Jan Mottlau

Senior Specialist
Utility and process design
NIRAS
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Compagny

- Engineer in NIRAS since 2014
- Professionel bear taster ISO9001, certified since 2016

Experience

Been working with classified facility area since 1994

- Client advice, Project management - and specialist functions
- Technical adviser for Hospitals, pharma, lifescience, Cleanroom, datacenters, Containment Facilities as BSL2-3 (Ag),

Hospitals Design, programming:

- **OR**-departments,
- **HLIU** facility, (High Level Insulation Units)
- **PCR**, (Polymerase Chain Reaction)
- **CGT** (Cell and gene therapy)
- **BSL3**, (Biosafety level 3) Pharmacy,

Jan Mottlau

Certificate

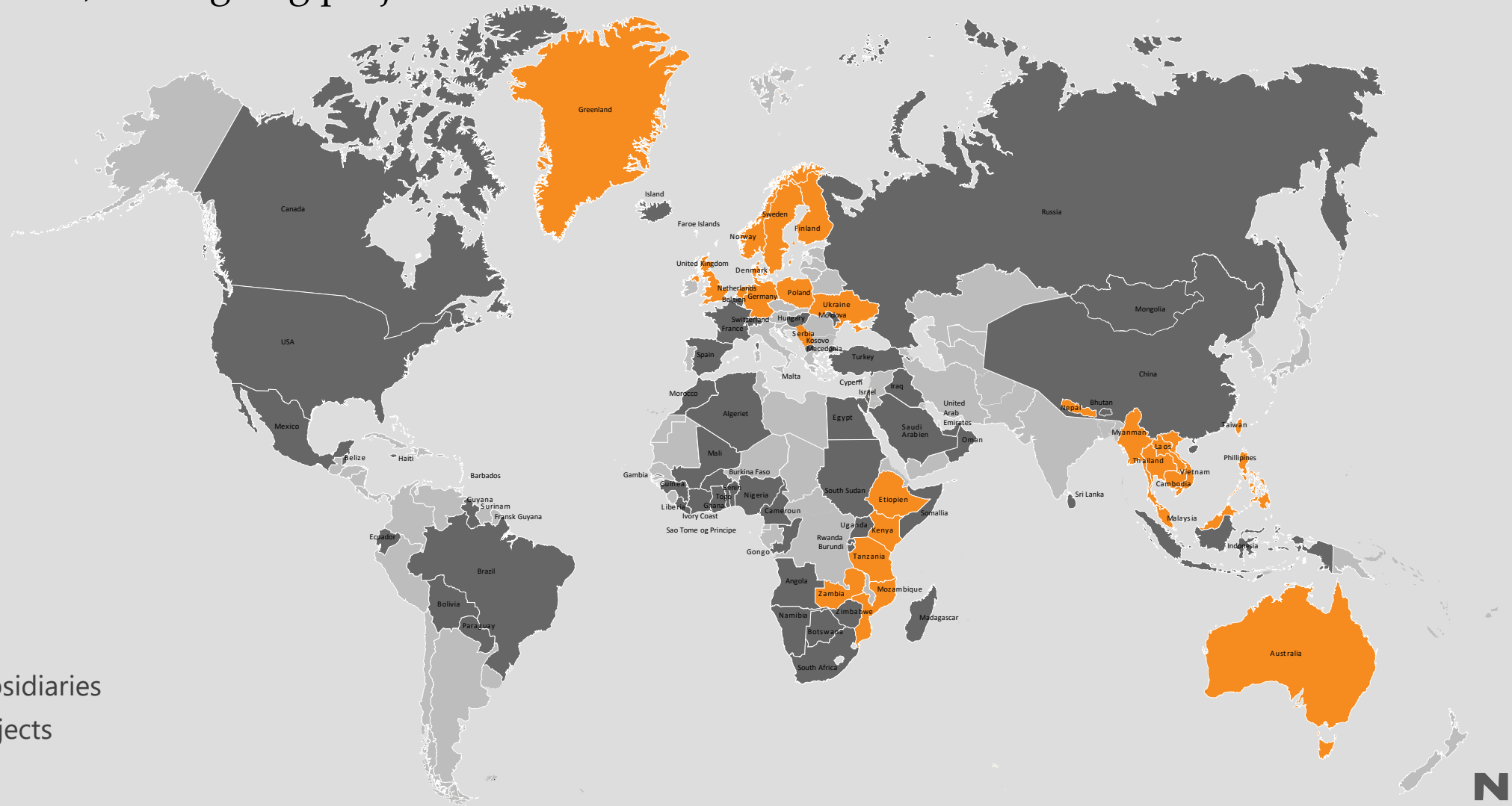
- **CTCB-i** Certified cleanroom tester

Committees:

- **R3-Nordic** (Hospital Symposium 23/24-5, Elsinore in Denmark)
- **ISPE** (International Society for Pharmaceutical Engineering)
- **FSTA** (Danish Union for Hospital, Technical & Architecture)
- **Danish Standard** DS/ S-438 - Cleanroom technology
- **ISO** TC209 WG 3, 5, 15. (ISO 14644)

Global Footprint

Over 7,000 ongoing projects in more than 30 countries



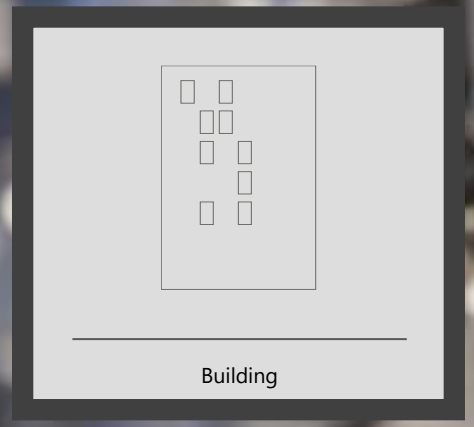
Subsidiaries

Projects

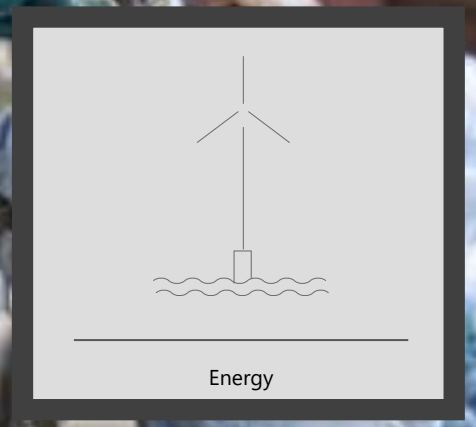
NIRAS

Broad range of services

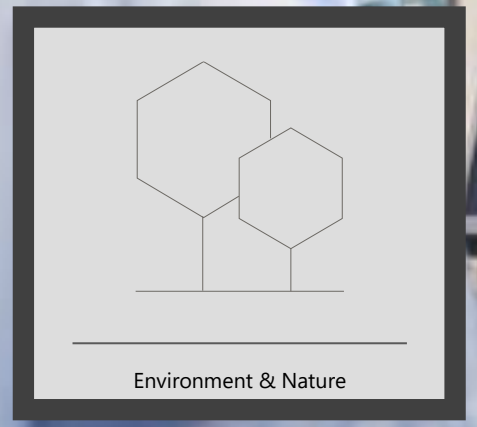
Across the NIRAS Group


Building

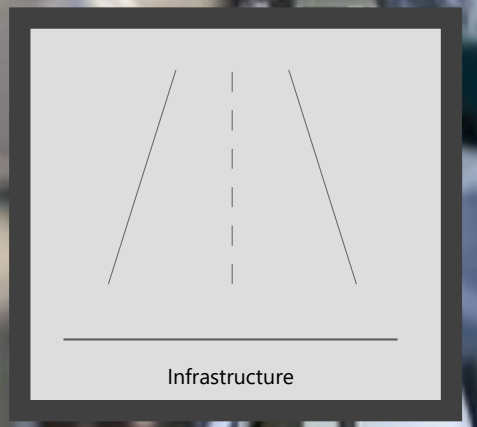

Process Industry

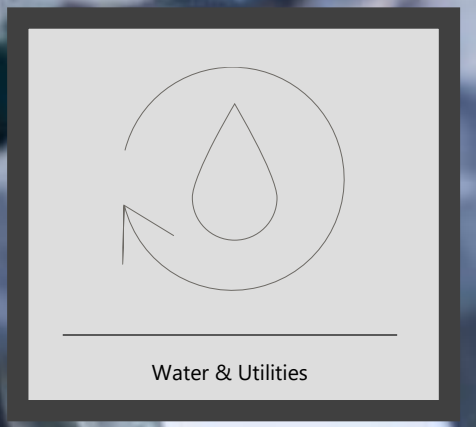

Energy

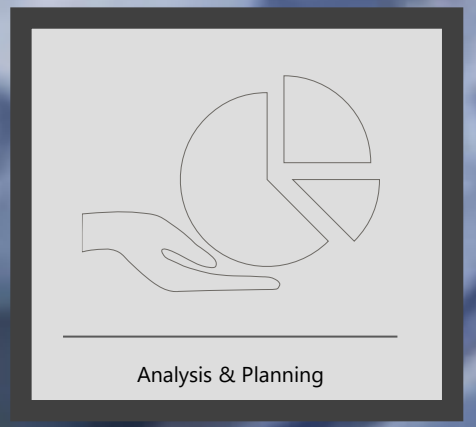

GIS, Geodata & Automation


Environment & Nature


Development Consulting


Infrastructure

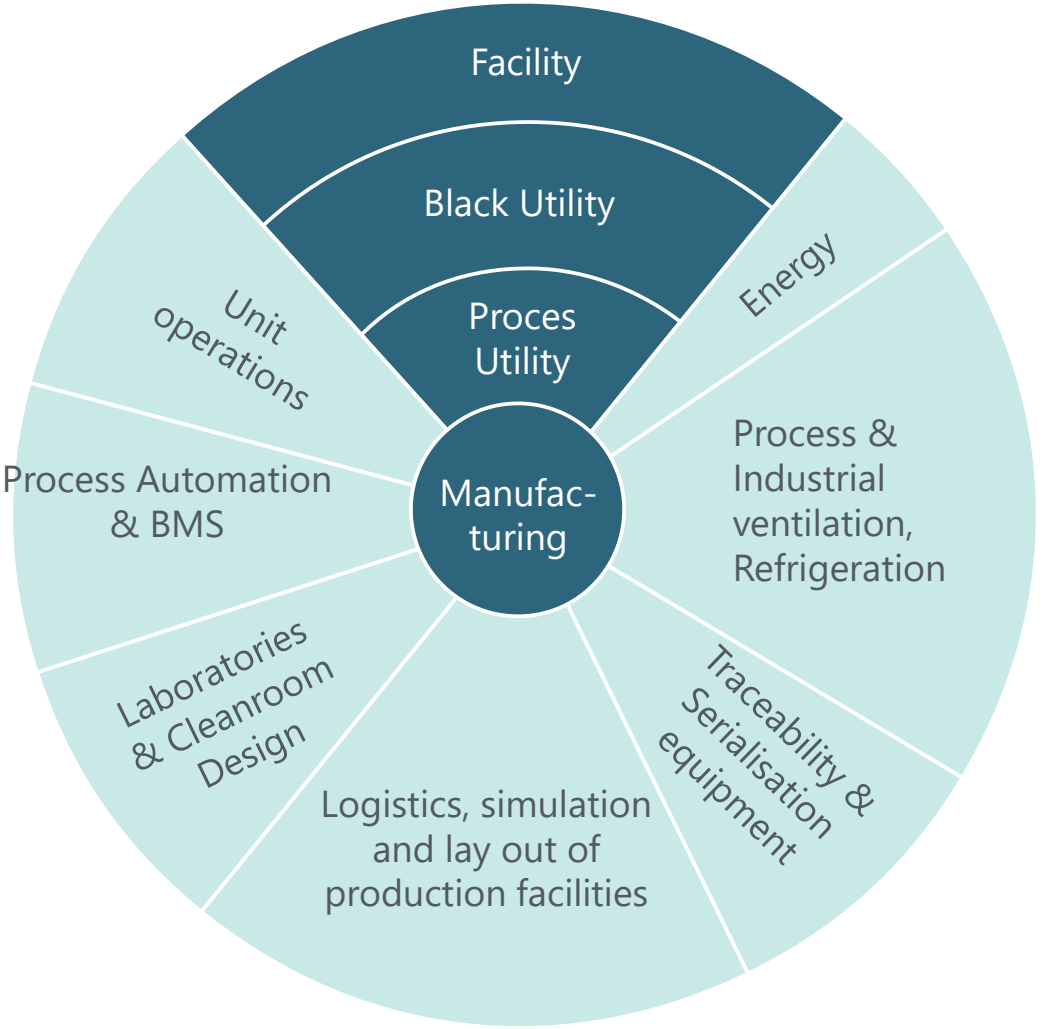

Water & Utilities


Analysis & Planning

We strive to move towards an enhanced sustainable future

Integration of the manufacturing in a quality demanding Life Science (GMP) market

Infrastructure
Environmental Services
Working environment
Permitting
Flodding
Chemicals & Waste



Facility Management
Facility Design
Construction
Offices
Warehouses
Bridges
Digitalisation

Project and Consultancy

Carefully designed project steps keep things in control

GMP services to ensure compliance

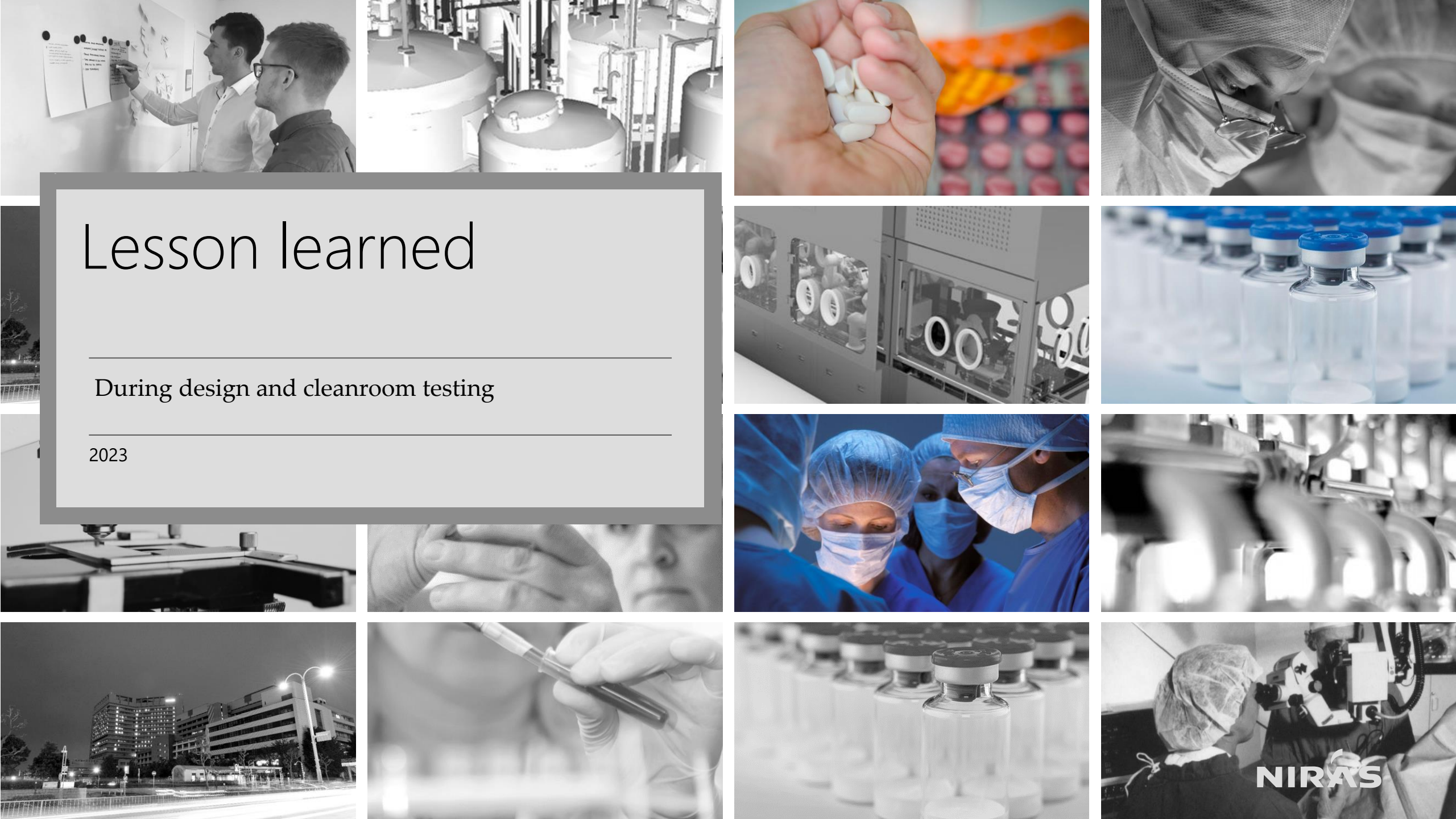
Front load project	Conceptual Brief / Conceptual Design	Basic Design / Detail Design	On site
• Integration of User Demands • Organization / Resource load • Financial requirements • GAP Analyze/Audits • Logistics • Development of master plan • Business Cases • Supply Chain • Due Diligence	• Total Cost of Estimate • Lay outs • Master Planning • Logistic, Manflows, • Facility planning & Design • Modular Engineering • URS • Overall Time Schedule • Project execution plan • ATEX & EX, • Long lead items	• Vendor selection & Tendering services • Review and Design qualification • Process Simulation, Virtual Reality • URS Review • Sparring in choice of technologies. • Sanity Check of TIC. • Process Flow Diagrams, PI&D • Automation Process & BMS	• Process Project Management • Vendor Coordination • Construction Management • Punch list management • Cost control • Scope control • FAT/ SAT, IQ, OQ, PQ • Training • Material Control • Approval of deliverables • Hand Over

Decision gateway

Decision gateway

Validtation master plan, Qauality plan, Consultancy, Advisory

Project execution plan, Procurement startegy, **Project Management**, Time Schedule, Financial reporting



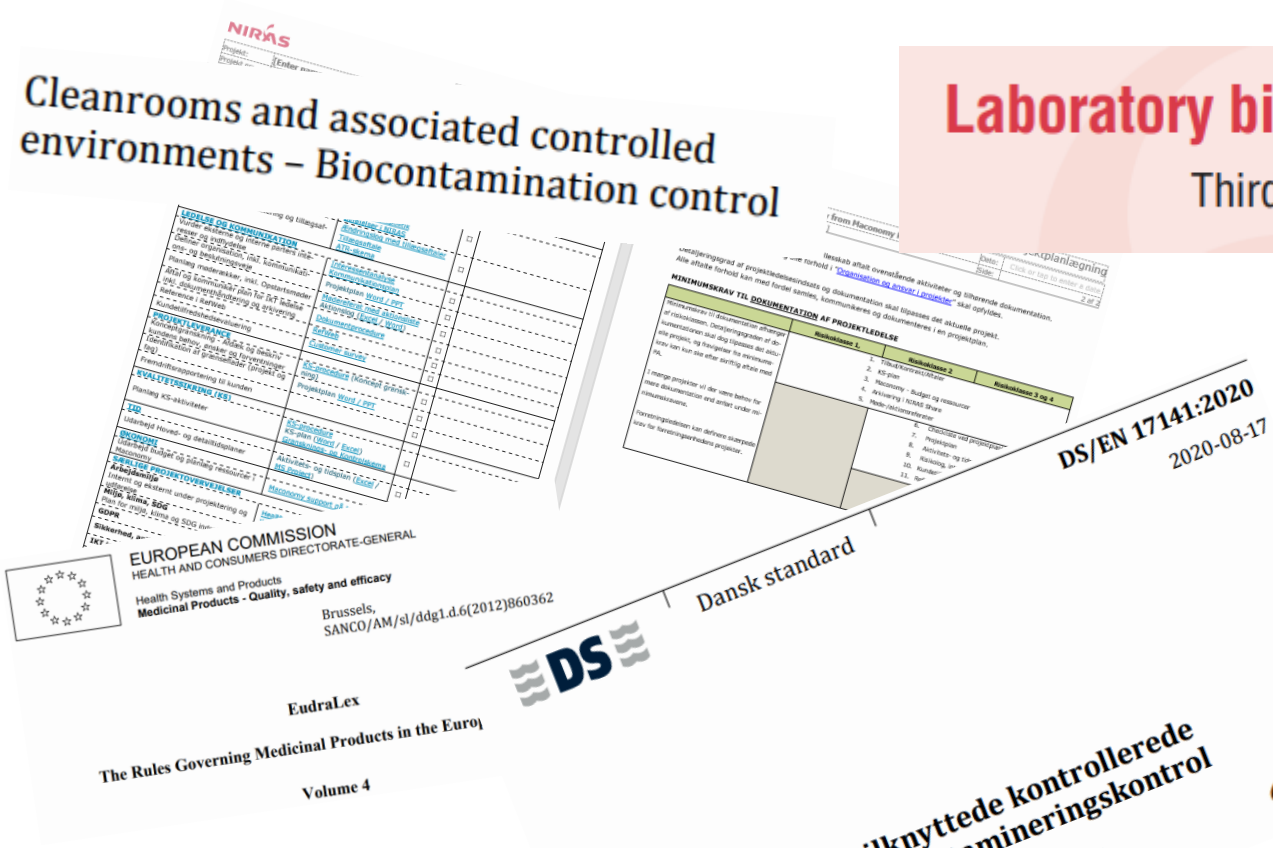
Lesson learned

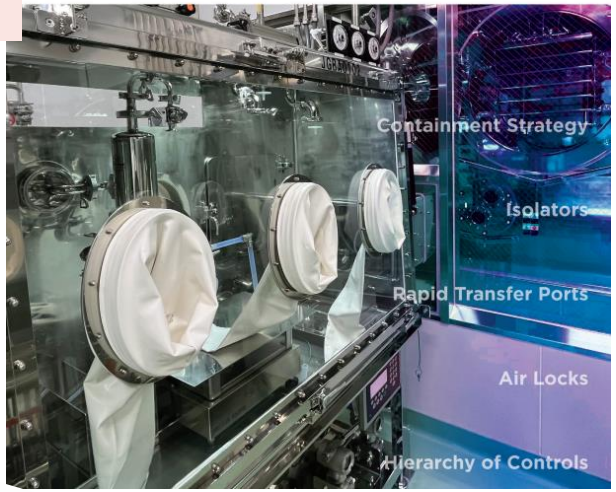
During design and cleanroom testing

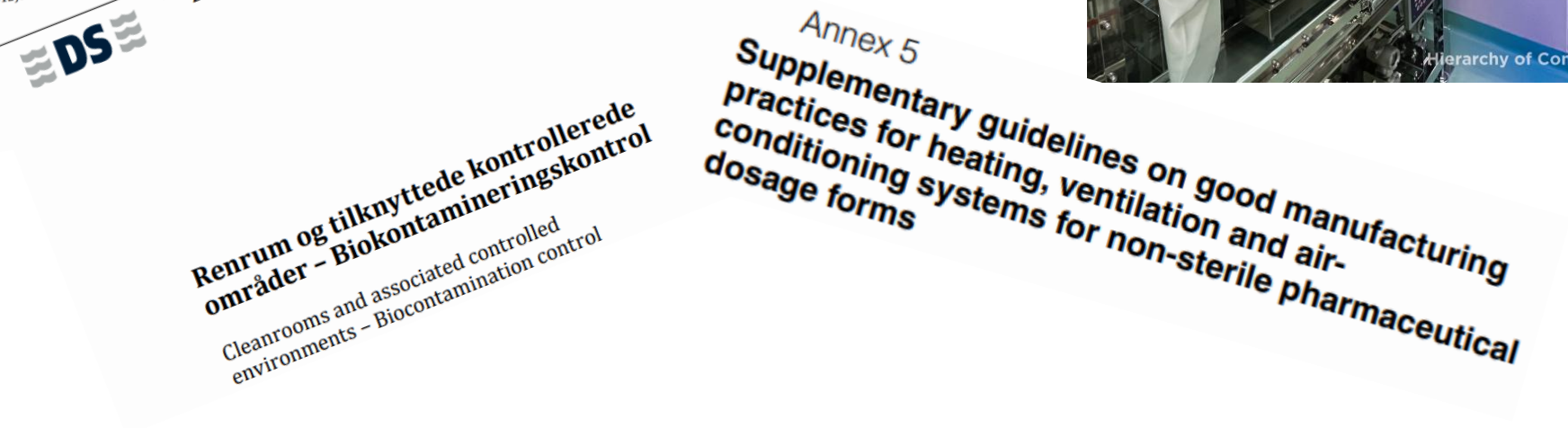
2023

Standards, guidelines internal doks.

Enough standards, guideline and internal procedures?







Always to remember:
Instructions, prescriptions and guidance is a delicate matter.
Simple small details gone wrong, can make everything go wrong.

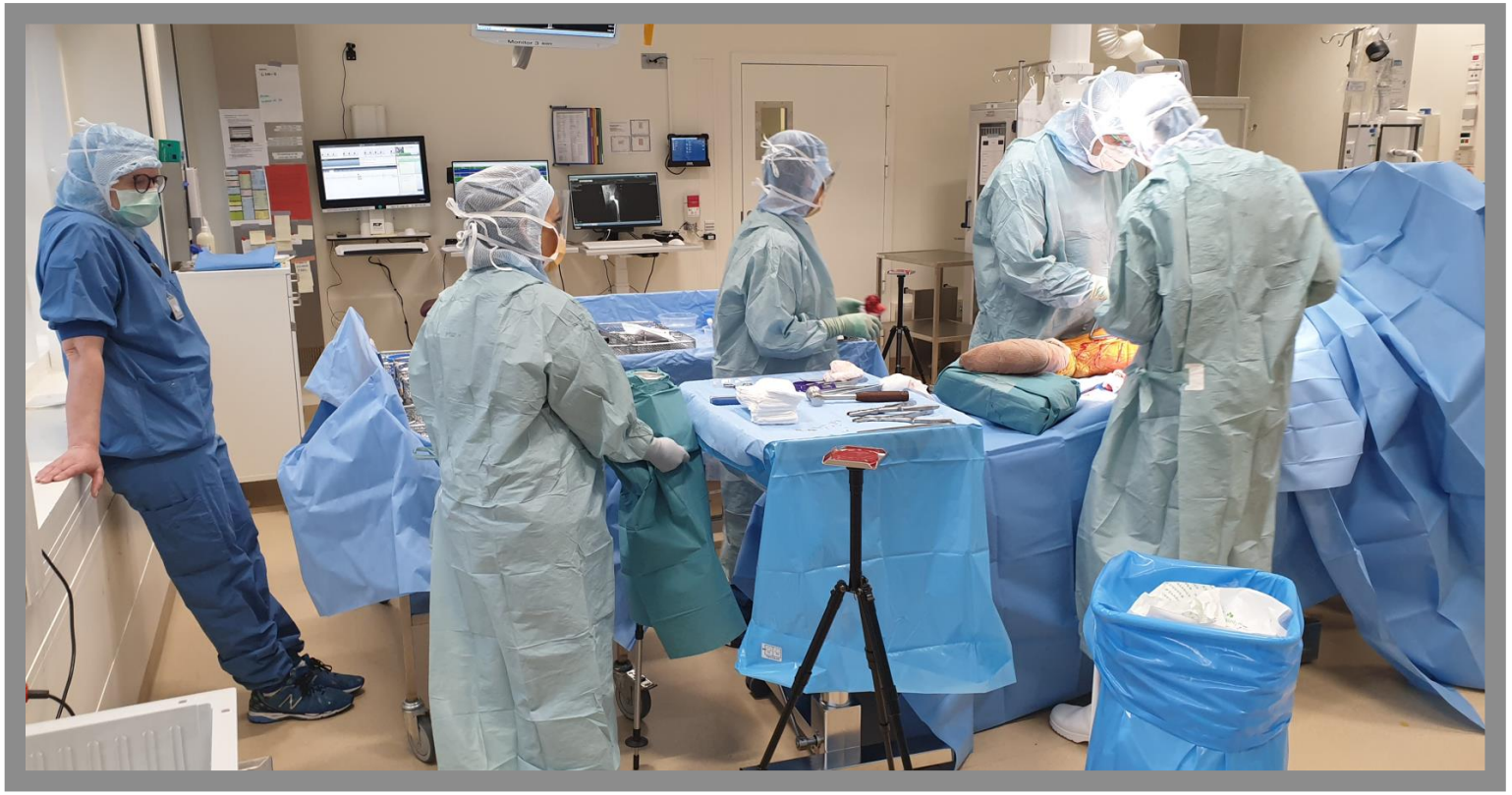
What did’t work

It works !!!

Quality assurance in several steps.

Requerments and facility -Do they match

Material in cleanroom, use of cleanroom



- Grade B cleanroom
- <10 CFU
- 5-10 persons
- Mixing ventilation
- 10 ACH
- No airlock
- Iso 7(5) – non classified

Oviously here is several things gone very wrong. Find easily 5 mistakes. - RIP

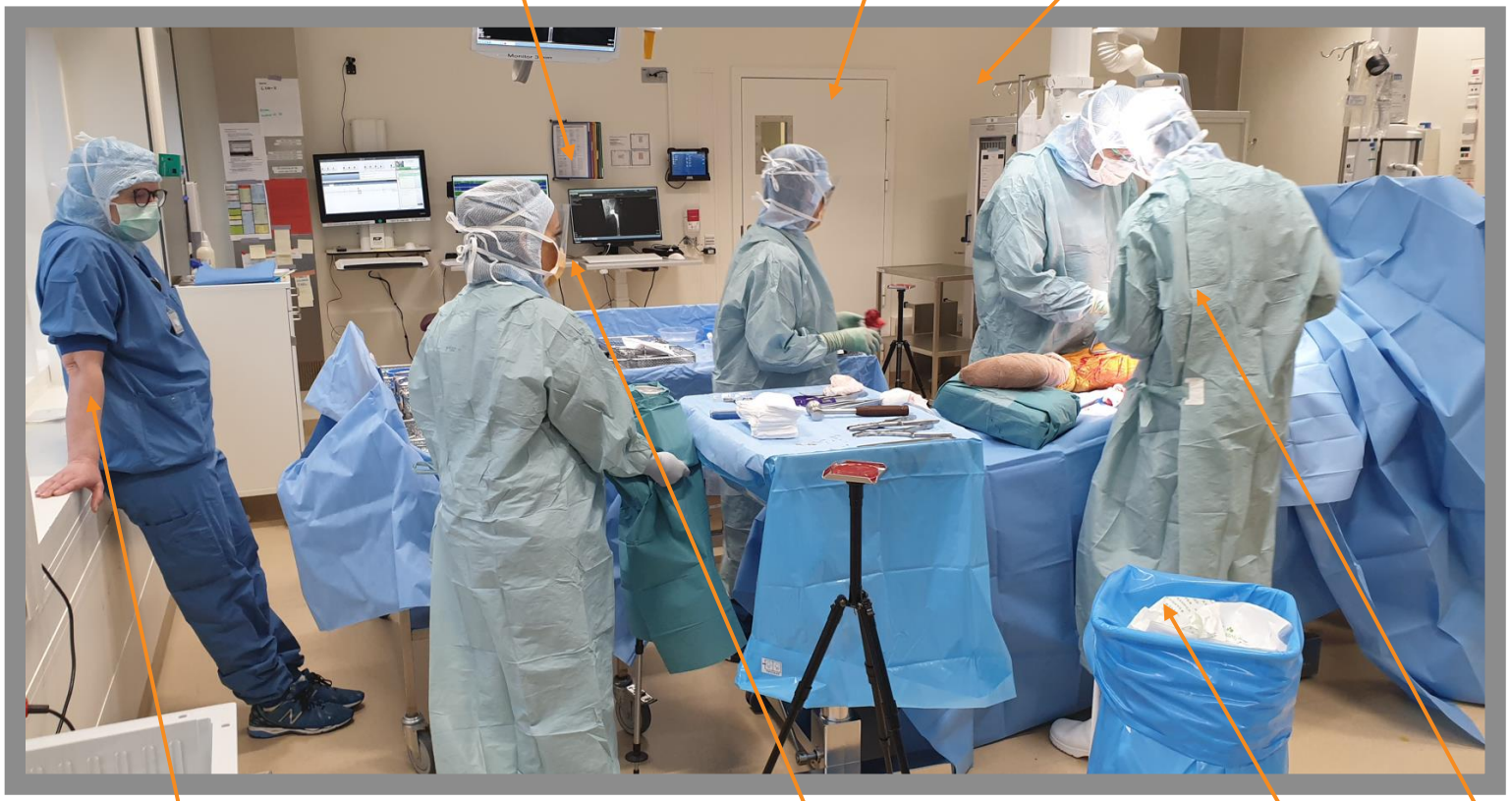
2: Requerments and facility -Do they match

Fast overview - faults

Unable to keep clean

No airlock to corridor

Airchange inadequate and simple mixing principle in Grade B facility, it's a no go.



Un covered arms in turbulent airflow

Use of cosmetic

Open dust spin and no protection zone to patient

Too low grade cleanliness clothing

- When operating in bones, the body can not recover from bacteria in the bone part, as no blood flow is present.
- Normally a totally different OR suite set up is necessary. To avoid Hospital acquired sickness.

Alternative

An optimised OR suite cost, extra Once: 140.000 EUR
Reoperation is approx. 90.000 EUR

Suite last 20 years.

One incident a week in 20 years = 1040 incidents.

If you want to save money, please make facility right first time.

How to start improving:

Start learning from: ISO14644- 1, 2, 3, 4, 5. ☺

Energy optimation – How far can you go ?

what can go wrong ?

”why can’t we just stop the HVAC unit, when we don’t work in the cleanroom”

I often get the question, ”why can’t we stop the HVAC unit when we don’t work in the cleanroom”

Issues is compliance “in Control” definition pressure and cleanliness must be obtained. Standard for setback there is none. But ISO 14644-4 describes to do a risk based analysis using:

- HACCP (hazard analysis Critical Control point),
- FMEA (Failure Mode Effects Analysis) or
- FTA (Fault Tree Analysis)

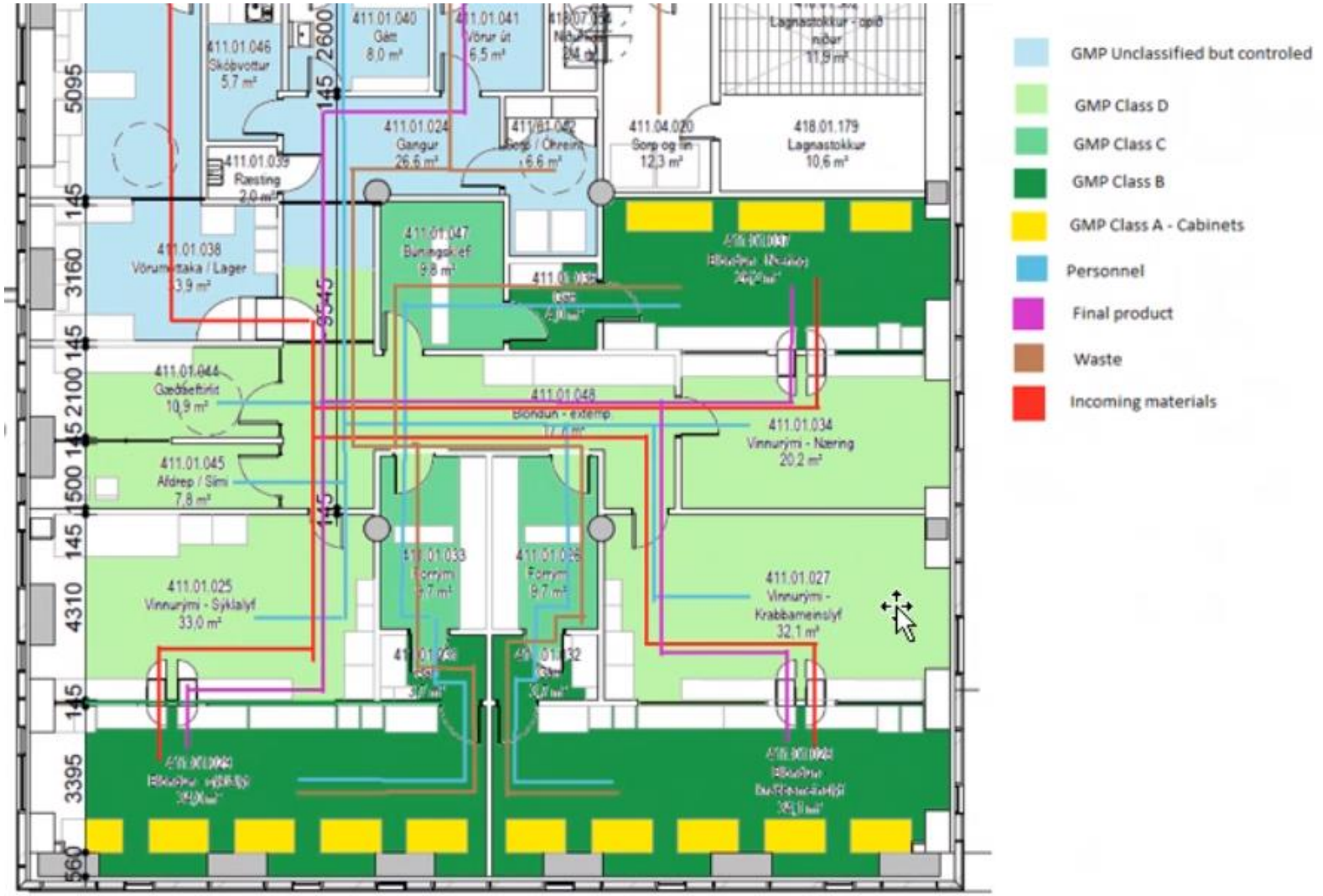
And set back is very relevant as people are the polluter in the room, and when they are not there, the source strength is much lower. And airchange needed to keep cleanliness is therefor much reduced. (cleanliness and pressure shall be obtained at all times, in order to be in control.

If you stop the ventilation, a full cleaning procedure and change of HEPA filters, shall be carried out, before next operation, in order to be “in Control”

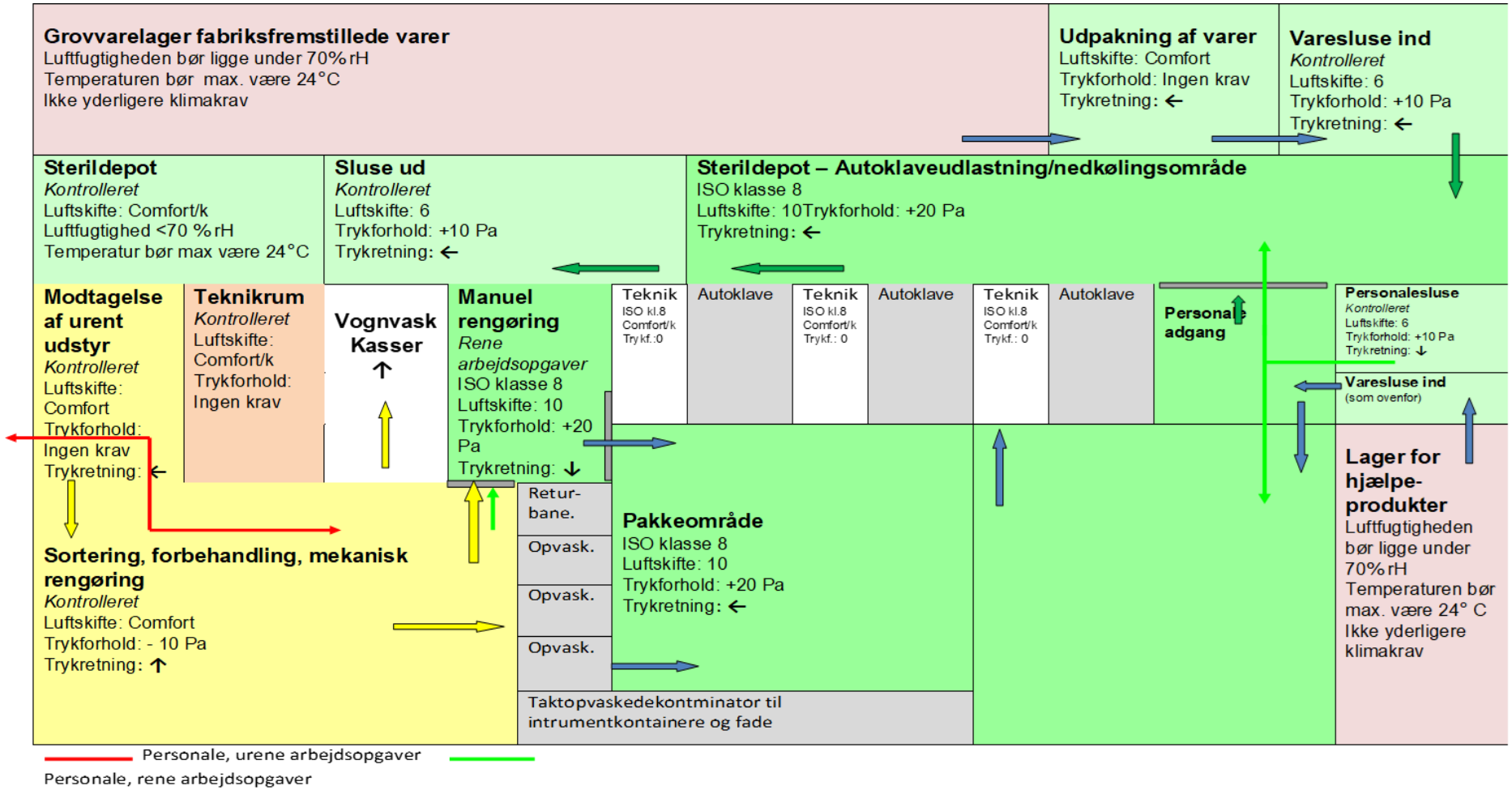
Ultra clean OR room in Denmark, is Iso Class 7 “in operation” and ISO class 5 “at rest” this is grade B.

Flow diagram for different processes

Basic flow – no timing.

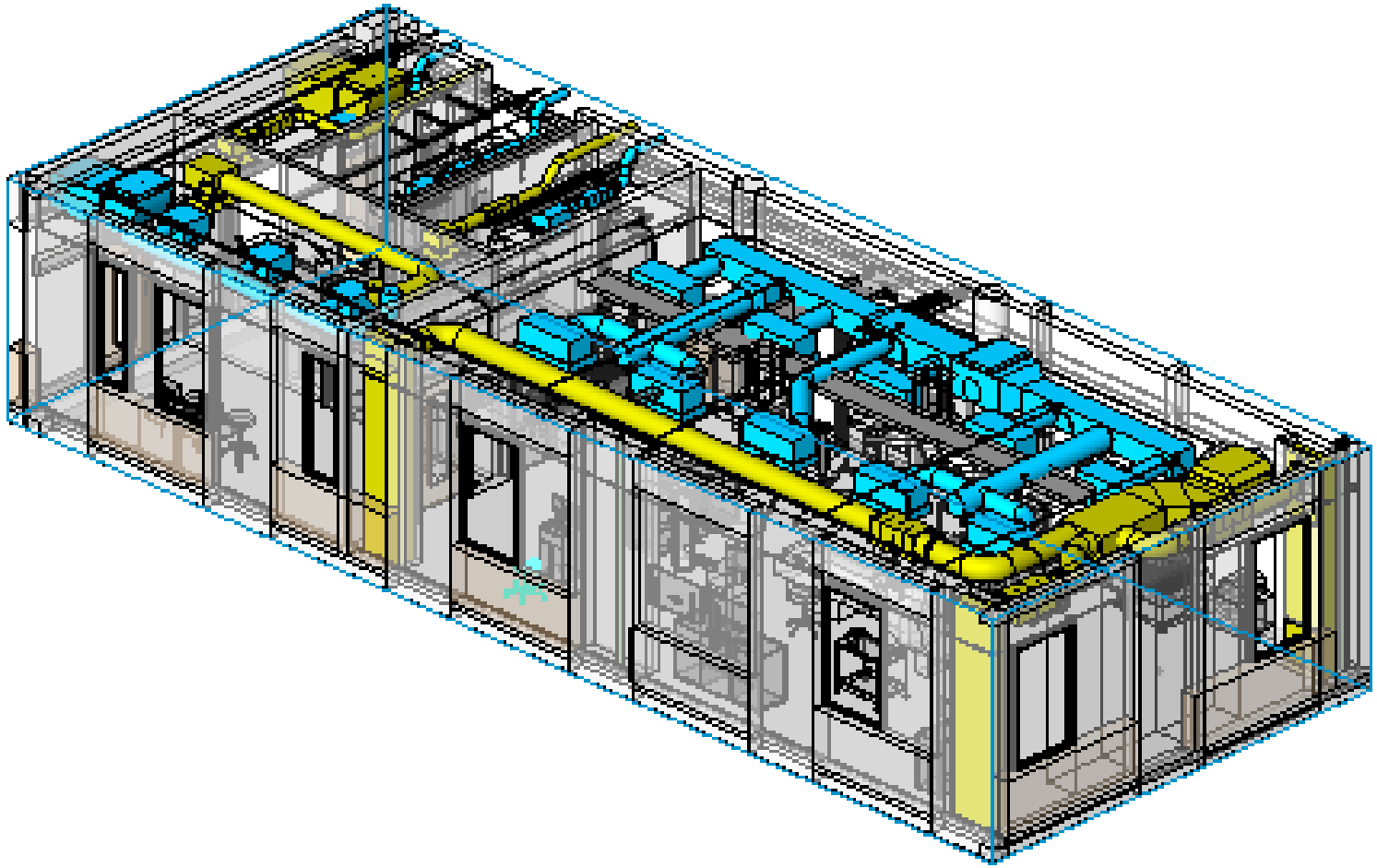


Design Sterilisation site
standard DS 2451-13 (NIR)



Service friendly installations

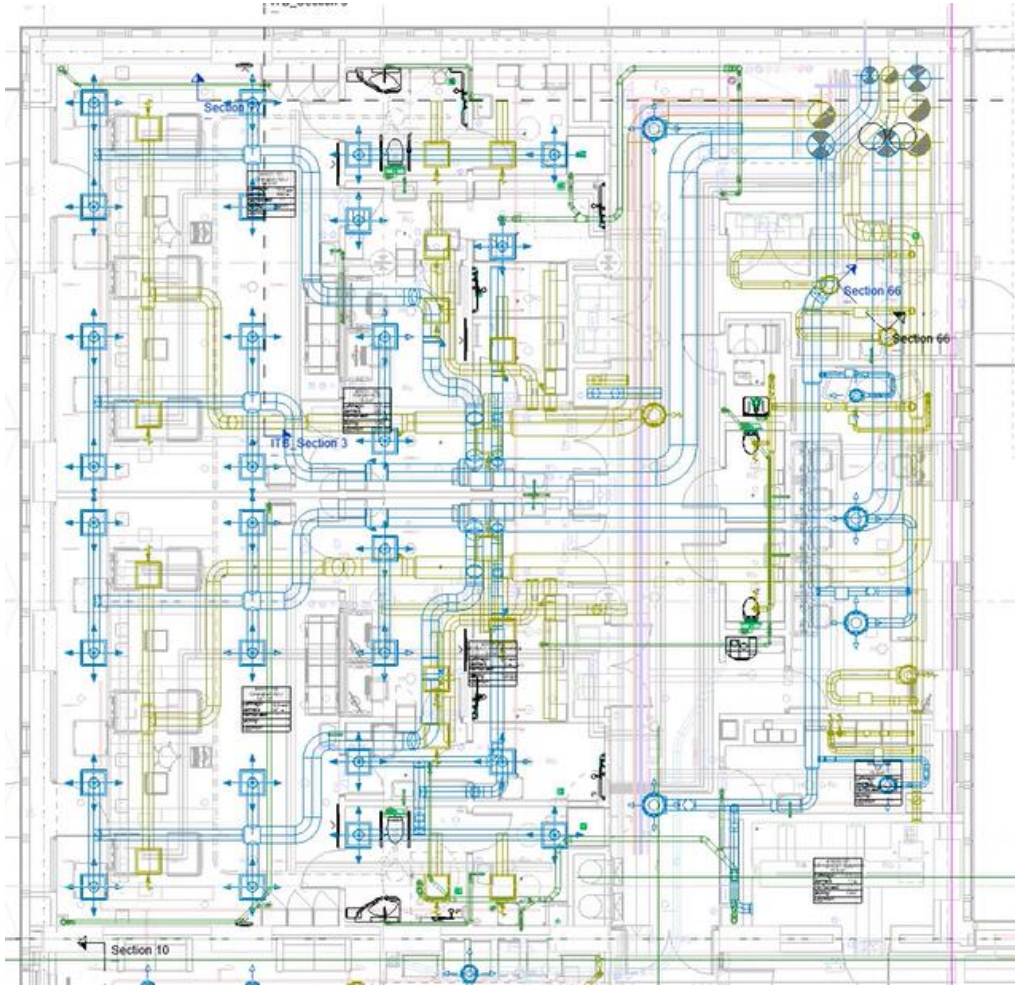
Is service possible ?



- Is service only possible in summer and Winther close down period ?
- Or accessible also in between ?
- Service demanding gear smart placed in the corridor
- Haches were needed
- Space so normal persons can do the job.
- Build safe work environment for maintainers

Accesability

After handover, how to ensure accessibility and service on all components



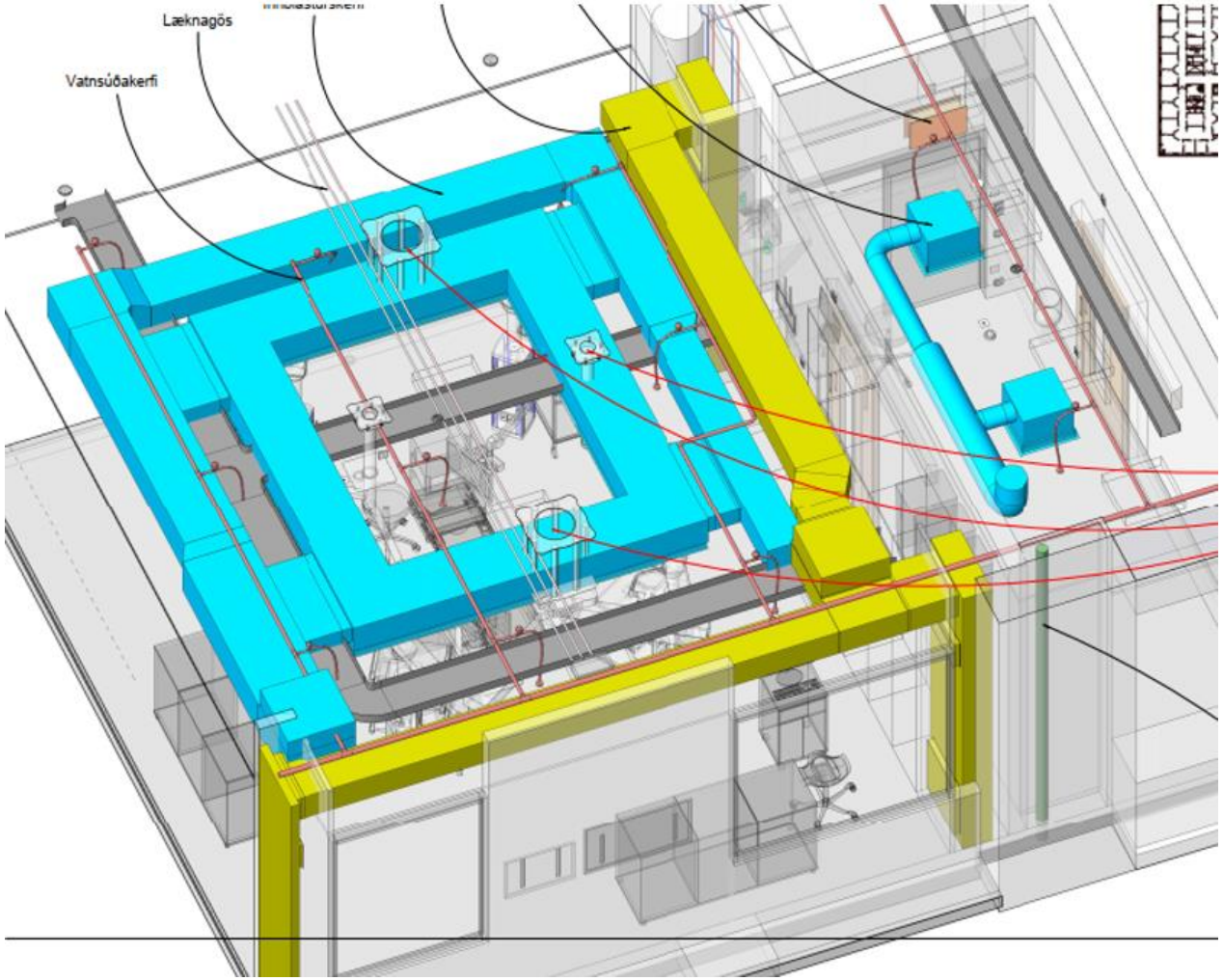
Example Containment areas as:

- BLS3 or
- HLIU High Level insulation Rooms

Collisions on drawings when installer work

What will happend ☺

During installation, if nothing is updated.

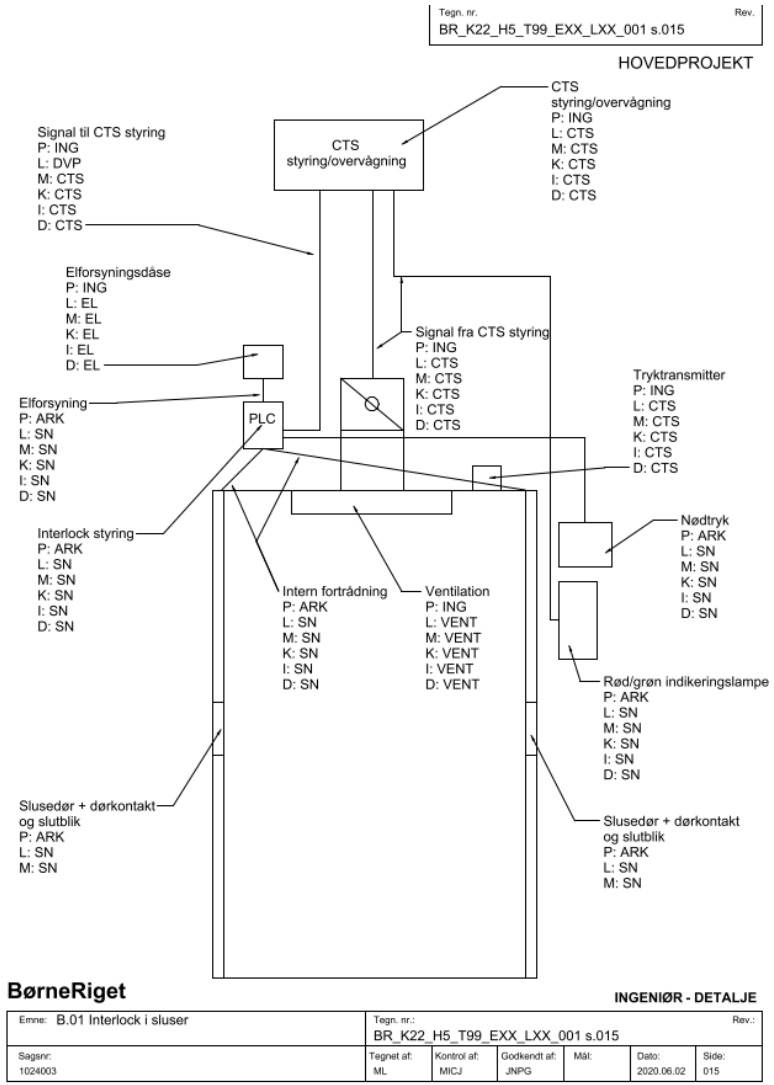


Borders, Equipment

Who do what, and when

During design, and construction need for Clear border lines, for the entreprenerd and engineers

Limits; gaps and doubt.

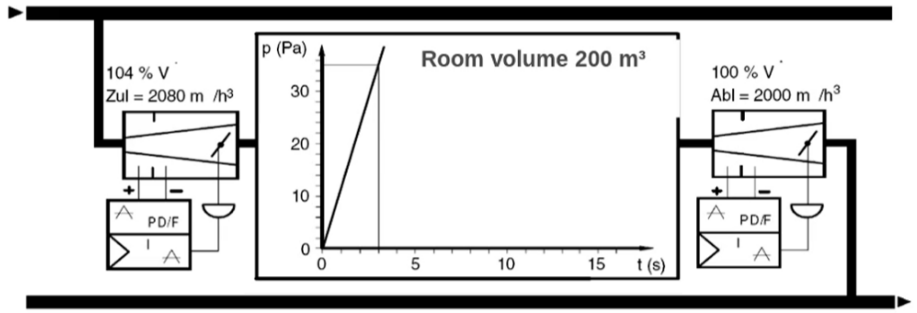


Exambles: on Borders for a interlock

Pressurisation -Tight room

Small air changes make pressure jump the tighter the worse

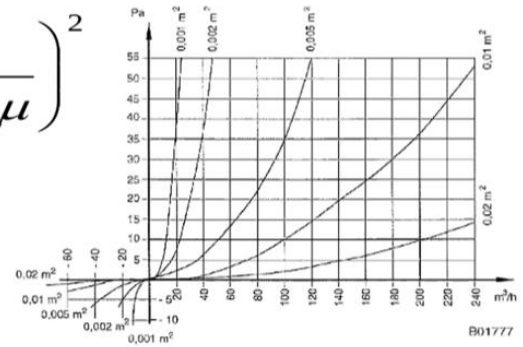
RELATION BETWEEN LEAKAGE, FLOW AND RESULTING NEGATIVE PRESSURE



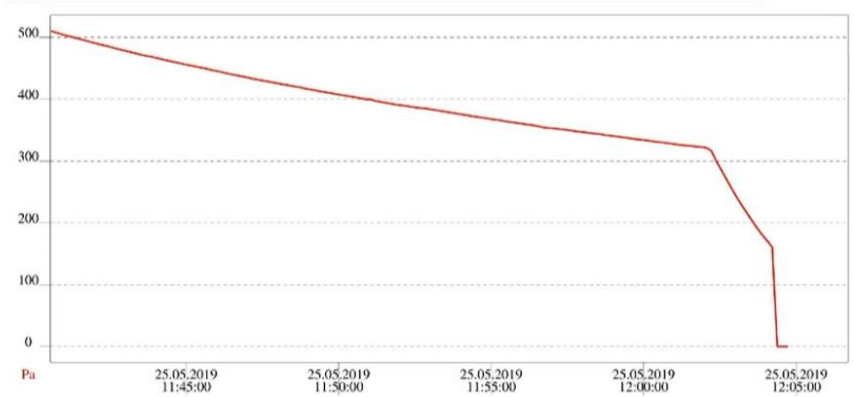
3 second = + 35 pa

RELATION BETWEEN LEAKAGE, FLOW AND RESULTING NEGATIVE PRESSURE

$$\Delta p = \frac{\rho}{2} \cdot \left(\frac{\dot{V}}{A \cdot \mu} \right)^2$$



TIGHTNESS TEST BY PRESSURE DECAY METHOD



TIGHTNESS TEST BY PRESSURE DECAY METHOD

$$Q = \left(\frac{P_i}{T_i} - \frac{P_f}{T_f} \right) \cdot \left(\frac{V}{R \cdot \Delta t \cdot 60 \cdot 1.201} \right)$$

V [m³] : Inner Volume of Test Object

P_i [Pa (abs)] : Initial Pressure

T_i [K] : initial Temperature

□t [min] : measuring time

P_f [Pa (abs)] : final Pressure

T_f [K] : final Temperature

Q [l/sec] : Leakage Air Flow

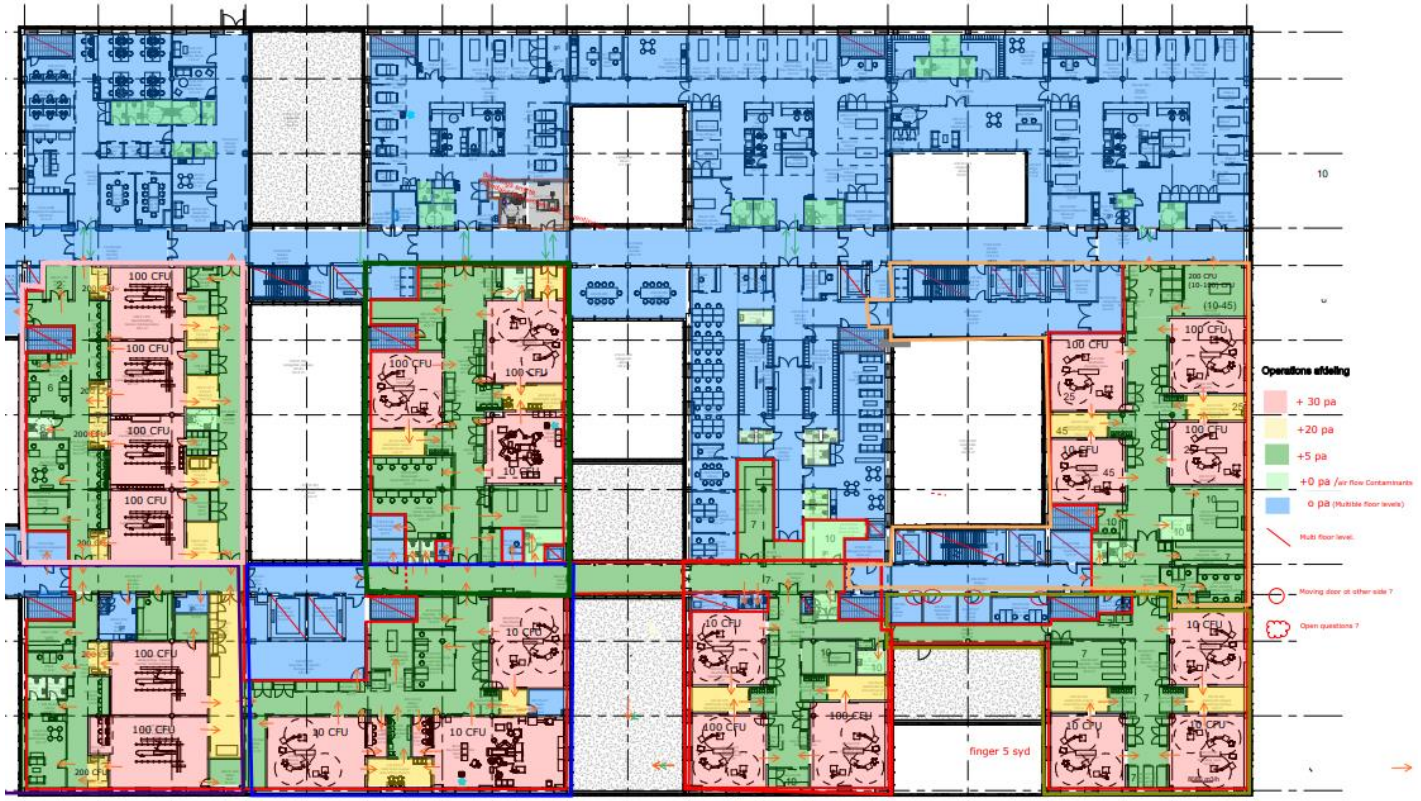
Pressurecascades - how to

Pressure and flow must be combined in order to keep pressure cascades right

What will happen if all light-red rooms opens up to green corridor ?

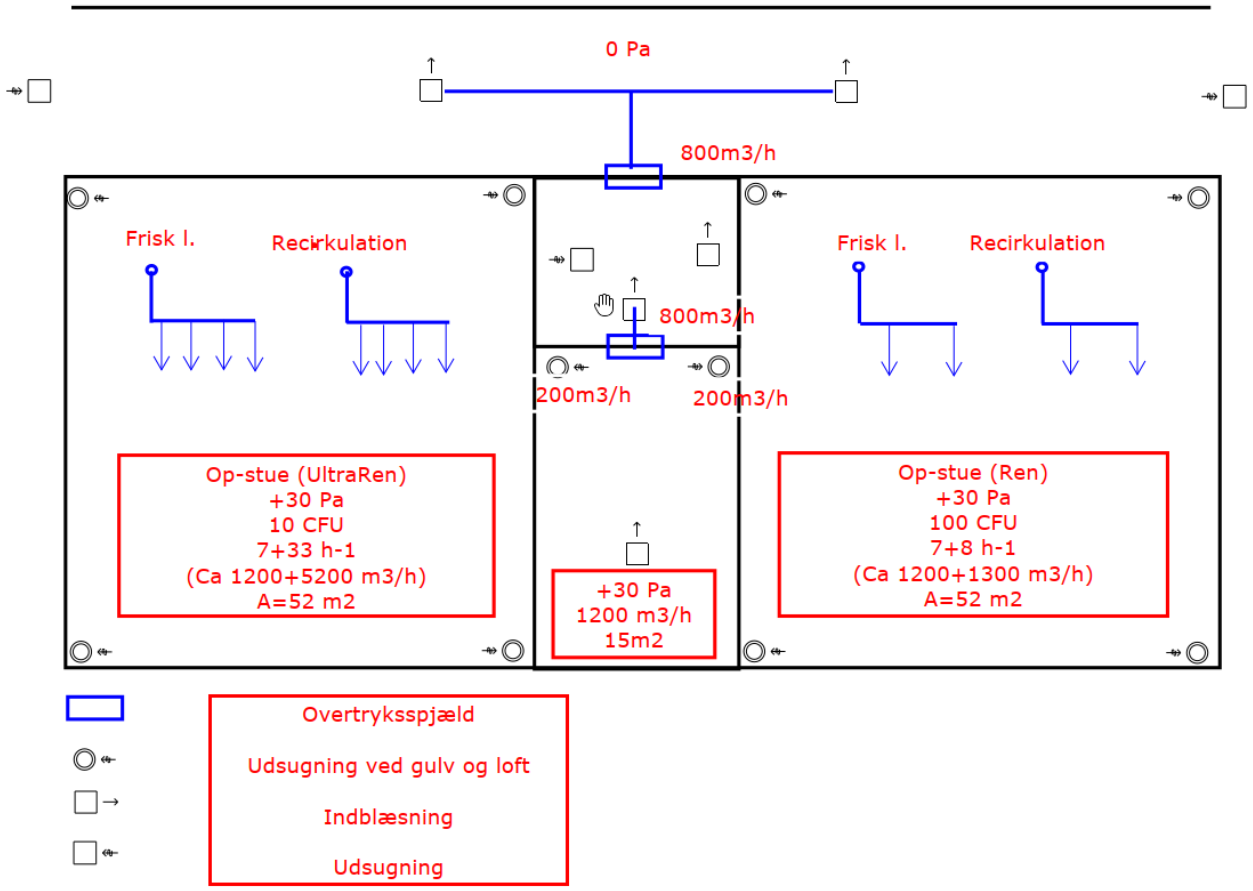
Pressure !

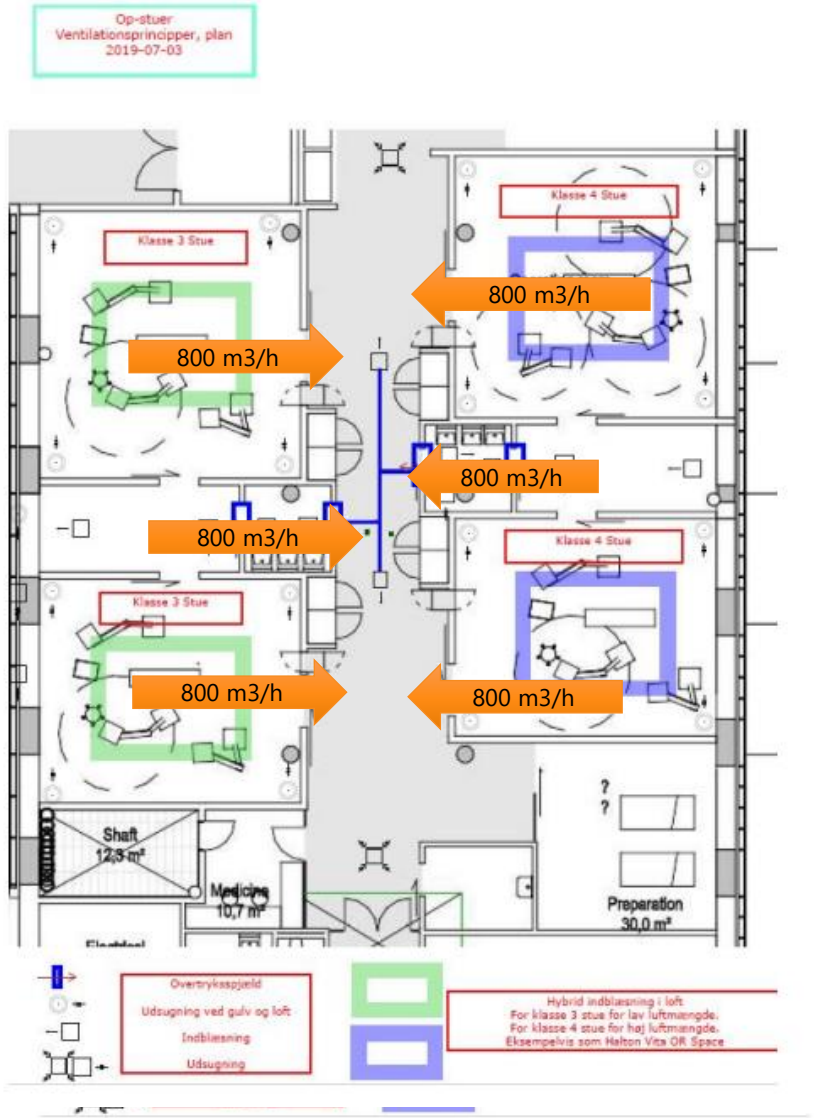
-Flow is faster than pressure to ajust.



Pressure - flow - control

Example on how to keep differential flow in cascade





Tight room – hard to pressure control

Small air change make pressure jump the tighter the worse

One way to reduce the sensibility for pressure ”jumps”
-is to install controlled stable leaks.

- Holes with HEPA filter in,
- Appreco balance pressure damper (picture)
- Faster loop for BMS
- Air consuming equipment is better synchronised
- With inlet. ”Open Gap” stabilises a workbench.
- Etc.

Airlock as clean barrier.

How to design.

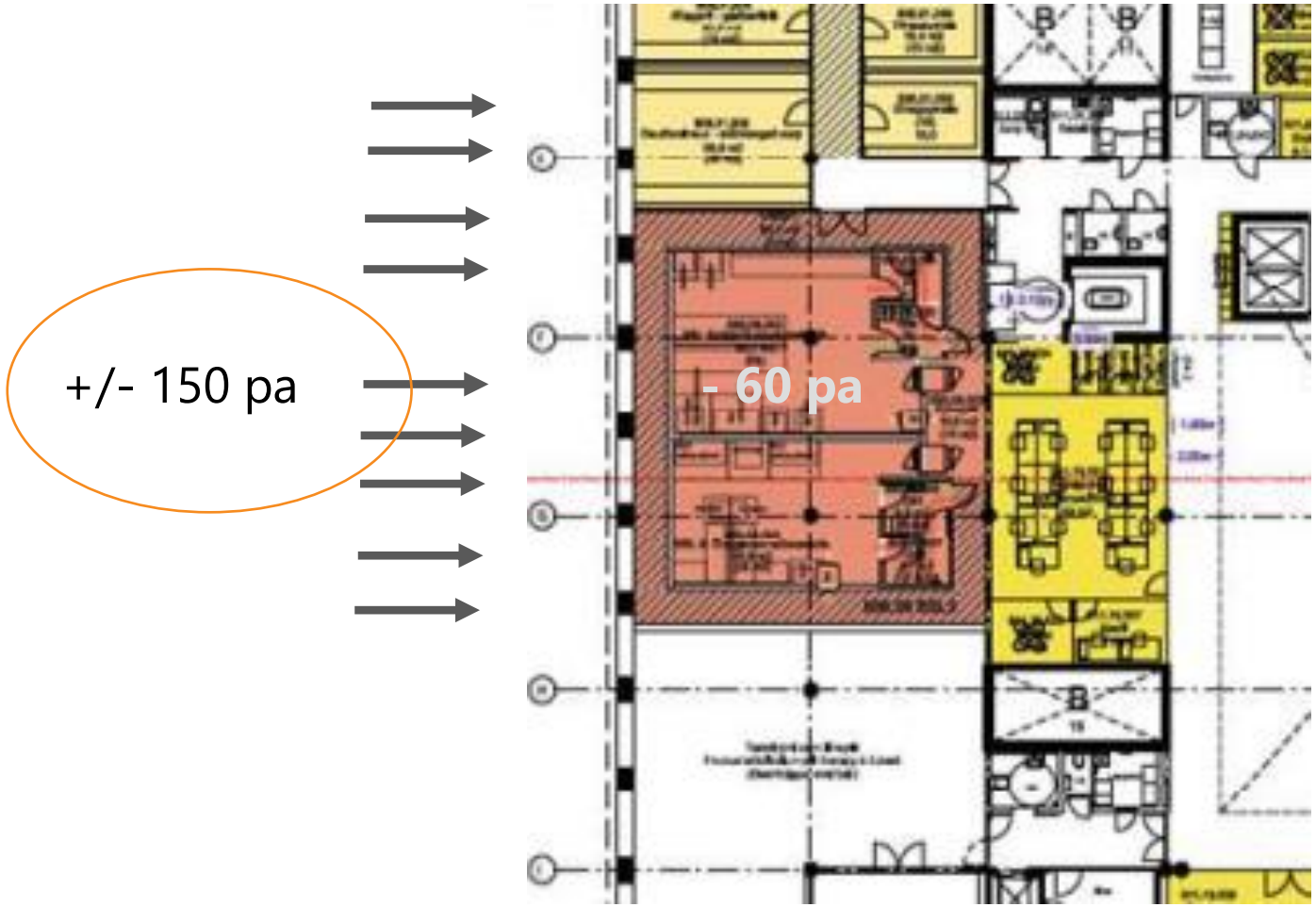
Capacity in airlocks by design.

Higher airchange =>
Lower particle concentration =>
Faster pass-through of personnel.

Concider if waiting time is only needed one way, the other no waiting time is needed.
(how to control interlock?)

Pressure cascades – and outdoor pressure

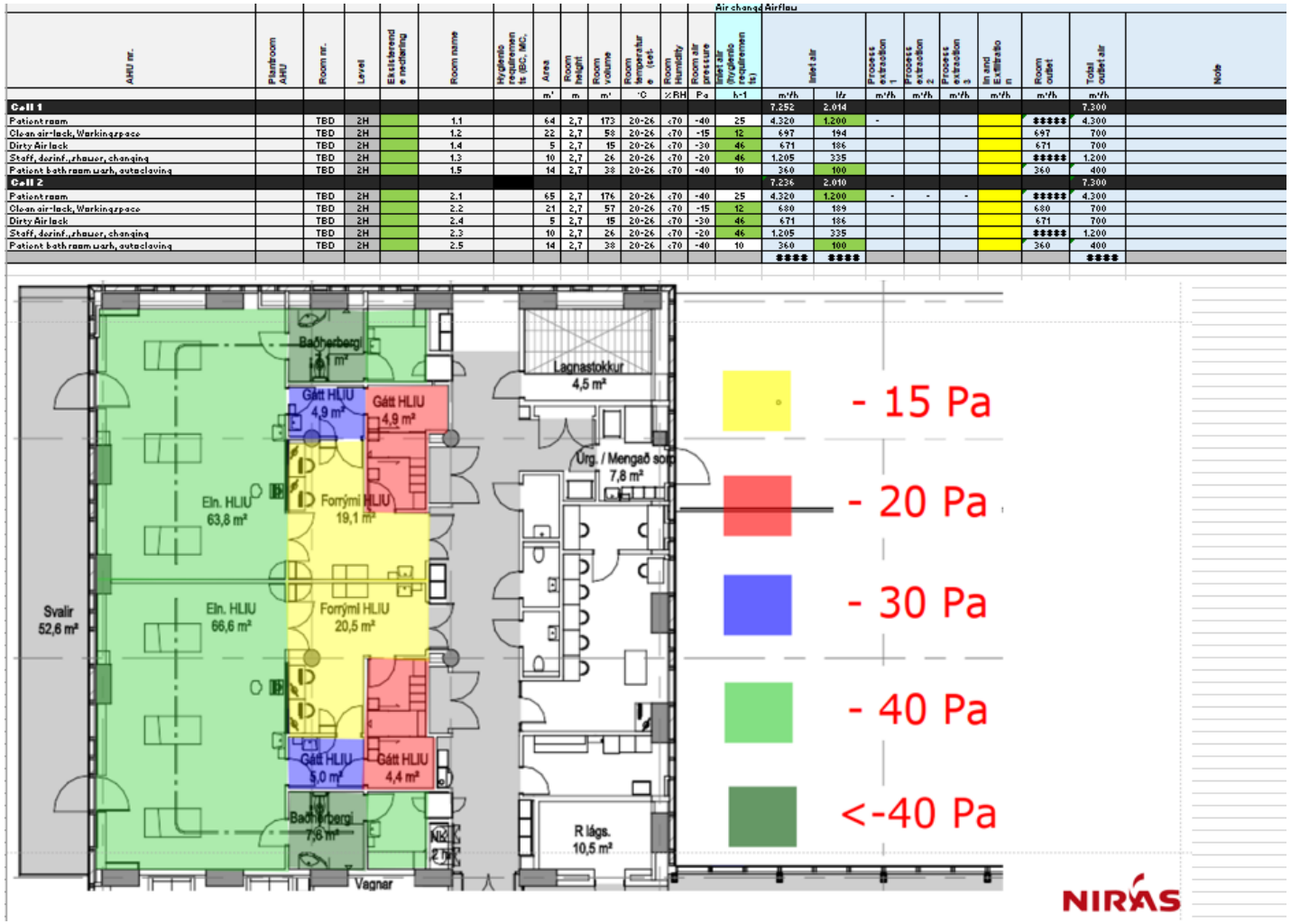
Room in room classified rooms – Here BSL3 facility.



In / Ex Filtration

Leaks have great inpact on the HVAC and the pressure.

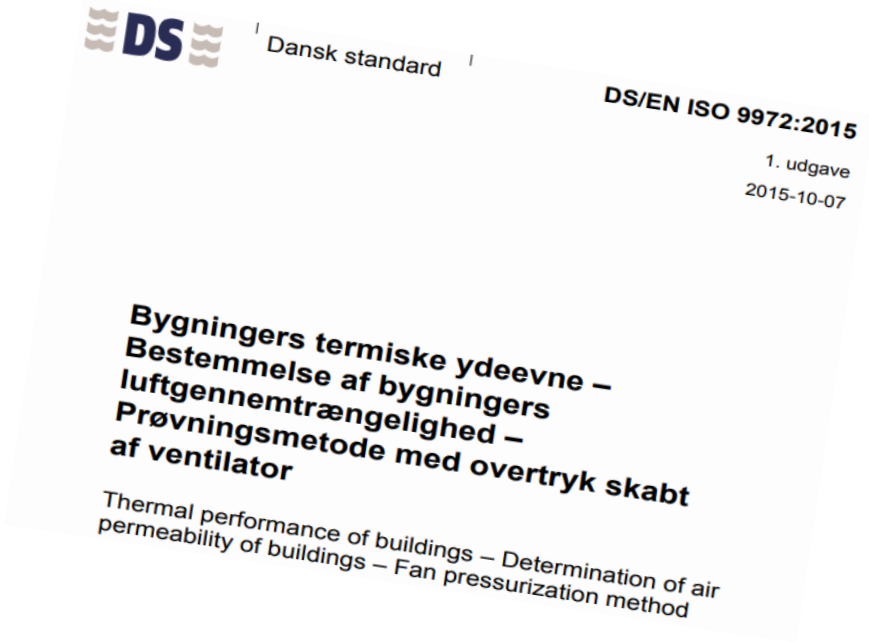
- Leak must be taken into account while designing cleanroom facilities.
- A sceme as above can be used t odescribe the level of leaks.



Leak level, in a facility before handover .

Examble is from a contamination facility.

Different ways to test and find leaks is normally by smoke and blowerdoor testing .

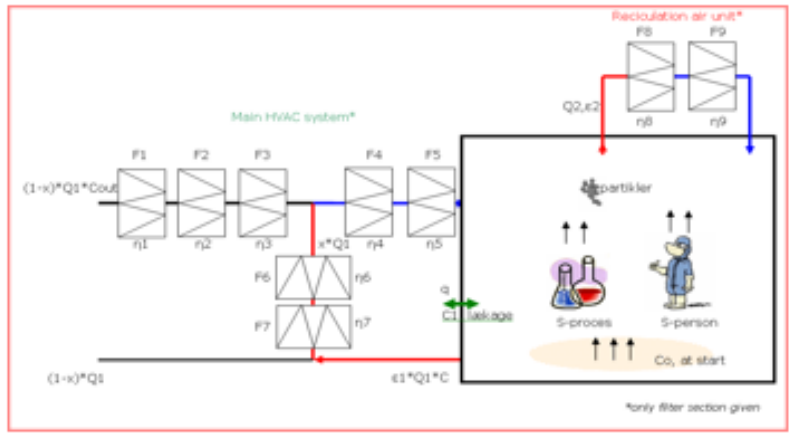


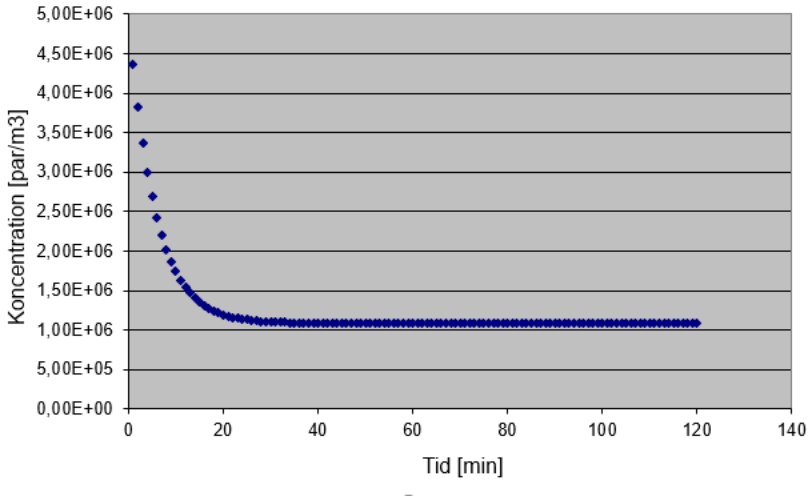
TIGHTNESS TEST BY CONSTANT PRESSURE METHOD

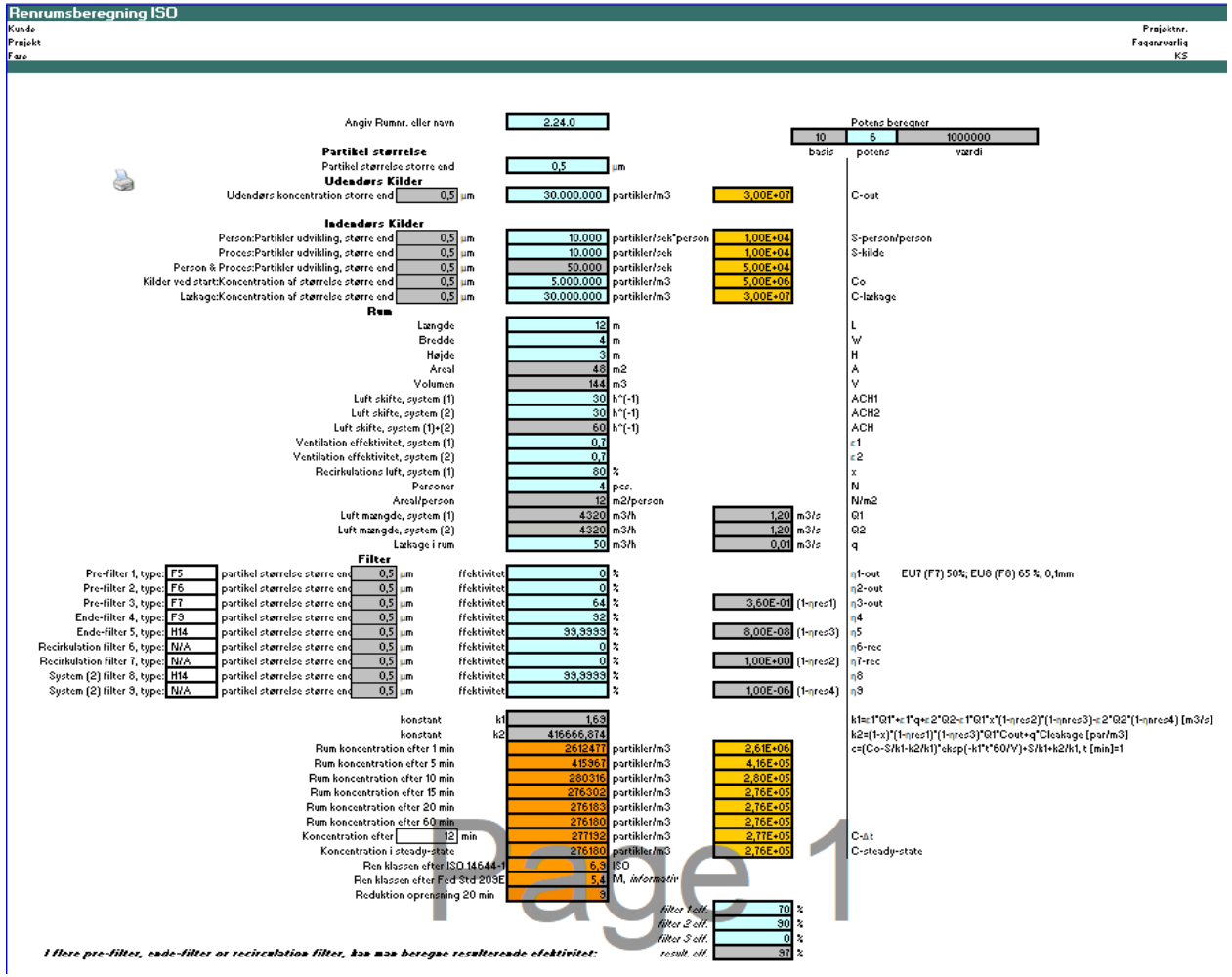
LEAK DETECTION BY ULTRASONIC

Cleanliness calculation

Example on how to calculate different scenarios to a cleanroom ISO14644-1







Recovery time - calculation

Example on calculaton on recover time

Renrumsberegning ISO

Kunde	Projektnr.
Projekt	Fagansvarlig
Fase	KS

Beregning af oprensningstid på baggrund af DS 14644-3 - B4 recovery test

Recovery rate

Rate		konstant	Tidskonstant	
1:10	0,1	-2,30	4	min
1:100	0,01	-4,61	4	min

Inddata fra cleanroom beregning

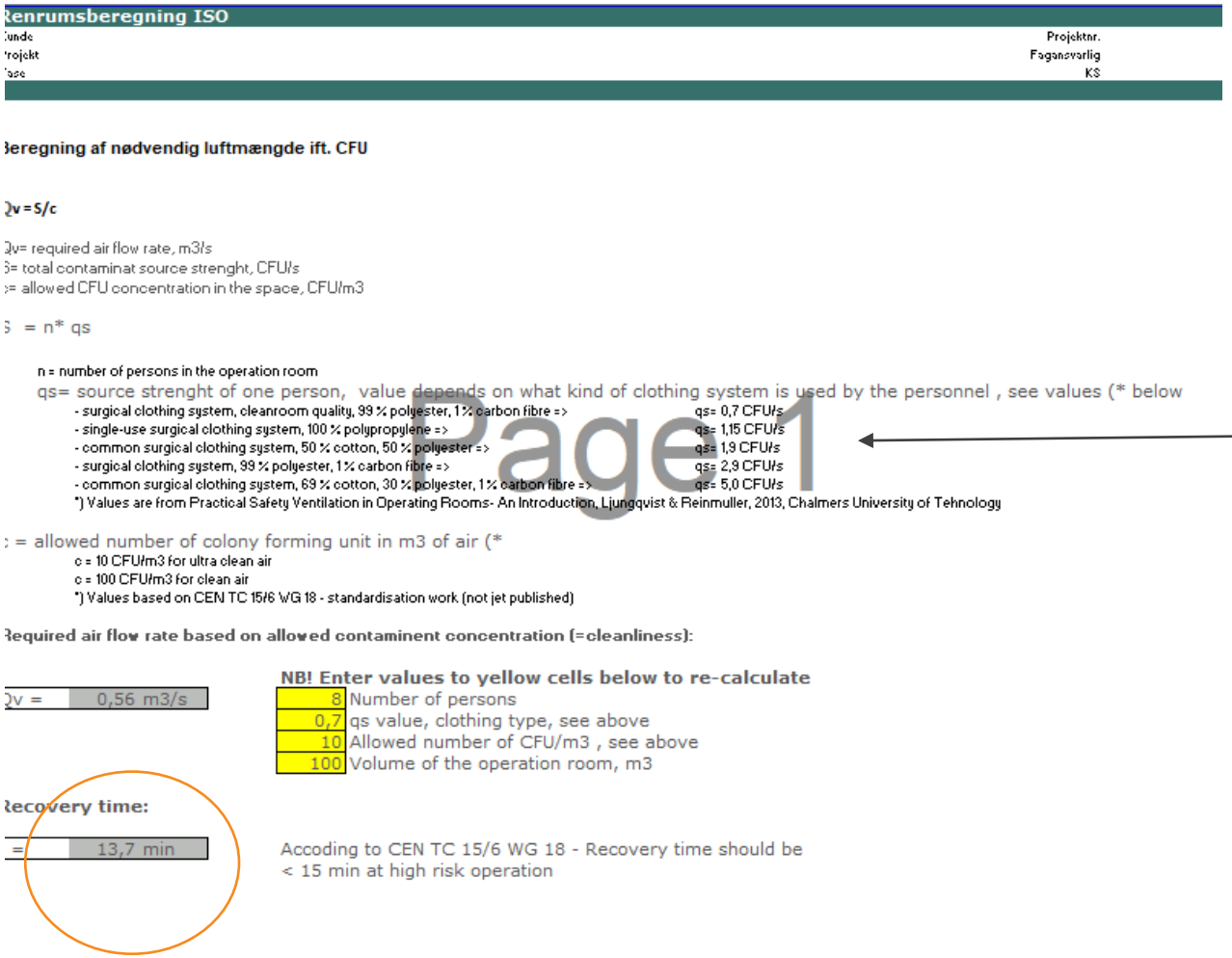
Total luftskifte (1+2)		15,0	h^{-1}
Ventilationseffektivitet		0,7	
Tidskonstanten	T	4	min

Oprensningstid 1:10	**-9,2**	**min**
Faktisk oprensningstid 1:10	**-13,2**	**min**
Oprensningstid 1:100	**-18,4**	**min**
Faktisk oprensningstid 1:100	**-26,3**	**min**

Note:
Opretningstiden er under forudsætning af, at der ikke tilføres infiltration
infiltration forlænger oprensningstiden

Recovery time

Number of people, gowning type, and cleanliness level required.



Renrumsberegning ISO

Kunde — Projektnr.
Projekt — Fagansvarlig
Fase — KS

Beregning af nødvendig luftmængde ift. CFU

Qv = S/c

Qv= required air flow rate, m3/s
S= total contaminat source strenght, CFU/s
c= allowed CFU concentration in the space, CFU/m3

S = n* qs

n = number of persons in the operation room
qs= source strenght of one person, value depends on what kind of clothing system is used by the personnel , see values (* below
- surgical clothing system, cleanroom quality, 99 % polyester, 1 % carbon fibre => qs= 0,7 CFU/s
- single-use surgical clothing system, 100 % polypropylene => qs= 1,15 CFU/s
- common surgical clothing system, 50 % cotton, 50 % polyester => qs= 1,9 CFU/s
- surgical clothing system, 99 % polyester, 1 % carbon fibre => qs= 2,9 CFU/s
- common surgical clothing system, 69 % cotton, 30 % polyester, 1 % carbon fibre => qs= 5,0 CFU/s
*) Values are from Practical Safety Ventilation in Operating Rooms- An Introduction, Ljungqvist & Reinmuller, 2013, Chalmers University of Tehnology

c = allowed number of colony forming unit in m3 of air (*
c = 10 CFU/m3 for ultra clean air
c = 100 CFU/m3 for clean air
*) Values based on CEN TC 15/6 WG 18 - standardisation work (not jet published)

Required air flow rate based on allowed contaminent concentration (=cleanliness):

Qv = 0,56 m3/s

NB! Enter values to yellow cells below to re-calculate

8	Number of persons
0,7	qs value, clothing type, see above
10	Allowed number of CFU/m3 , see above
100	Volume of the operation room, m3

Recovery time:

= 13,7 min

Accoding to CEN TC 15/6 WG 18 - Recovery time should be
< 15 min at high risk operation

Huge difference in particle emission of particles.

Requerments is in ISO14644-3 for recovery time

New equiptment solves problems and gives new problems

Instrumentcontainer

Smart new technology

How to make it safe

When they turn they rip up the floor if not extremly stable.

Questions

A simulation by

www.niras.com

Simulering

RSR_SterilCentra l_2017_10_30.mp4