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.
"Just your husband's feet will suffice Mam."
## DISINFECTANTS AND HOW THEY FUNCTION

<table>
<thead>
<tr>
<th>Desinfectant</th>
<th>Bactericidal</th>
<th>Fungicidal</th>
<th>Virucidal</th>
<th>Sporicidal</th>
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<tr>
<td>Alcohols</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
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<tr>
<td>Aldehydes</td>
<td>+</td>
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<tr>
<td>Chlorine</td>
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<td>+</td>
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<tr>
<td>Fenol-producten</td>
<td>+</td>
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<td>+/-</td>
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<tr>
<td>Quat. Ammonium producten</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>
SENSITIVITY TO DISINFECTANTS

Vegetative Cells → Easy → Enveloped virus

Mould Spores → Hard → Non-enveloped virus

Bacteria Spores
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
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

- plan
- act
- do
- check
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 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)

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 that 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