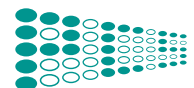


PHARMACEUTICAL
CONSULTANCY
SERVICES

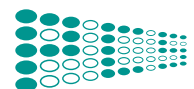
Cleaning and Disinfection

AGENDA

- Definition
- Types of Disinfectants
- Basic Principles of Cleaning/Disinfection
- Cleaning/Disinfection in Practise
- Monitoring
- Validation



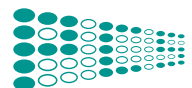
DEFINITIONS



THE IDEAL DISINFECTANT

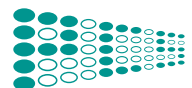
- Effective against all micro-organisms
- Works at every temperature, pH etc.
- Works on every surface
- Does not corrode the surface
- Does not expire
- Not toxic to humans
- No residues
- Cheap

**But unfortunately,
it does not exist!**



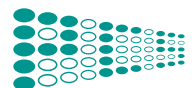
DEFINITIONS

- Bacteriostatic (not for disinfectants but for antibiotics)
 - Slows bacteria down
- Bactericide
 - Kills bacteria (not their spores)
- Virucide
 - Kills viruses
- Fungicide
 - Kills moulds and yeasts
- Germicide
 - Kills all micro-organisms
- Sporicide
 - Kills all spores



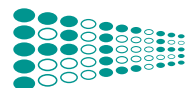
CLEANING AND DISINFECTION (1)

- Cleaning
 - Removing (chemical) materials, dust
 - Vacuuming / Soap / Water
- Disinfecting
 - Reducing the number of micro-organisms
 - Only if sterilization is not possible, or when it is less important
- Sterilizing
 - Killing “all” micro-organisms (max. 1 per 1,000,000 is left alive)

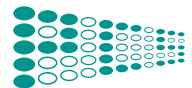


CLEANING AND DISINFECTION (2)

- What will be cleaned?
- What will be disinfected?
- What will be sterilized?

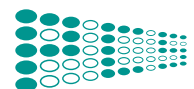


TYPES OF DISINFECTION



DISINFECTANTS AND HOW THEY FUNCTION

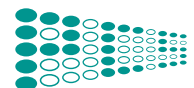
- **Quaternary ammonium compounds** change the surface tension so that structures (pili) on the cell wall are removed
- **Aldehydes** damage the protein structure
- **Halogens** (chlorine, iodine) and **Peroxides** oxidate organic materials
- **Alcohol** coagulate proteins
- **Peracetic Acid, Peroxides** oxidizes the outer cell-membranes of the micro-organism



**FOOT & MOUTH
DISINFECTION
AREA**



"Just your husband's feet will suffice Mam".



DISINFECTANTS AND HOW THEY FUNCTION

desinfectant	bactericidal	fungicidal	virucidal	sporicidal
alcohols	+	+/-	+/-	-
aldehydes	+	+	+	+
chlorine	+	+	+	+
hypochloriet	+	+	+/-	+/-
waterstofperoxide/perazijnzuur	+	+	+	+
fenol-producten	+	+	+/-	-
quat. Ammonium producten	+	+	+/-	-



SENSITIVITY TO DISINFECTANTS

Vegetative Cells

Easy

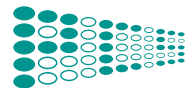
**Enveloped
virus**

Mould Spores

**Non-enveloped
virus**

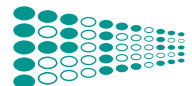
Bacteria Spores

Hard

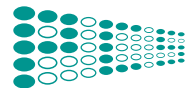


TYPES OF DISINFECTANTS

- What will be used?
- Is there circulation?
 - Why?
- Combination cleaning/disinfectants

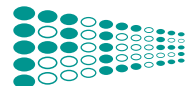


BASIC PRINCIPLES CLEANING/DISINFECTION



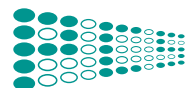
WHAT CAN INFLUENCE THE DISINFECTION

- Contamination
- Contact (surface and fumigation)
- Exposure Time
- Types of Micro-Organisms
- Disinfectant
 - Concentration
 - Material
 - Solvent
- Surface material
- Temperature



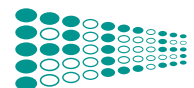
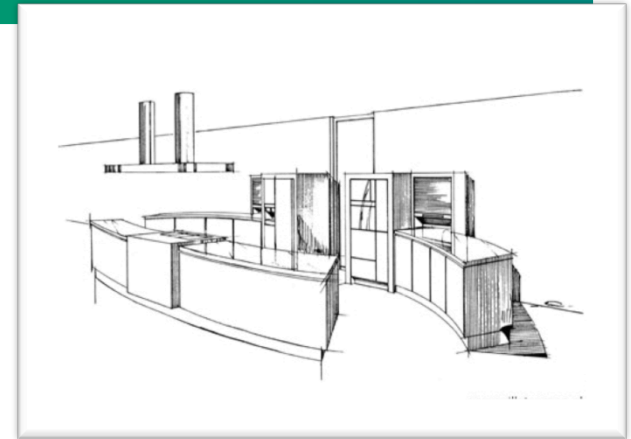
THE USE OF CLEANING

- Removing visible contamination, because contamination
 - Reacts with disinfectants
 - Shield micro-organisms
 - Are a source of nutrition for micro-organisms
- With vaccine- or bio-technological production:
 - Disinfection (killing a specific organism)
 - Cleaning
 - Disinfection
 - Washing



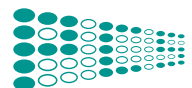
PRINCIPLES; DESIGN

- Smooth surfaces, not porous
- No edges
- No corners, smooth surface
- Use materials that can handle disinfectants
- No non-essential materials in the clean room
- No shelves, ridges, etc.
- Sanitary Design



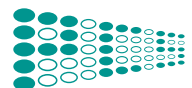
PRINCIPLES; USE

- Make sure that as little is possible is present in the clean room
- A clean room is not a storage room
- Clean everything up first
- Make sure everything is accessible
- Leave no materials behind
- Store materials (where?)



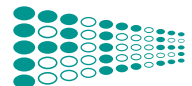
PRINCIPLES: CLEANING/DISINFECTION

- Work from high to low
- Work from clean to dirty
- Work from back to front (or to the door)
- Make sure that cleaning/disinfection is not spreading contamination
 - Ensure the use of sterile solvents
 - Ensure clean/sterile aids
- Keep cleaning materials away from production
- Cleaning- and disinfectants may (usually) leave no residues (wash afterwards)



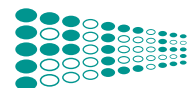
TYPES OF CONTAMINATION

- Depends on the process
- Glas
- Product
- Metal (aluminium)
- Skin, hairs
- Micro-organisms

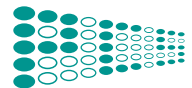


PRINCIPLES: CLEANING

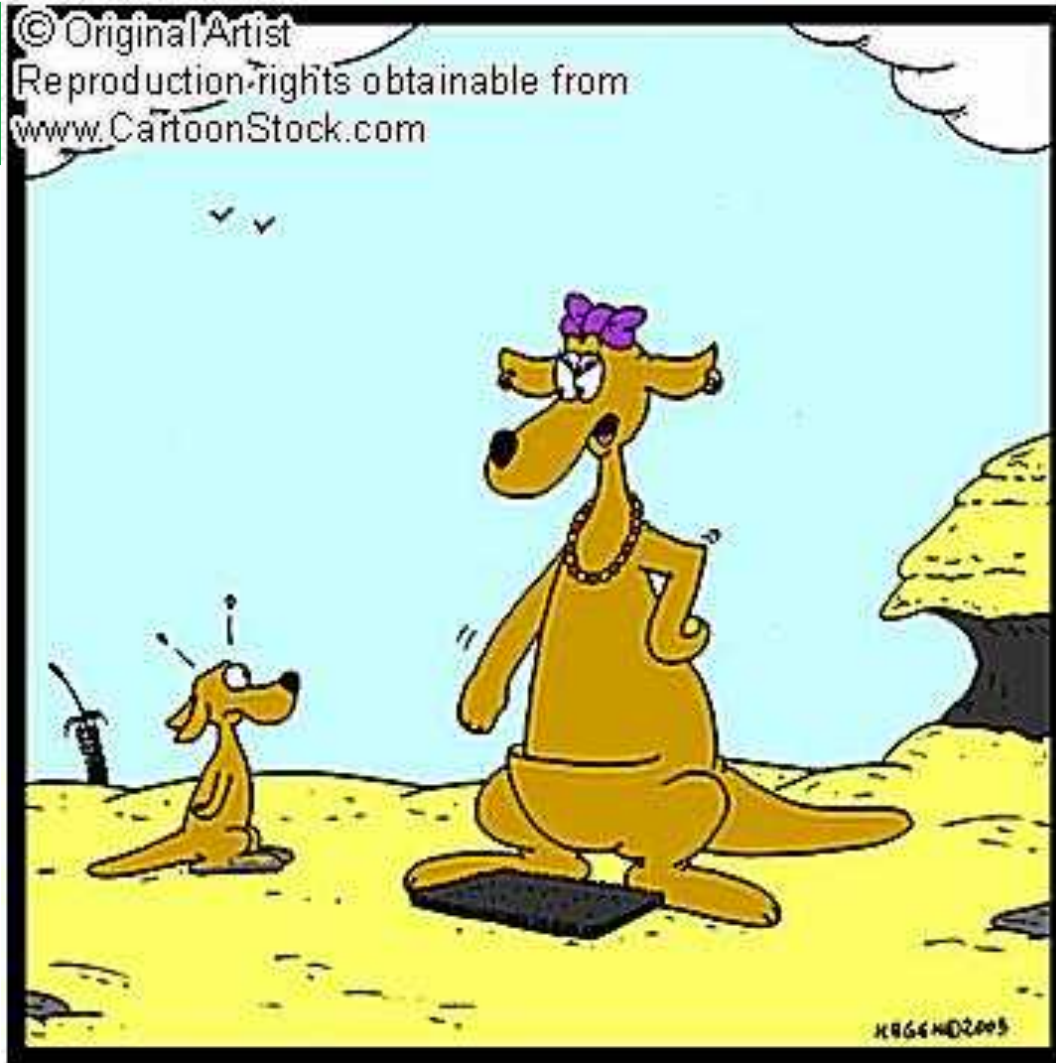
- Proper exposure time
- Proper concentration
- Correct scheduling
- Right type of cleaning agent/
disinfectant
- Keep to all the behavioral rules



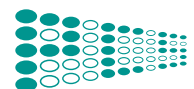
CLEANING/DISINFECTION IN PRACTICE



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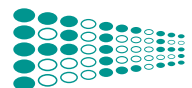


**I'm fed up with cleaning your room!
From now on, wipe your feet!**



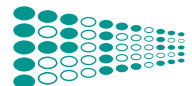
CLEANING AND DISINFECTION IN PRACTICE

- Procedure
 - Frequency (how long will a room remain clean?)
 - Rotation regime
 - Is this always necessary? It is, according to the guidelines
 - Concentration
 - Making the agents, expiration dates
 - Exposure times
 - Follow-up



CLEANING AND DISINFECTION IN PRACTICE

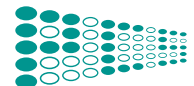
- Procedure
 - What rooms, spaces?
 - All positions always or changing schedule
 - Will cleaning agents/disinfectants be qualified, if so which tests?
 - Cleanroom disinfectants will have to be sterile before use
 - During the infeeding of materials into the cleanroom, a sporicide is advised to be used (PIC/s)



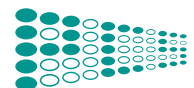
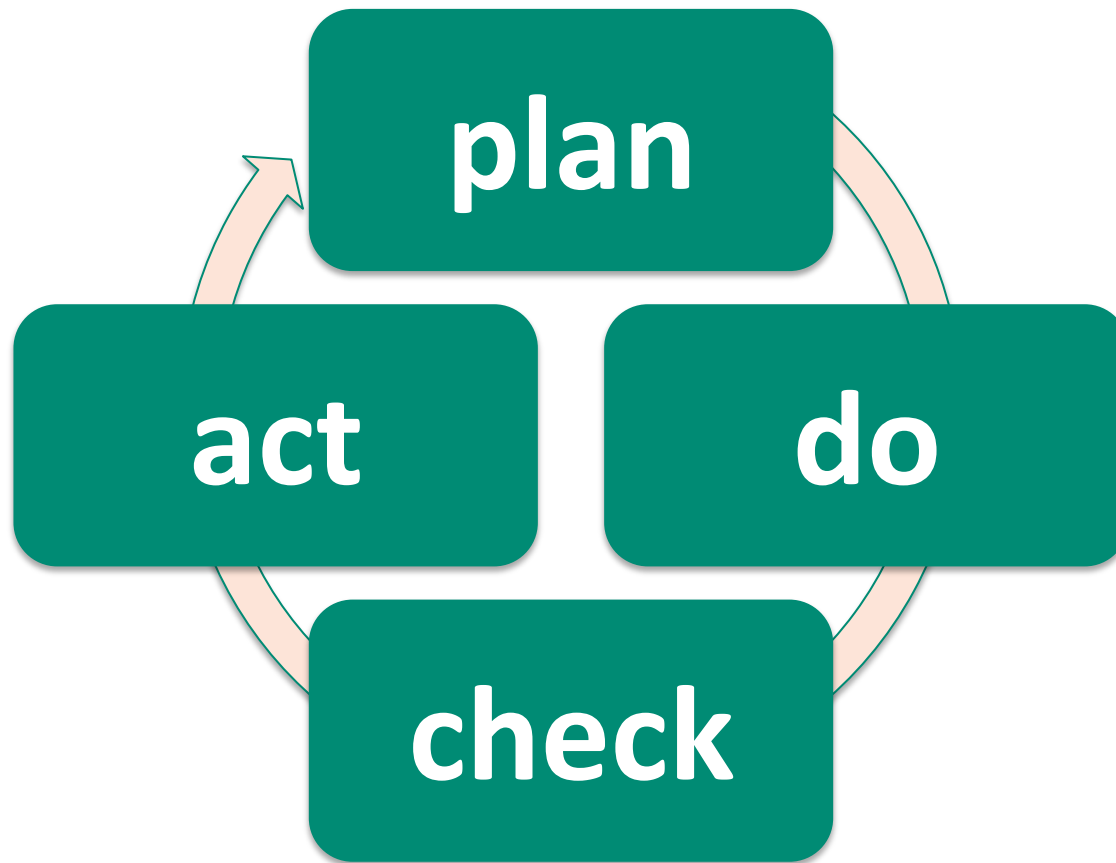
CLEANING AND DISINFECTION IN PRACTICE

Reporting:

- Used materials
- Creating materials
- What materials have been used?
- Cleaner/operator
- Date/time
- Specifics
- Signing off by supervisor and customer?
- Logs



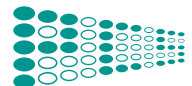
CLEANING AND DISINFECTION IN PRACTICE



CLEANING AND DISINFECTION IN PRACTICE

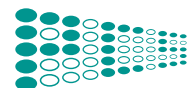
Outsourcing:

- How do you know if cleaning and disinfection is done adequately?
- Who checks and how?
- Do the cleaners know what to do when?
- Where have the cleaners been earlier?
- Hygiene rules apply to cleaners too!
- Contract
- Audit
- How is feedback handled?
- Replacing cleaners when there are absentees

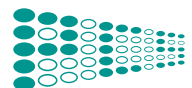


CLEANING AND DISINFECTION IN PRACTICE

- Training
 - Training in GMP
 - Personal Hygiene
 - Basic principles microbiology/disinfection
 - Dress qualification
 - Practical training cleaning en disinfection
 - Filling in logs
 - Who checks this and how?

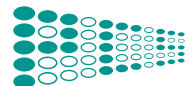
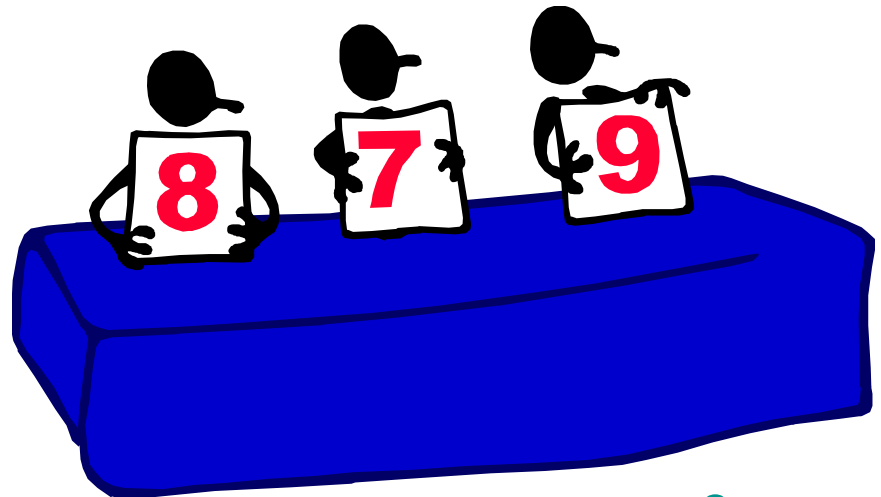


MONITORING

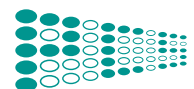


MONITORING

- How can cleaning/disinfection be monitored?
 - Log
 - Visual checks
 - Presence during cleaning
 - EM-results

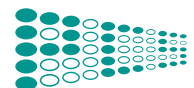


VALIDATION



VALIDATION OF DISINFECTANT

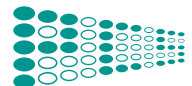
- US
 - USP 1072
 - Disinfectant should show a reduction of log 2 for bacterial spores, log 3 for vegetative bacterial cells within 10 minutes after application
- Europe
 - EN 1040, EN 1276, EN 1650 and many others
 - 3 phase program
 - Show a reduction of log 3 for viruses, log 4 for bacteria, mycobacteria and fungi
- WHO
 - No discernible guidelines



CLEANING VALIDATION (WHO)

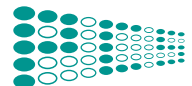
- **TSR 937 Annex 4: Supplementary guidelines on good manufacturing practices: validation**
 - **Appendix 3: Cleaning Validation (p127 – p135)**

Website: http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/



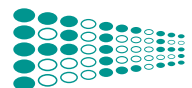
CLEANING VALIDATION (WHO)

- Setting acceptable limits should be practical, achievable and verifiable
- The rationale should be logical and based on knowledge of materials
- Additional screening may be required



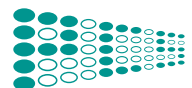
CLEANING VALIDATION (WHO)

- Commonly used criteria
 - Visually Clean
 - No more than 10 ppm of one product will be discovered in a subsequent product
 - No more than 0.1% of a therapeutic dose of one product will be discovered in a subsequent product
 - **Use most stringent!**
 - Certain allergenic ingredients and highly potent material should be undetectable by the best available analytical methods (i.e. penicillin)



CLEANING VALIDATION (WHO)

- Sampling
 - Direct Surface Sampling
 - Rinse Recovery
 - Recovery of >80% is **good**,
 - Recovery of >50% is **reasonable**
 - Recovery of <50% is **questionable**
 - Batch Placebo
- WHO prefers combination of direct surface sampling and rinse recovery
- Limits can be expressed as ppm or mcg/cm²
- Resampling should be prevented before or during cleaning



CLEANING VALIDATION (WHO)

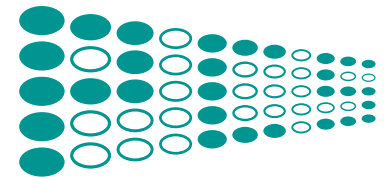
- Validated analytical methods used should be able to detect residuals or contaminants and be sufficiently sensitive to detect the acceptable level of residue and/or contaminants
- I.E.
 - HLPC
 - GC
 - HPTLC



QUESTIONS



THANK YOU FOR YOUR ATTENTION



PHARMACEUTICAL
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.....

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