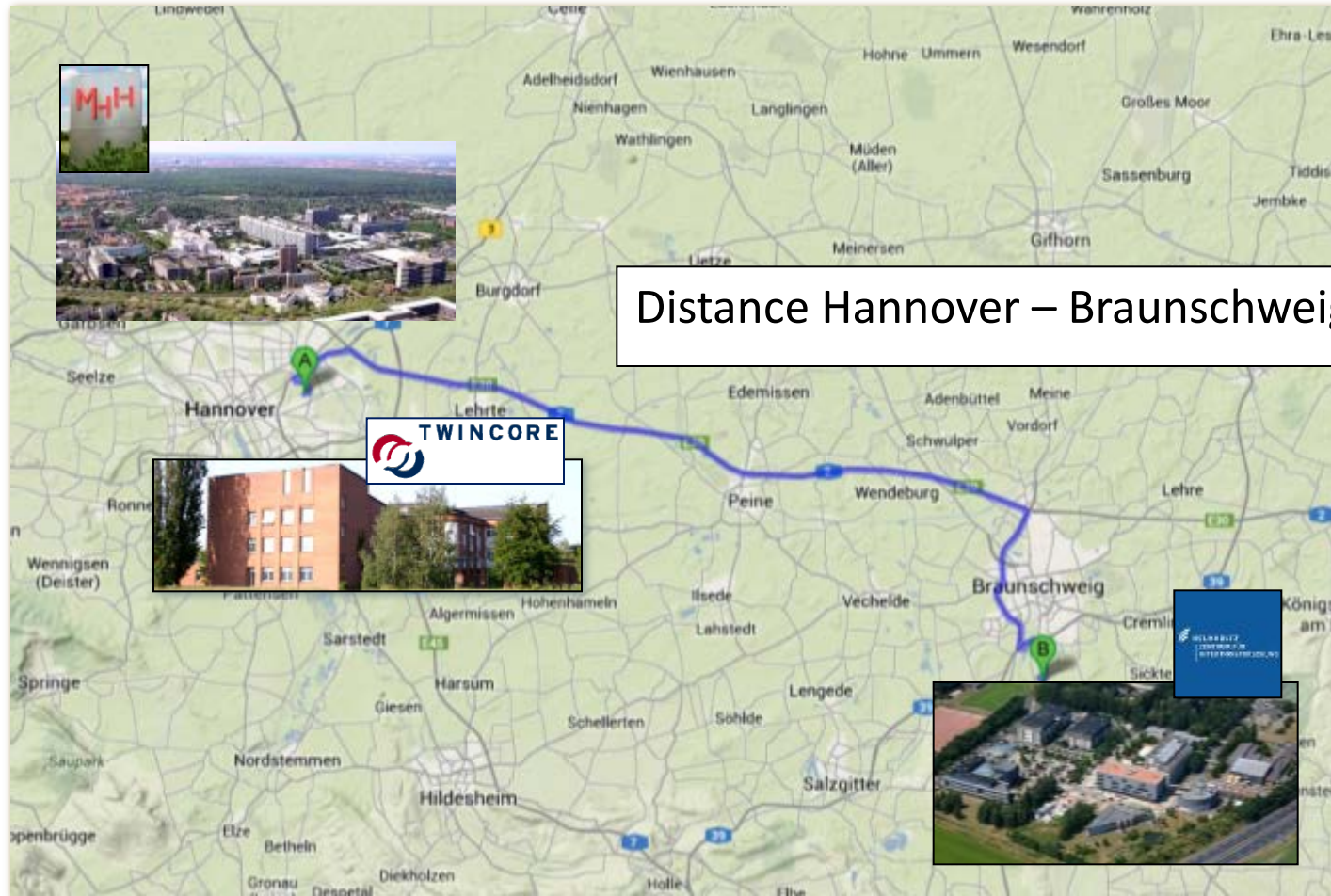


The focus of research is the search for new strategies for diagnosis, prevention and treatment of infectious diseases. The route to this is translation - the close interlinking of basic and clinical research.

# TWINCORE – Organisation chart



# TWINCORE - Centre for Experimental and Clinical Infection Research, Hannover

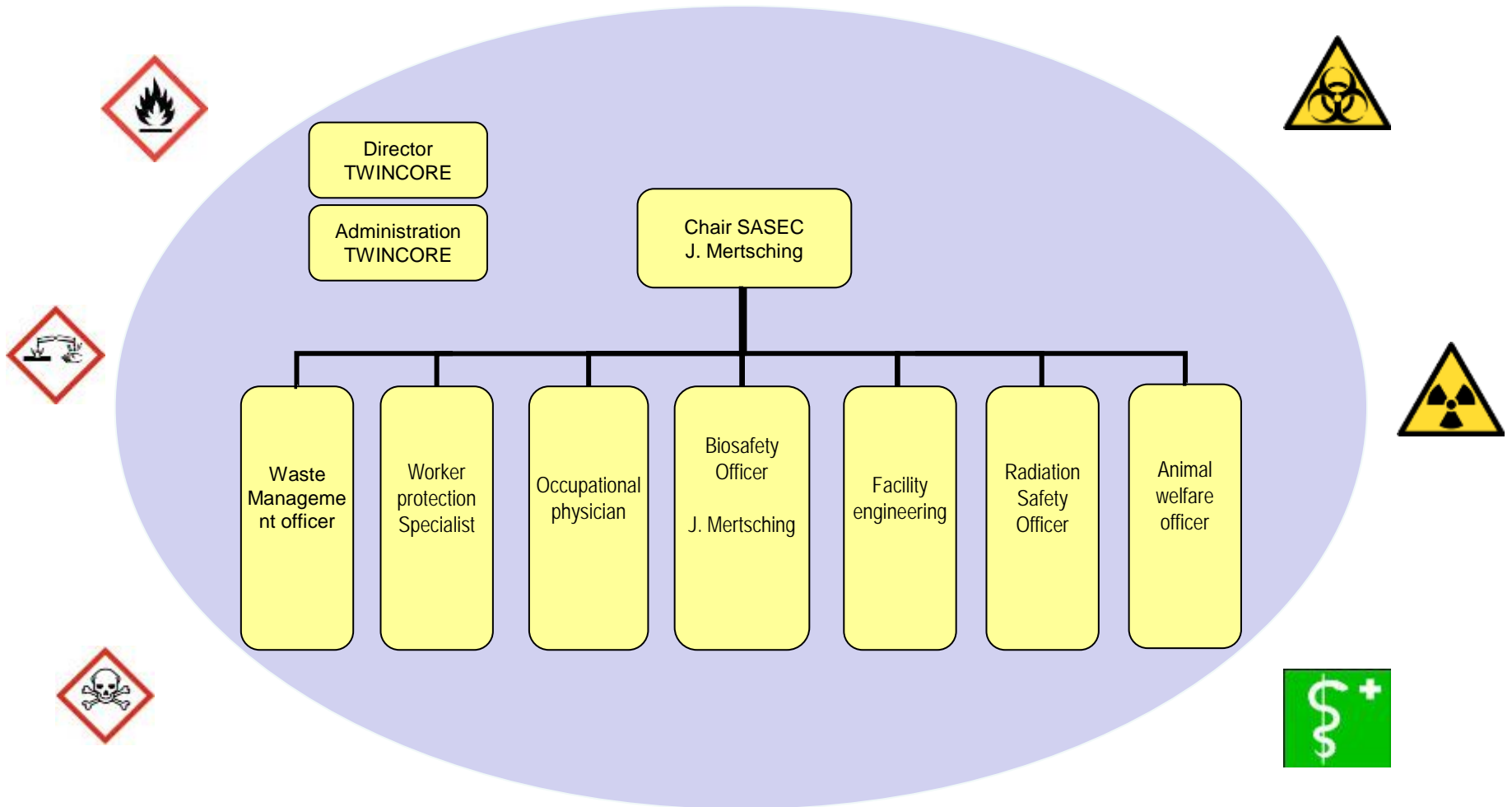


# Question of the manager who is going to hire one person for biosafety, chemical safety, radioactivity, and ...





# Safety Service Committee (SASEC) at TWINCORE



# Why do we need effective biorisk management?



# Laboratory-acquired infections (LAI)



American Journal of Infection Control

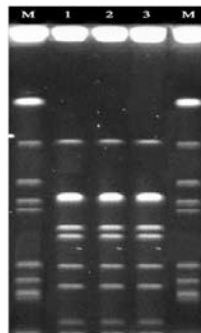
Volume 44, Issue 8, 1 August 2016, Pages 935–937



Brief Report

Laboratory-acquired skin infections in a clinical microbiologist:  
Is wearing only gloves really safe?

Yucel Duman  , Yusuf Yakupogullari, Baris Oflu, Mehmet Sait Tekerekoglu  
Medical Microbiology Department, Inonu University Medical Faculty, Malatya, Turkey



*Emerging Infectious Diseases* • [www.cdc.gov/eid](http://www.cdc.gov/eid) •  
Vol. 12, No. 1, January 2006

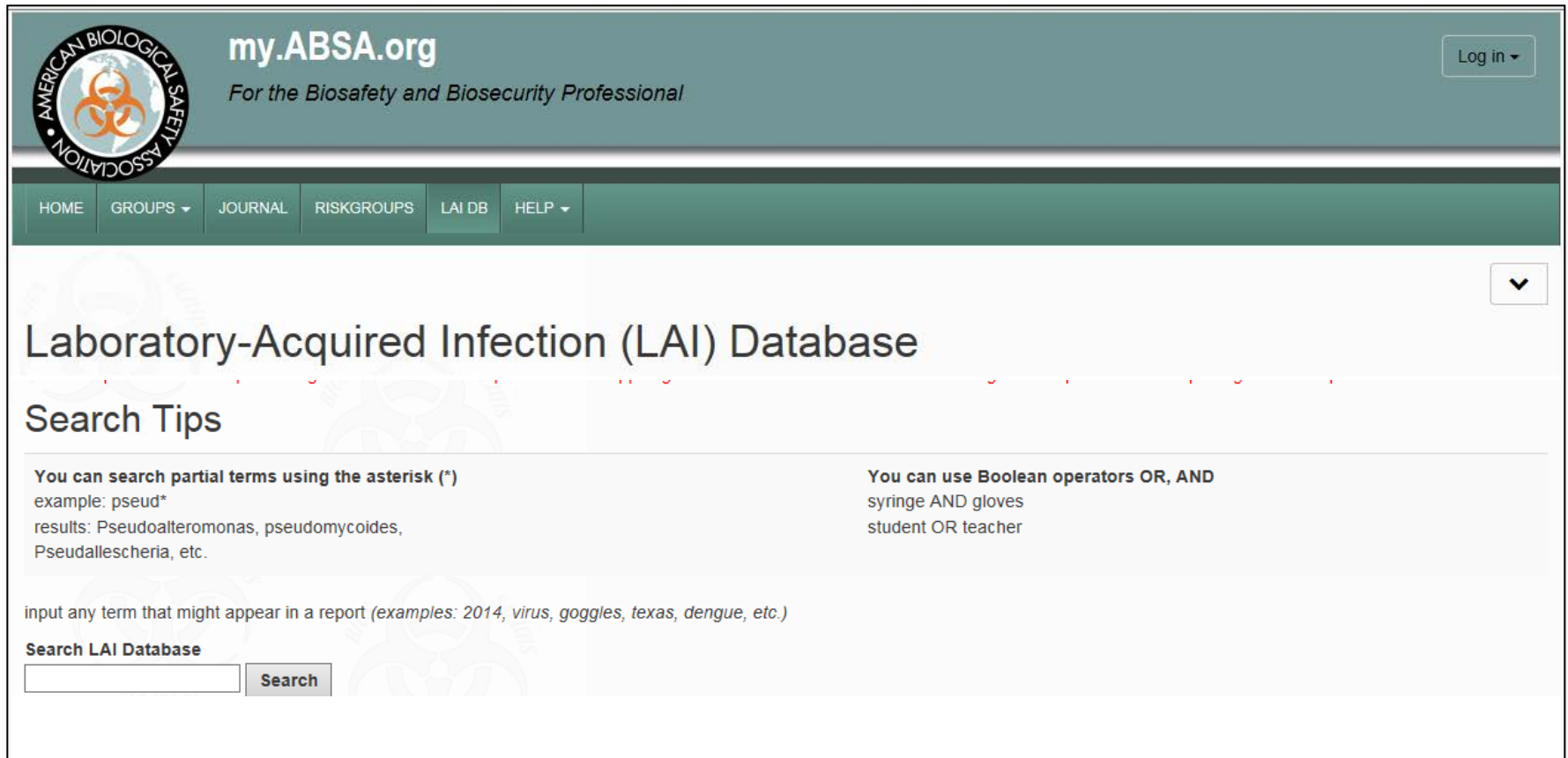
## *Ocular Vaccinia Infection in Laboratory Worker, Philadelphia, 2004*

*Felicia M.T. Lewis,\*† Esther Chernak,\*  
Erinn Goldman,† Yu Li,† Kevin Karem,†  
Inger K. Damon,† Richard Henkel,†  
E. Claire Newbern,\* Patrina Ross,\*  
and Caroline C. Johnson\**



# ABSA – American Biosafety Association

⇒ <https://my.absa.org/LAI>



**my.ABSA.org**  
For the Biosafety and Biosecurity Professional

Log in ▾

HOME GROUPS ▾ JOURNAL RISKGROUPS LAI DB HELP ▾

## Laboratory-Acquired Infection (LAI) Database

### Search Tips

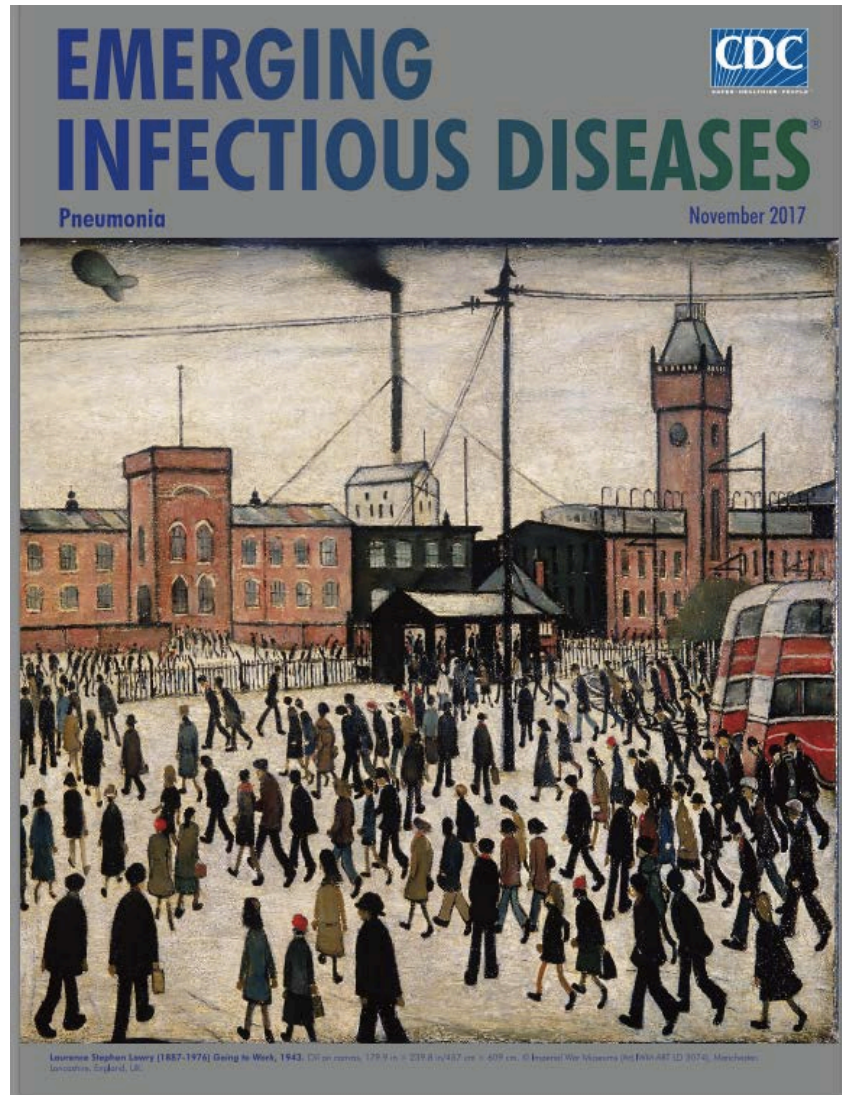
**You can search partial terms using the asterisk (\*)**  
example: pseud\*  
results: Pseudoalteromonas, pseudomycoides, Pseudallescheria, etc.

**You can use Boolean operators OR, AND**  
syringe AND gloves  
student OR teacher

input any term that might appear in a report (examples: 2014, virus, goggles, texas, dengue, etc.)

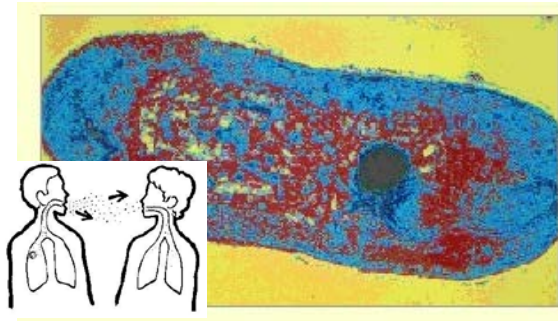
**Search LAI Database**

# New Emerging Infectious Diseases



## Is Tuberculosis still an Issue?

- 2 billion people (1/3 of world population) infected with *TB bacilli*
- 9.4 million new cases/year (95.1% in the developing world)
- 1.7 million deaths/year (98% in the developing world)
- TB incidence growing world-wide at 1% a year (mostly Africa)



*(Global Tuberculosis Control, WHO Report)*

# TB-Diagnosis Laboratory



Solid Agar Cultures

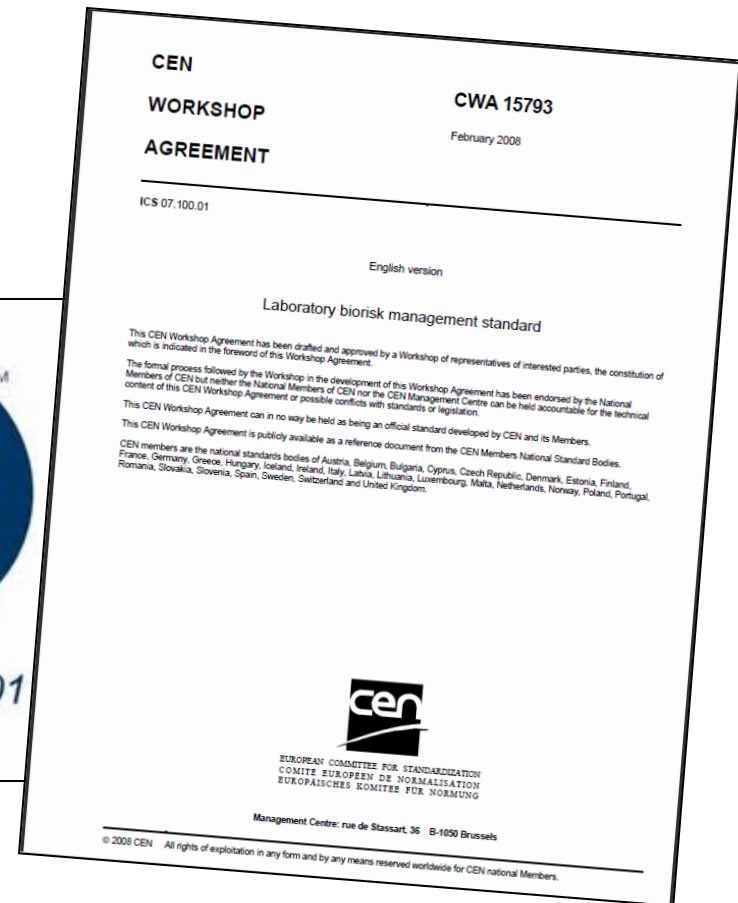


Automated Liquid Culture System

We want to be pro-active ...



# CWA 15793:2011 – Quality for Management of Biorisk



CWA 15793:2011 can be easily adapted to existing quality management systems.

# Laboratory Biorisk Management Standard CWA 15793



Result of a series of CEN workshops  
(CEN = EUROPEAN COMMITTEE  
FOR STANDARDIZATION)

Scope: To set requirements necessary  
to control risks associated with  
infectious biological agents and toxins.

Management system approach

# Participation in development



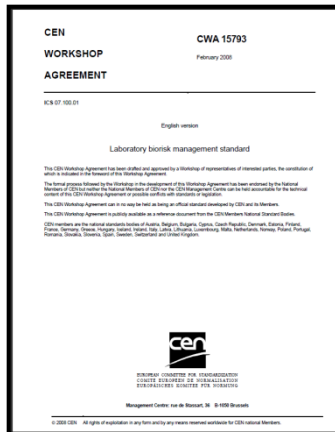
72 participants from 24 countries

# Management system integration

This laboratory biorisk management standard is compatible with the EN ISO 9001:2000 (Quality), EN ISO 14001:2004 (Environmental) and OHSAS 18001:2007 (Occupational Health and Safety) management systems standards, in order to facilitate the integration of all such management systems of an organization.

(CWA 15793 p. 6)

# Laboratory Biorisk Management Standard CWA 15793

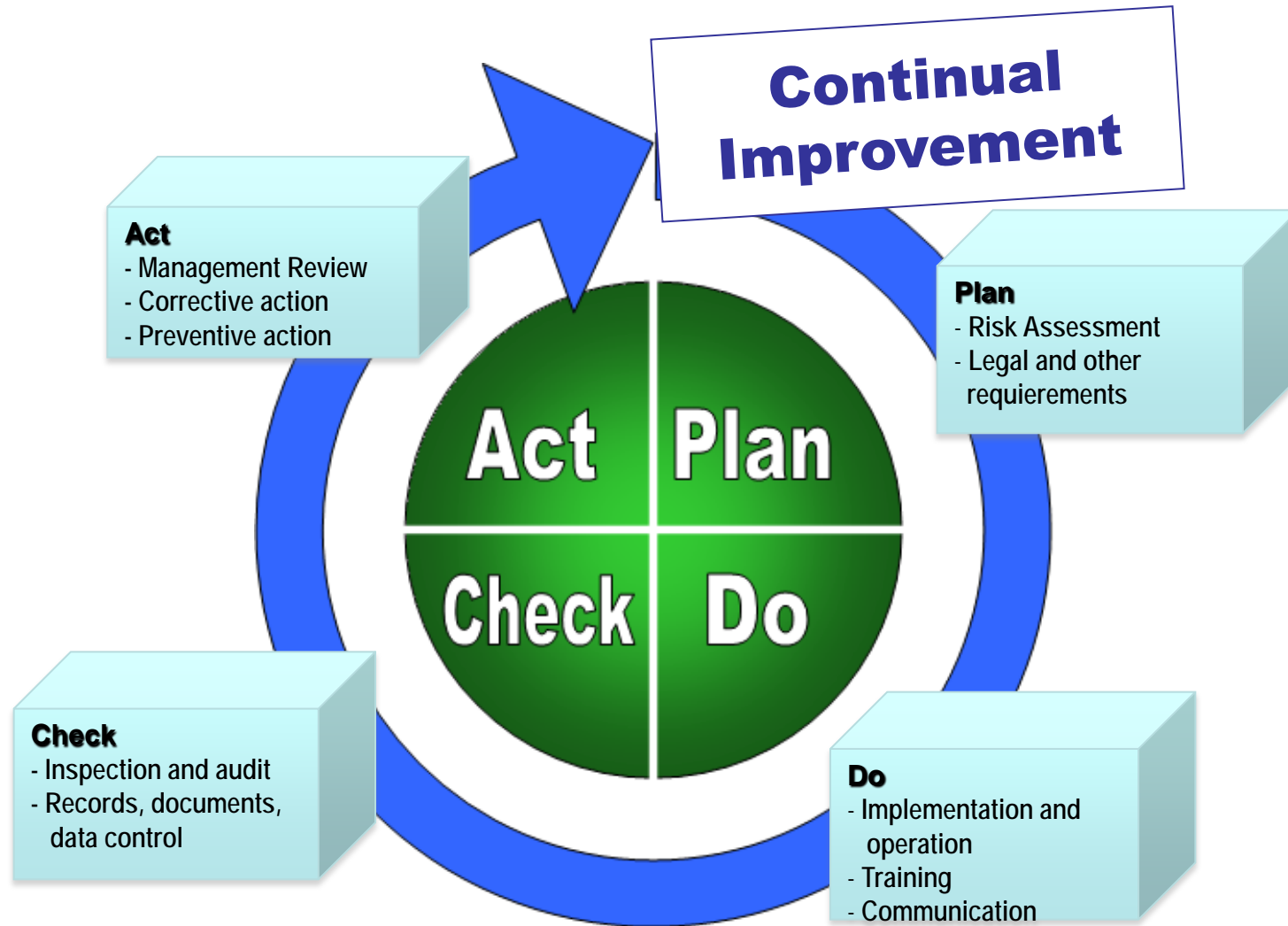


## Key messages:

- Plan – do – check – act cycle
- Management commitment
- Clearly define roles, responsibilities and accountability
- Continual improvement



# Laboratory Biorisk Management Standard (CWA 15793)



# Prescription vs. performance

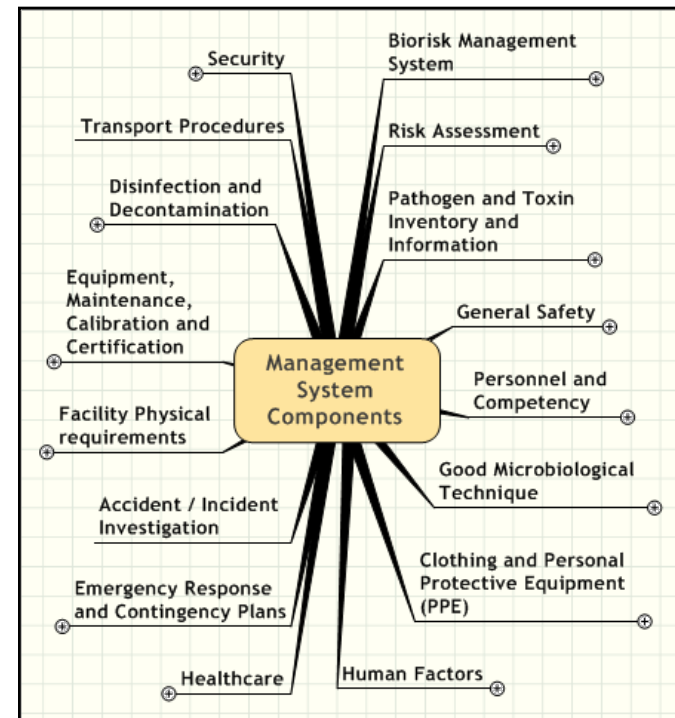
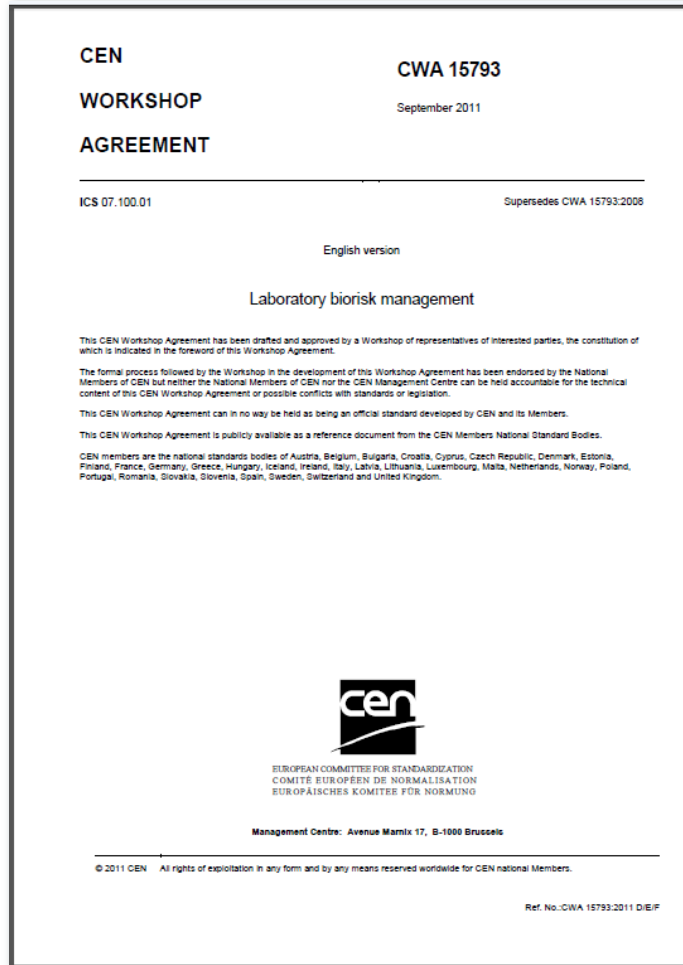
- Prescriptive-based standard
  - Spells out the detailed (technical) requirements for the output
- Performance-based standards
  - Spells out the functional requirements for the output
  - Performance-based standard describes what needs to be achieved
  - How to do it is up to the organization



# How ?



# Implementation of a biorisk management at TWINCORE - Centre for Experimental and Clinical Infection Research, Hannover

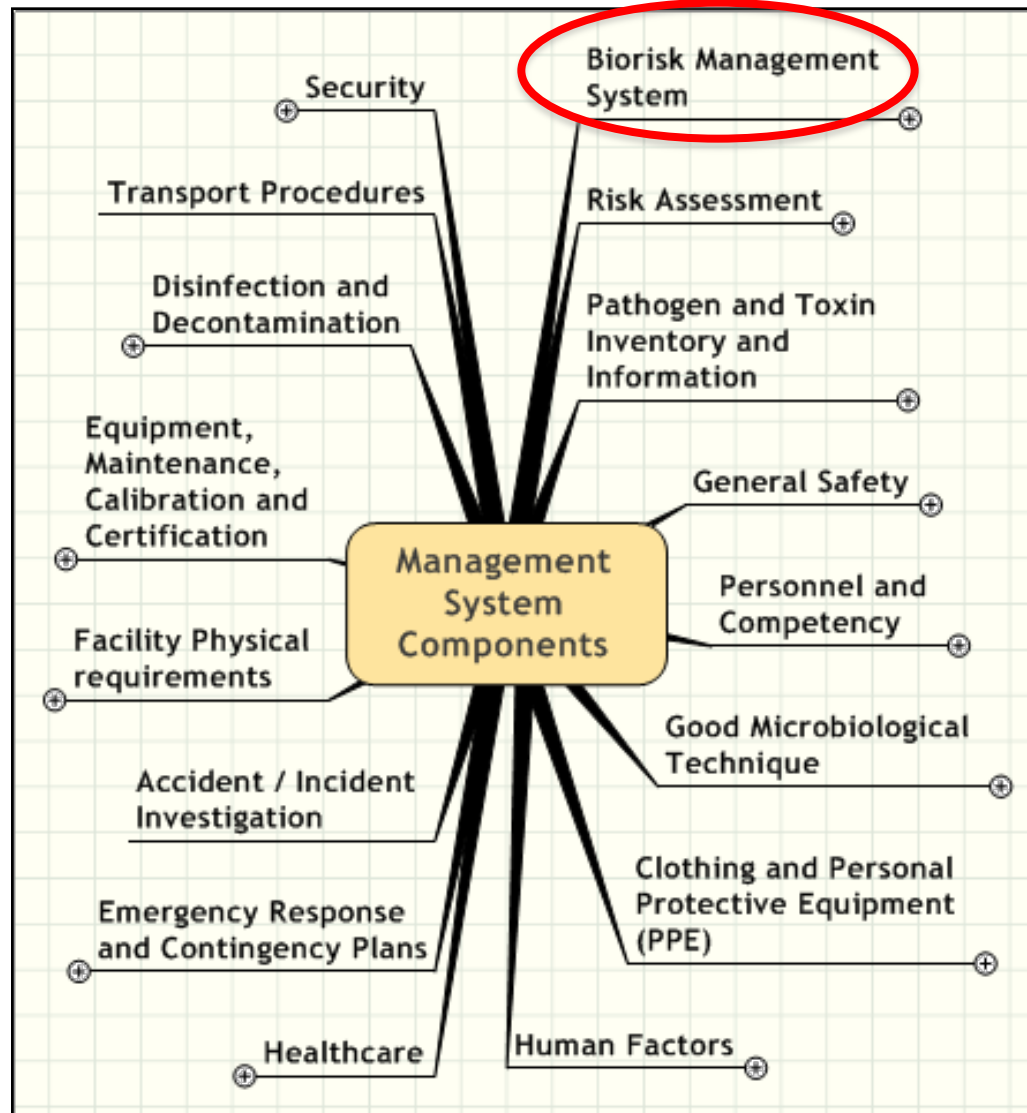


## First Question:

### What are the Needs of the Management Board?

- protect staff, contractors, visitors from biological agents and toxins that are stored or handled within the facility
- comply with all legal requirements
- achieve a high degree of transparency within the institute as regards the different infectious agents, the diverse mouse models,
- be effective, save time
- ...

# Laboratory Biorisk Management, CWA 15793:2011



# Safety Policy of TWINCORE

1. All employees of TWINCORE handle safety relevant issues clearly and responsibly.
2. All employees of TWINCORE are aware of their duty to inform society.
3. TWINCORE regulates all matters relevant to safety and security in such a way that all legal regulations are met and a high level of legal certainty is achieved.
4. All employees of TWINCORE apply a common system for operations relevant to safety and security.
5. All employees of TWINCORE know, recognize and minimize risks to avoid injuries to persons and damage to equipment.
6. The health of the staff is protected by regular occupational health checks and consultations.
7. All employees of TWINCORE handle waste responsibly, try to minimize waste and protect the environment.
8. The base for our safety and security guidelines are German laws and internationally approved rules. Therefore our scientists are internationally competitive with respect to safety and security.



# Safety Policy of TWINCORE

1. All employees of TWINCORE handle safety relevant issues clearly and responsibly.

Mistakes happen to all employees.

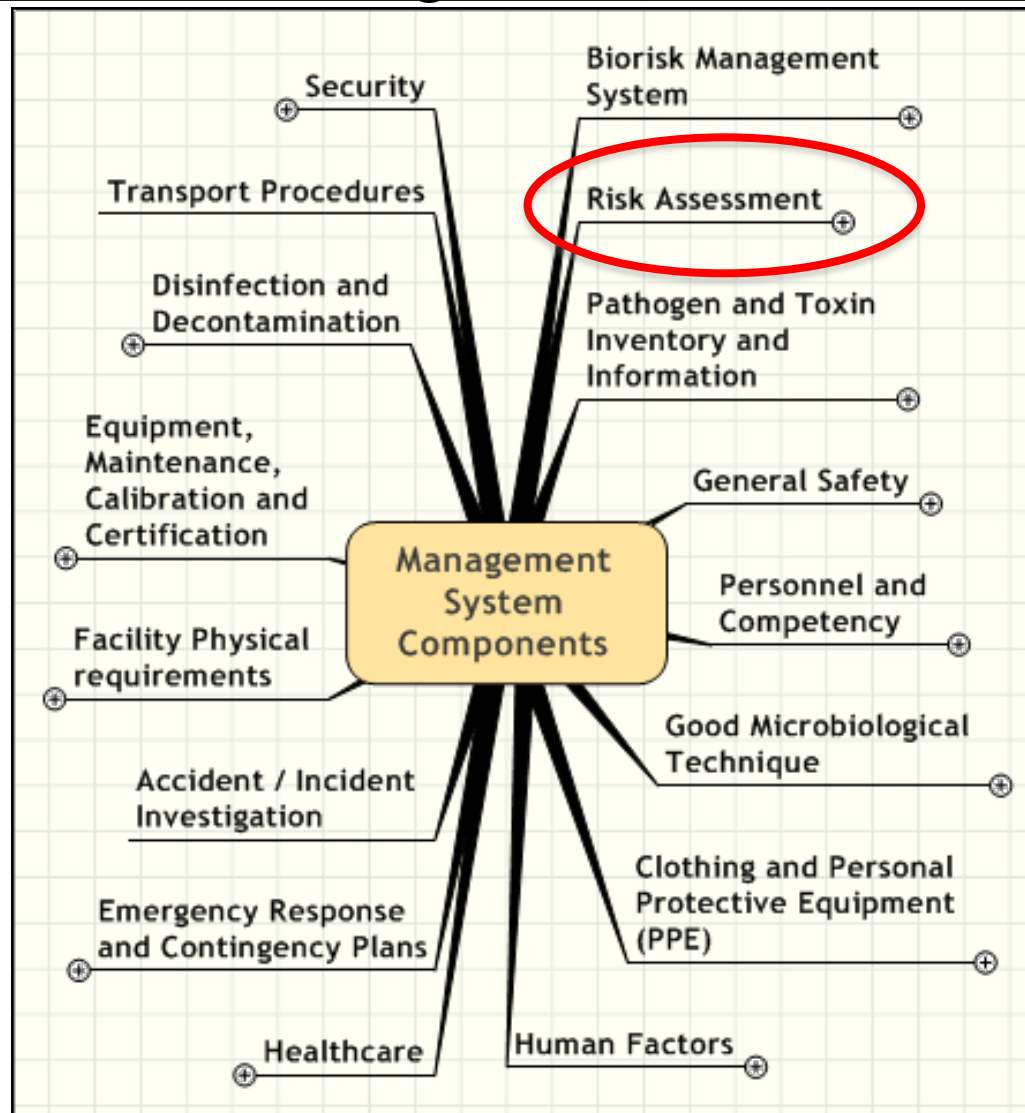
It is crucial

- to communicate mistakes
- to identify the source
- to be able to act appropriately
- to change procedures, if necessary.



**We are striving for a safety culture,  
not for a blame culture!**

# Laboratory Biorisk Management, CWA 15793:2011



# Risk Assessment

## EU Directive 2000/54/EC



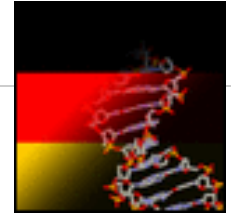
### Article 3

#### Scope — Determination and assessment of risks

...

2. In the case of any activity likely to involve a risk of exposure to biological agents, the nature, degree and duration of workers' exposure must be determined in order to make it possible to **assess any risk** to the workers' health or safety and to lay down the measures to be taken.

## Gentechnikgesetz



### § 6 Allgemeine Sorgfalts- und Aufzeichnungspflichten, Gefahrenvorsorge

(1) Wer gentechnische Anlagen errichtet oder betreibt, gentechnische Arbeiten durchführt, ..., hat die damit verbundenen Risiken für die in § 1 Nr. 1 genannten Rechtsgüter vorher umfassend zu bewerten (**Risikobewertung**) und diese Risikobewertung und die Sicherheitsmaßnahmen in regelmäßigen Abständen zu prüfen und ... zu überarbeiten.

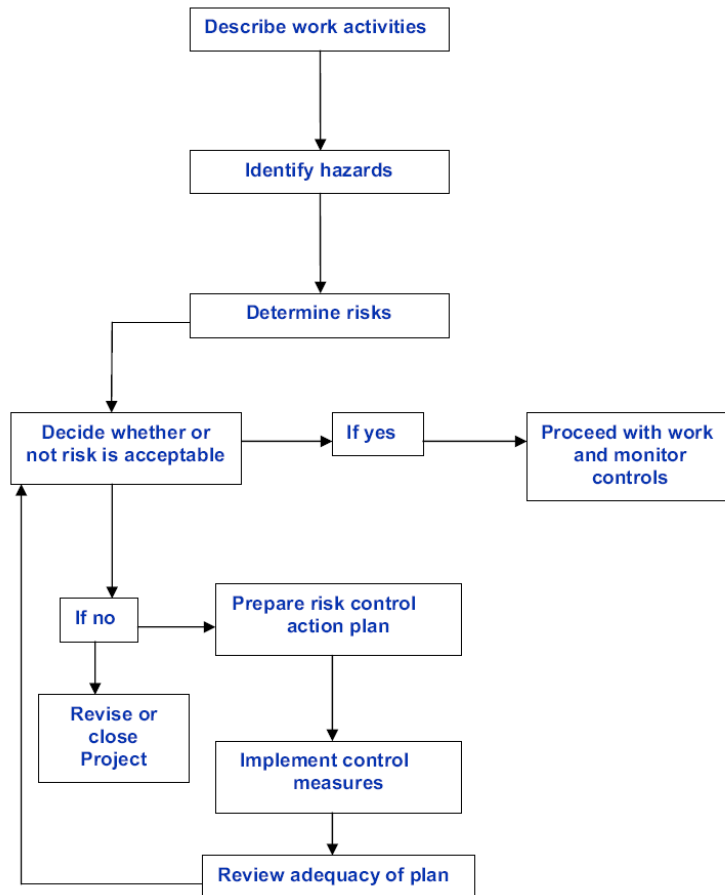
# Risk assessment



Process of evaluating the risk(s) arising from a hazard, taking into account the adequacy of any existing controls and deciding whether or not the risk(s) is acceptable.



# How to perform a risk assessment: The strategy



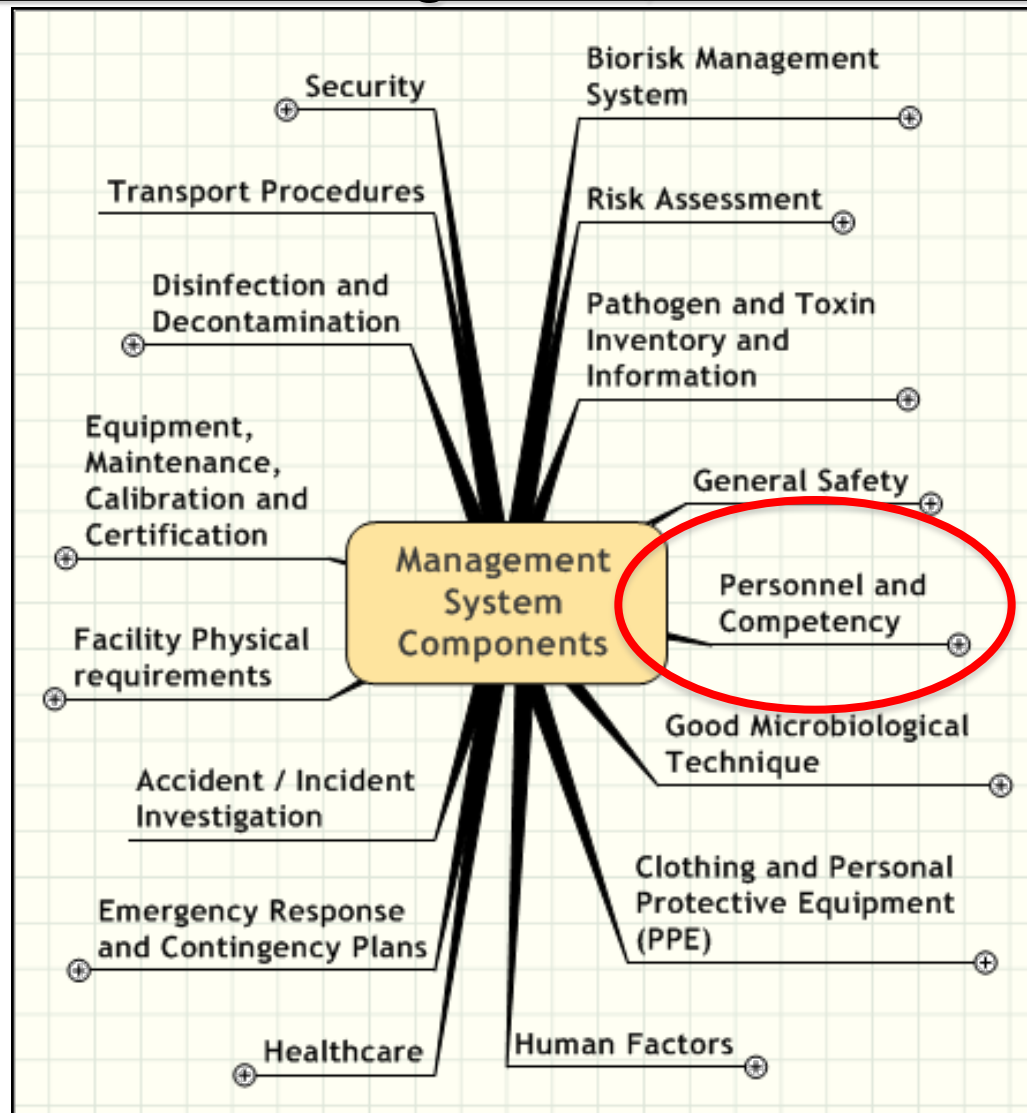
- 1) **Information** on working steps and organisms
- 2) **Hazard identification**  
Hazards associated with the infectious agents.
- 3) **Risk analysis**  
The agent  
The host  
The procedures
- 4) **Protective Measures**  
What risk mitigation measures exist?
- 5) **Recommendations and Documentation**  
Prescribe adequate measures and define appropriate facility designs and procedures to prevent or reduce the risk.

# Second Question: What are the Needs of the Scientists, Animal Caretakers, Technicians,...?

- **Management functions**
  - Strategy
  - Objectives and tasks of TWINCORE
- **Critical processes**
  - Operating instructions
  - SOPs
  - ...
- **Supportive actions**
  - General instructions
  - Hygiene plan
  - Workers protection
  - Fire protection
  - ...



# Laboratory Biorisk Management, CWA 15793:2011



# Training (CWA 4.4.2.4):

The organization shall ensure that requirements and procedures for biorisk-related training of personnel are identified, established and maintained.



**MHH** Medizinische Hochschule Hannover  
BETRIEBSANLEISUNG  
gem. GUV-E 8537 Stand November 2004  
Arbeitsbereich/Status/Funktion  
Datum/Übersicht:

Arbeitsplatz: Krankenvorsorge (auch IP-Studien) und Labore  
Tätigkeit: Injektionen, Blutentnahmen, Wundversorgung, operative Eingriffe, etc.

### Gefährdungsart

Umgang mit spitzen und scharfen medizinischen Einmalartikeln wie z. B. mit Spritzen, Kanülen, Lanzetten und Skalpell (im Folgenden "Kanülensicherungen" genannt)

### RISIKOFAKTOREN

Infektionen, z. B. mit

- HIV-Virus
- Hepatitis B-Virus
- Hepatitis C-Virus

### SCHUTZMASSNAHMEN UND VERHALTEN

Grundsätzlich sorgt jeder **s e f s i f** für sofortige und sachgerechte Entsorgung

- Kein Wiedereinsatz von Rückkäufen auf geleerbte Kanülen (kein Recycling)
- Kanülen und Spritzen getrennt trennen
- Entsorgungseinheit unmittelbar nach Gebrauch komplett in die gelben Kanülenabwurfbox abgeben
- Bei Problemen ein abweichendes, unkonventionelles Vorgehen zu vermeiden, bei dem über Kanülenabwurfboxen zu berichten, bevor die Öffnung von oben einsehbar ist! (Haut)
- Die Beschäftigten sind über Infektionsrisiken durch Stich- und Schnittverletzungen vor Aufzug regelmäßig, mindestens jährlich, mündlich anhand dieser Betriebsanweisung anzuhören! Die durchgeführte Unterweisung ist vor dem Beschäftigten schriftlich zu bestätigen! (Haut)

### Gesicherter Umgang

Gezielte Kanülenabwurfboxen anfordern (MüllADK) und für sicheren Platz

- Scharfe und spitze Gegenstände ggf. in vorgesehene Kanülenabwurfbox entsorgen
- Kanülenabwurfboxen nur soweit fällen, dass ein gefahrloses Abwerfen und Verschluss der Kanülenabwurfbox zu erwarten ist, bevor die Öffnung von oben einsehbar ist! (Haut)
- Kanülenabwurfboxen sind stets geschlossen zu halten, bis sie durch den Mitarbeiter gefüllt sind
- gefüllte Boxen sofort verschließen und entsorgen, wenn Kanülenabwurfboxen benutzt werden
- beschädigte oder überfüllte Kanülenabwurfboxen in größere oder ersatzfähige Kanülenabwurfboxen ggf. verschieben in die nächste Müllabwurfbox

### Prevention / Erste Hilfe

Sich **s e f s i f** um ausreichenden Impfschutz kümmern (Grundimmunisierung)

Der Betriebsärztliche Dienst (Tel.: 3403) berät Sie gerne und führt Impfungen bei:

- Bei Stich-, Schnittverletzungen
- Stülcklöcher durch Ausweichen in Richtung Wunde
- Chronisches Geschwür der Extremitäten, Phlebotrombose, Entzündung in der Extremität
- bei größeren, stark blutenden Verletzungen sollte die Zentralen Antibiotikastation bei Laborarbeiten darüber informiert werden, falls eine Verletzung von Biobioaktivem Material vorliegt

### SACHGERECHTE ENTSORGUNG

Abfallkennzeichnung: Einheits- 18 01 04, Örtliche Betriebsvorschriften sind zu beachten (Müll-Entsorgung) Anmerkungen: Abs. 3, 2.1.8 in der GUV-Anspruchspartner: DE 1362 Tel. 5952 www.mh.uni-hannover.de

420197.32.25-11/04

**UNTERWEISUNGSNACHWEIS-BIOSTOFFVERORDNUNG!**  
§ 12 Abs. 2 Biostoffverordnung

Thema: **Schutz vor Infektionen Vorgehen nach Stich-, Schnittverletzungen und Kontaminationen mit potenziell infektiöser Material! Persönliche Schutzausrüstung!**

Inhalt der Unterweisung: Vorkommen relevanten Infektionserreger (Hepatitis B-, C- und HIV-...), Ursachen und Adäquanz der Stich-, Schnittverletzungen (Beratungsleistung/ Kanülenstichverletzung; Bioblog-Verbot; geeignete beim Betriebsärztlichen Dienst oder UVA, HfH - Populationsprophylaxe); Anwendung von persönlicher Schutzausrüstung: Ess-, Rauch- und Trinkverbot; Beachtung der Hygienevorschriften; Anwendung von Hautschutz- und Hautpflegemitteln; Durchführung der arbeitsmedizinischen Vorsorgeuntersuchung im Impfgebiet.

Hiermit bestätige ich, dass ich an der Unterweisung **abwesend** teilgenommen habe und inhaltlich über die oben aufgeführten Themen informiert wurde.

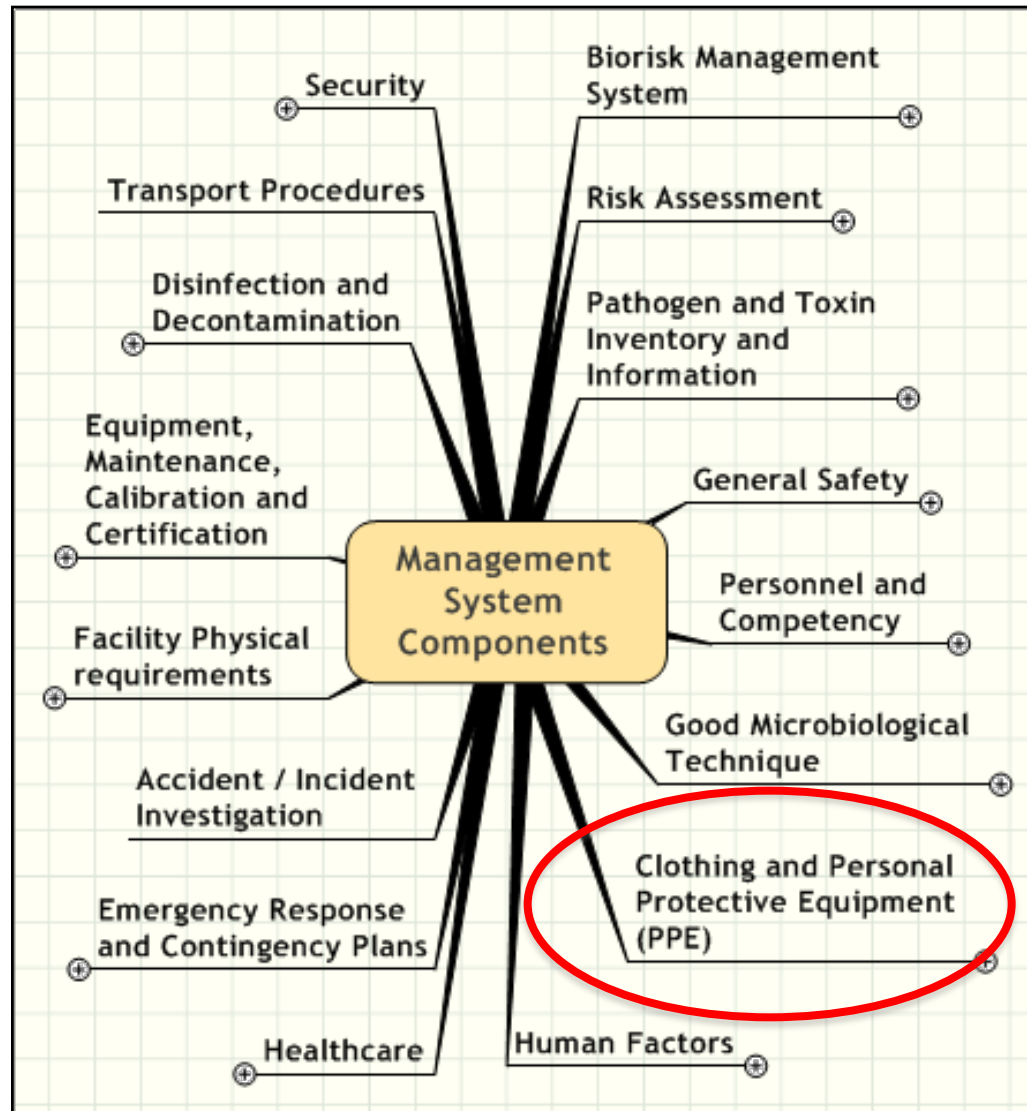
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Die Unterweisung wurde durchgeführt von:

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# Laboratory Biorisk Management, CWA 15793:2011



## Personal Protective Equipment CWA (4.4.4.5.4):

The organization shall ensure that PPE needs are identified and suitable equipment is specified, made available, used and maintained appropriately within the facility.



# Personal Protective Equipment – Disposable gloves



## Gloves are prohibited ...



- in the kitchen
- in the seminar room
- making phone calls
- working with the computer keyboard.



# Personal Protective Equipment – Safety glasses

Handling concentrated  
disinfectants:  
**Use safety glasses!**



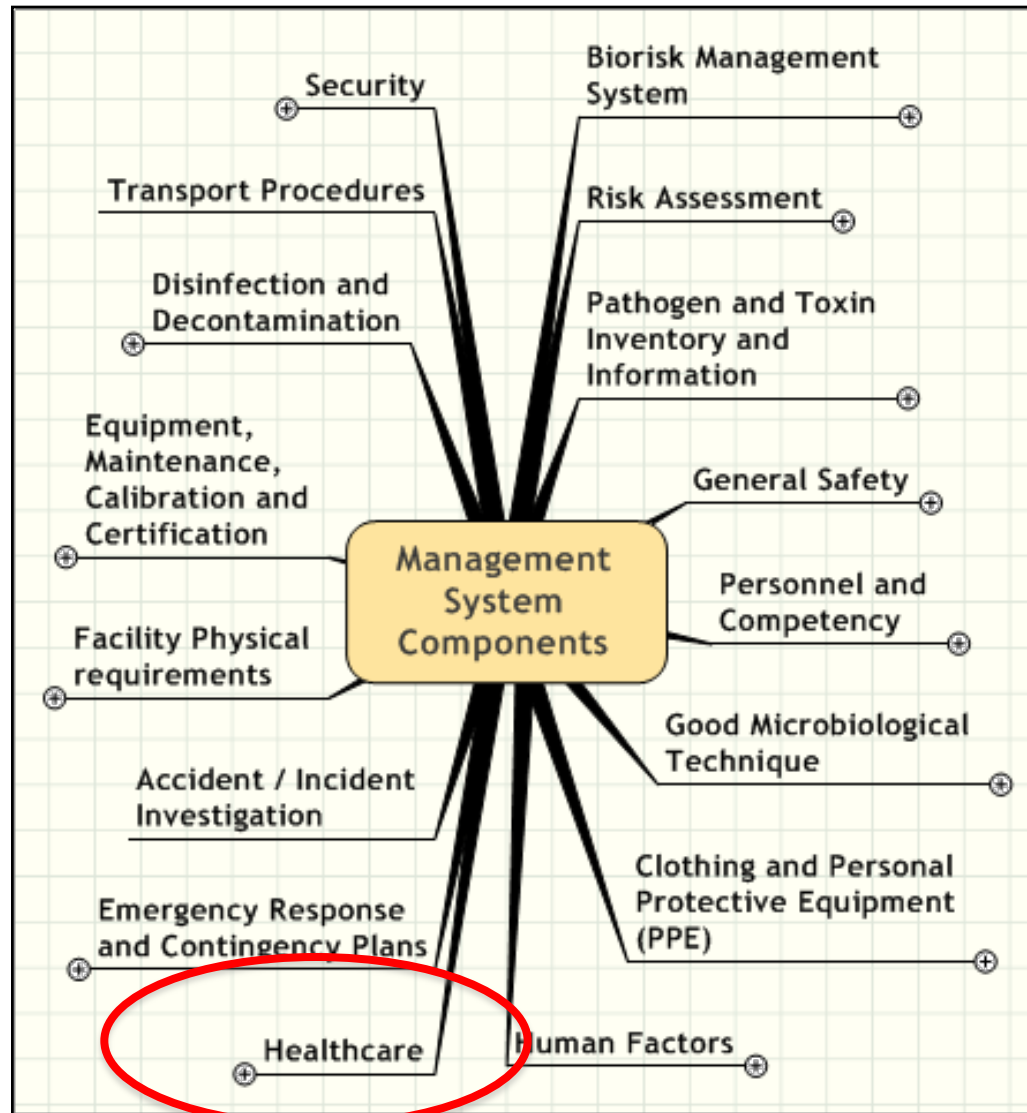
If pressure is created:  
**Use safety glasses!**



Handling hazardous  
chemicals:  
**Use safety glasses!**



# Laboratory Biorisk Management, CWA 15793:2011

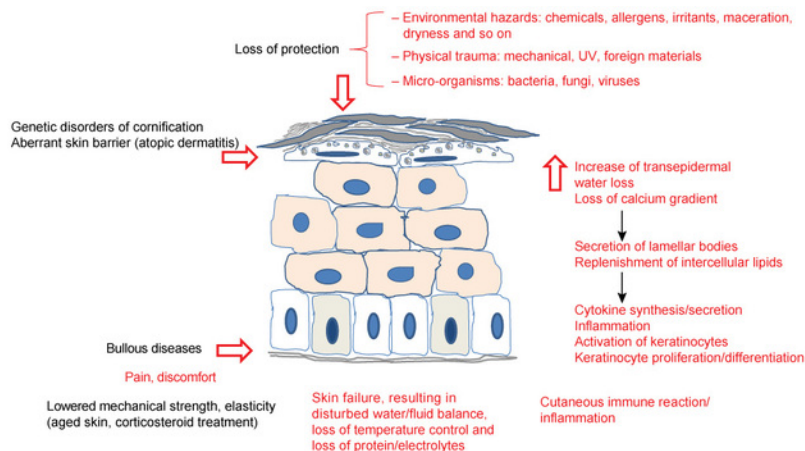


## Worker health programme (CWA 4.4.4.6):

The organization shall ensure that risk to worker health, and that of other personnel whose health could be directly impacted by exposure to biological agents and toxins, is managed effectively including prevention and protection measures.

### Wearing disposable gloves over hours ...

Skin occlusion may increase percutaneous absorption of applied chemicals, with some exceptions. It also obstructs the normal ventilation of the skin surface and increases stratum corneum hydration and hence compromises skin barrier function.



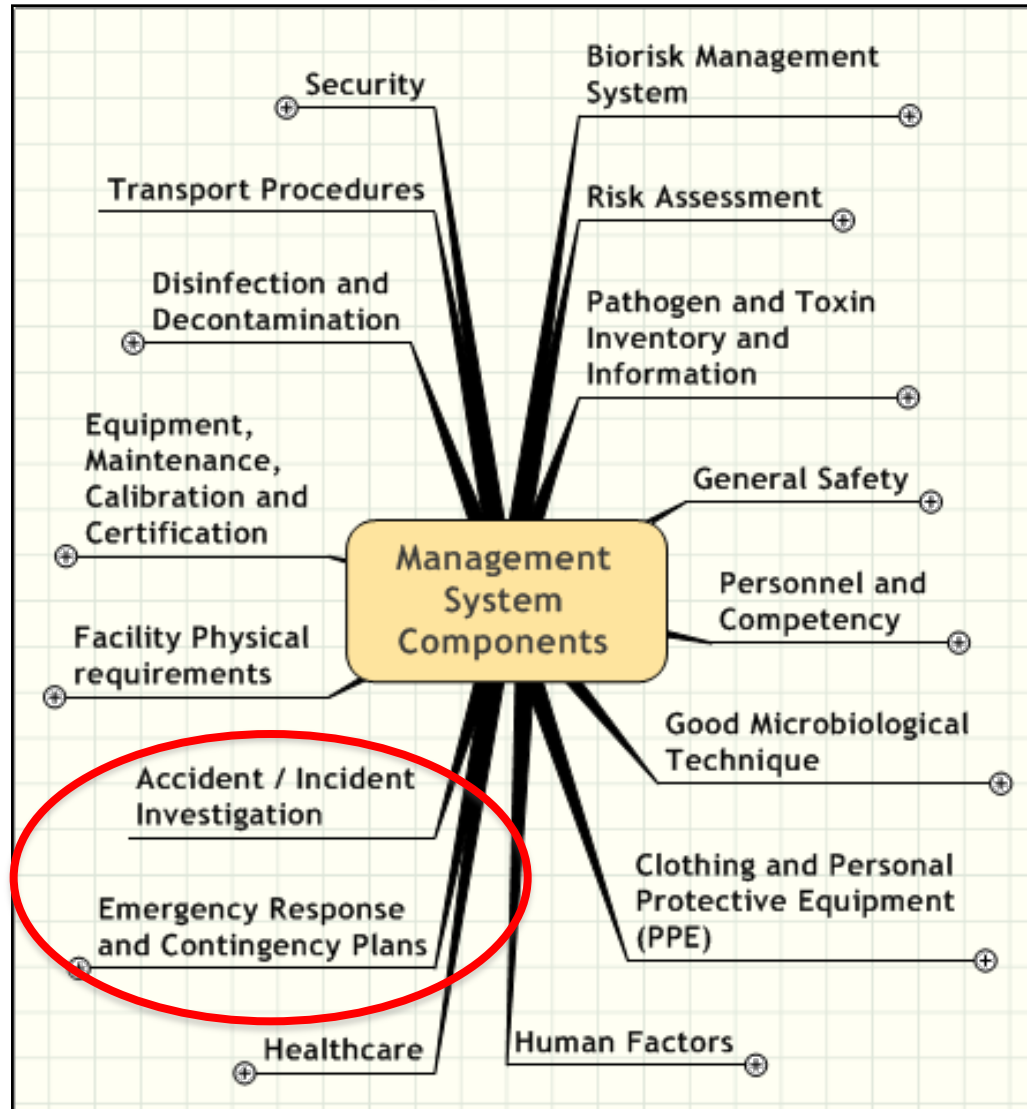
# Allergic reactions to glove materials

Selected Synthetic Glove Materials and Brands Glove Material	Brand Names	Accelerators
Polyisoprene	Dermapreen, Isotouch (Ansell); Biogel (Biogel / Molnlycke Health Care); Esteem (Cardinal Health); Sensicare (Medline Industries)	Carbamates or Thiurams/Thiazoles
Vinyl (polyvinyl chloride)	Duratouch/Trutouch (Ansell, Maxxim), Triflex (Allegiance)	No accelerators, Allergic contact dermatitis has rarely been reported from vinyl glove additives
Nitrile (butadiene copolymer)	Safeskin (Safeskin Corp.) ; Sensicare (Maxxim Medical); Tillotson Pure Advantage and Dual Advantage (Tillotson); SmartCare (SmartCare, Inc.) Allegiance Flexam Nitrile Examination Glove (Allegiance); Adenna NPF Nitrile Powder Free Exam Gloves (Adenna Inc.)	Carbamates, thiazoles
Nitrile (butadiene copolymer) accelerator free	True Advantage (Tillotson) , N-Dex (Ansell, Best Glove), Aspen2100 (Hourglass Indust.), SemperSure (Sempermed)	No accelerators
Neoprene (polychloroprene polymer)	Dermaprene (Ansell); Biogel Neoprene; Duraprene (Allegiance); Neolon (Maxxim)	Thiourea, diphenyl guanidine, carbamates
Polyurethane	Sensicare (Maxxim Medical)	No accelerators



<http://www.research.northwestern.edu/ors/safety/general/ppe/documents/allergic-reactions-to-gloves.pdf>

# Laboratory Biorisk Management, CWA 15793:2011



**Incidents, Accidents and Emergency Preparedness (CWA 4.4.3):**  
The organization shall establish and maintain plans and procedures to identify the potential for incidents and emergency situations involving biological agents and to prevent their occurrence.

*That is what we need to prevent:*  
*Damage in a laboratory after a fire*



<http://www.rp-online.de/region-duesseldorf/duesseldorf/nachrichten/hoher-schaden-bei-laborbrand-in-duesseldorf-1.875408>

# Fire extinguisher, Emergency shower, Emergency switches

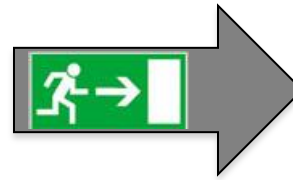


- Look in your lab where the things are !



CO<sub>2</sub> Fire extinguisher

# Main escape route = Staircases



In addition:  
Emergency balcony stairs





# Emergency Exit – Emergency release

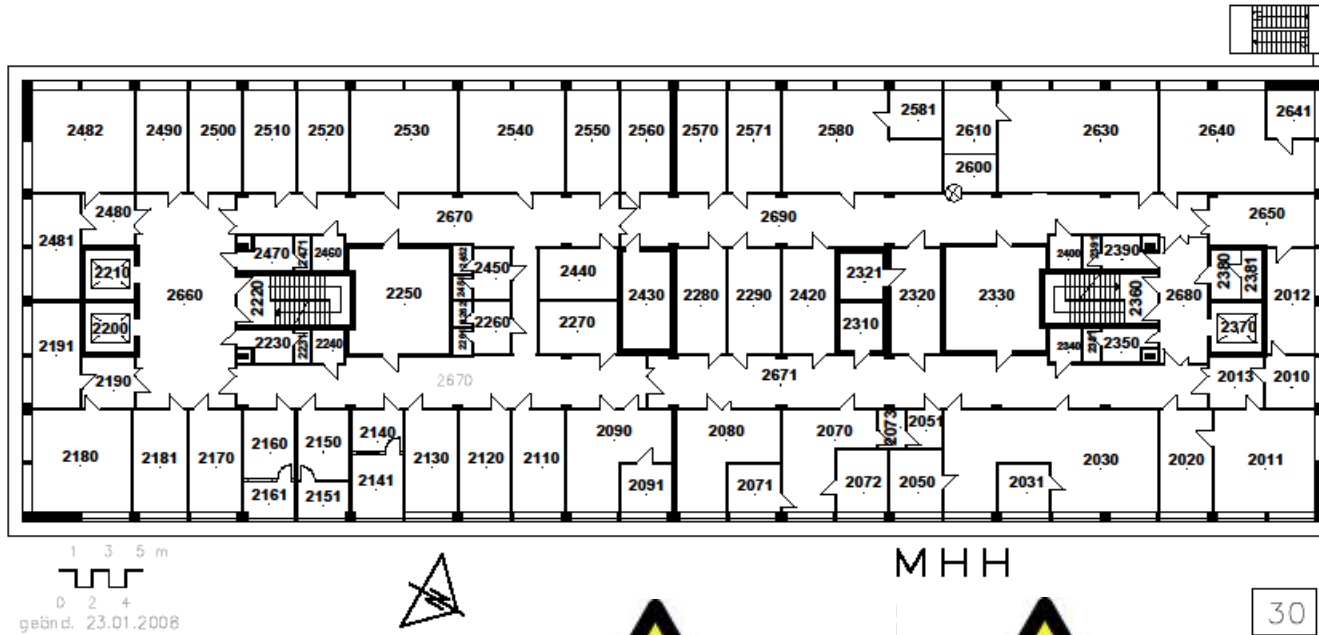


# Laboratory Biorisk Management, CWA 15793:2011





# Facilities



S1 Genlabor

S2 Genlabor  
Zutritt nur mit  
Berechtigung

S3 Genlabor  
Zutritt nur mit  
Berechtigung

**Change management CWA 4.4.4.4):** The organization shall ensure that all changes associated with the design, operation and maintenance of the facility are subject to a defined and documented change management process.



**RED LIGHT:**

- ventilation error (+ acoustic alarm)

**PUSH RED LIGHT:**

- acoustic alarm off

**YELLOW LIGHT:**

- ventilation in reduced mode (caused by lowering to certain times or by an error)

**GREEN LIGHT:**

- normal ventilation mode

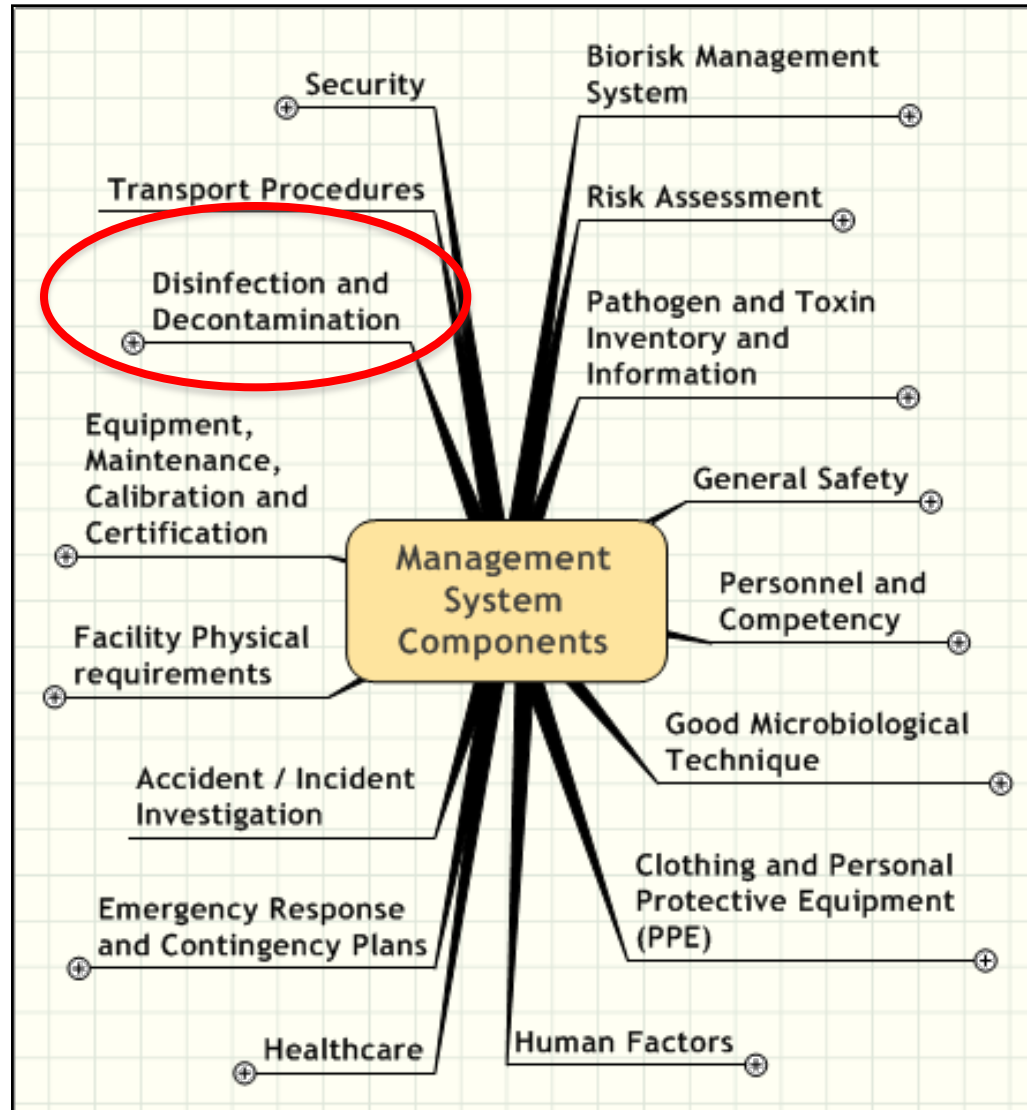
**PUSH GREEN LIGHT:**

- additional 120 minutes of normal ventilation

**LIGHT SWITCH**

Working in the laboratory: The ventilation system must be functional.

# Laboratory Biorisk Management, CWA 15793:2011



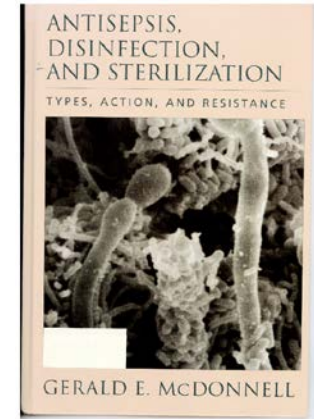
# Criteria to choose the right disinfectant



- Efficacy against the respective bacteria, virus and fungi
- Occupational health aspects for usage
- Cost-effectiveness for the purchase department
- Environmental considerations
- Stability / Storage

# Disinfectants used (Examples)

- **Bacillol AF** contains alcohol  
→ routine surface disinfection
- **Sterillium / Sterillium virugard** contains 99% Ethanol  
→ hand disinfection
- **Incidin perfekt** contains aldehydes  
→ used when working with VSVg pseudotypes
- **Korsolex basic** contains aldehydes  
→ disinfection of liquid waste and devices
- **Sekusept plus** contains glucoprotamin  
→ disinfection of liquid waste
- **Perform** contains active oxygen  
→ in case of contaminations



Important:

- ✓ Right concentration
- ✓ Sufficient incubation time



# Accidents with concentrated disinfectant at MHH



During the last years three accidents with ocular injuries involving concentrated Incidin have been reported. While preparing a diluted solution, employees got splashes of concentrated disinfectant into the eyes. (Protective glasses were not worn). With two of the employees there were no serious ocular injuries, because ocular showering was available and could be used. A third person ended up with serious injuries to the cornea.



## Solution: Automated Dilution of Disinfectant



# Laboratory Waste Management

## Regular waste



Plastic packaging

(No gloves and tips)

## BIO-S1



E.coli + Plasmid HCV partial genome  
E.coli + Plasmid HIV vector, retroviral or adenoviral vector,  
Cell lines: Huh-7, HuH6, 293T, Huh-7+HCV replicon

## BIO-S2



E.coli + Plasmid HCV complete genome  
Lenti-, retro- or adenovi. vectors  
Transduced 293T cells directly after,  
Cells with VSV-GFP/Luc

## Sharps Container (autoclavable)



Sharps  
Syringes  
Pasteur Pipettes

# Transport to the autoclave within TWINCORE



The bags with S1-waste has to be transported only in these waterproof pans.



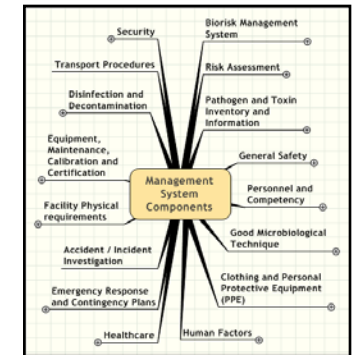
# Transport to the autoclave within TWINCORE



S2-waste must be transported only in the metal containers.



# Safety management at TWINCORE



- Cooperation
- Communication
- Creativity