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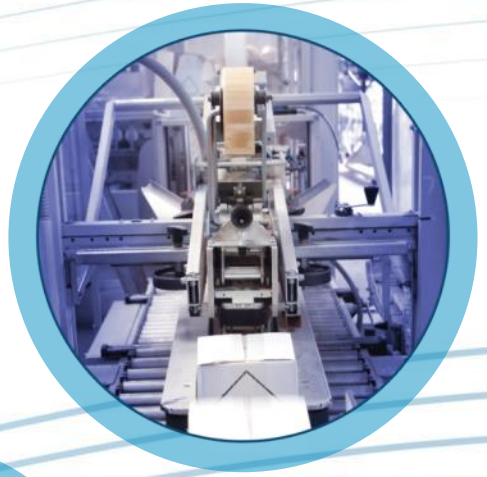
Effective Shop-Floor Oversight and Good Training Methods



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Important Aspects about

- Shop Floor Oversight
  - General Guidance and References
  - Quality Culture & Aseptic Processing at the Shopfloor
  - How to prepare Shop Floor Monitoring Reports
  - Experiences

- Effective Training Methods in Aseptic Processing
  - Lessons learnt from > 25 years
  - What works, and what not
  - Examples

References for “oversight”

FDA Aseptic Guide:

- Supervisory personnel should routinely evaluate each operator´s conformance to written procedures during actual production.

- The process simulation should be observed by the QC …

EU Annex 1 (2022)

8.16 There should be an authorized list of allowed and qualified interventions, both inherent and corrective, that may occur during production (see paragraph 9.34). Interventions should be carefully designed to ensure that the risk of contamination of the environment, process and product is effectively minimized. The process of designing interventions should include the consideration of any impact on air-flows and critical surfaces and products. Engineering solutions should be used whenever possible to minimize incursion by operators during the intervention. Aseptic technique should be observed at all times, including the appropriate use of sterile tools for manipulations. The procedures listing the types of inherent and corrective interventions, and how to perform them, should be first evaluated via risk management and APS and be kept up to date. Non-qualified interventions should only be used in exceptional circumstances, with due consideration of the risks associated with the intervention and with the authorisation of the quality unit. The details of the intervention conducted should be subject to risk assessment, recorded and fully investigated under the manufacturer's PQS. Any non-qualified interventions should be thoroughly assessed by the quality department and considered during batch disposition.

8.19 Aseptic operations (including APS) should be observed on a regular basis by personnel with specific expertise in aseptic processing to verify the correct performance of operations including operator behaviour in the cleanroom and address inappropriate practices if detected.

PDA Aseptic Processing Ptc 1

Topic E: Supervision in the Aseptic Processing Area

Problem Statement

What is the degree of oversight necessary to effectively monitor an aseptic processing area?

Recommendation

Oversight of aseptic processing should be performed by individuals who are trained and qualified in the aseptic procedures for the areas being reviewed. These persons should have a thorough understanding of the process and the potential contamination risks. This oversight is best performed by physical presence in these areas with consideration on limiting microbial contamination risks (e.g., by monitoring the areas through windows or cameras when possible).

Aseptic processing areas that contain viewing windows may allow observation of some aspects of aseptic processing from outside the aseptic processing area.

The degree of oversight needed may depend on the level of physical separation of the operators from the exposed products and product contact surfaces and the level of process automation.

Proper oversight is required but not limited to cleaning, maintenance, production on all shifts, or any activity that can negatively impact the aseptic conditions within the aseptic processing area.

The quality unit is also responsible for reviewing the oversight program for the aseptic area.

PDA Aseptic Processing Ptc 1

Rationale for Recommendation

Maintaining a successful aseptic operation is dependent on operational discipline and on the conduct of personnel in the way that they have been trained to perform, regardless of internal or external factors that may negatively influence their performance (e.g., pressure to complete a manufacturing run in a short time). Manufacturers should be able to demonstrate that operational discipline is maintained, and oversight is a key methodology to achieve this.

WHY is personnel important ?

- Personnel is running the aseptic filling line inside the cleanroom.
- They are very close to sterile product / product – and indirect product contact services
- They perform the set-up, which is in most cases a risky part in the process
- They are primary source of microbial contamination of aseptic processing areas is personnel (PDA PTC I)
- Audits – company is very vulnerable through exposure of „clean room operators“

It´s all about .....PEOPLE

… good human behaviors, and to treat all people with respect !

…. acknowledge and recognize the personnel at the shop-floor

… and sometimes there is a deficiency in „LEADERSHIP“ of the management (examples ….)

What is a BAD Quality Culture in Aseptic Processing ?

- Inadequate (outdated) Quality Management System (e.g. Senior Management is focused on sales and numbers)
- Installation of low-priced filling lines, wrong design or even disassembly from other sites
- No investment in advanced aseptic processing lines (Isolators/ RABS/ RTPs/ …)
- Supplier-Management based on a one day audit (including API supply: is very serious in case of sterile API)
- Low recognition of shop- floor personnel by supervisors and management
- No periodic QA (and supervisor) oversight

What is a BAD Quality Culture in Aseptic Processing ?

- Training and (Re) Qualification of operators not effective and convincing
- If production staff performs the QC – controls: no QA oversight and no EM surveillance monitoring
- No Feedback to operators & vice-versa no information from cleanroom operators to QA / Supervisors
- Mainly recently hired operators have to work within clean rooms
- No Bonus salary for qualified, good working operators

What is a BAD Quality Culture in Aseptic Processing ?

- Clean room staff includes part time / leasing operators
- High pressure on cleanroom operators with regard to EM-results (Risks: false- negative trending data and Data Integrity)
- Deviations/ Investigation Reports : Focus in producing a high numbers of pages without a real value for quality (e.g. Investigation Reports, Fisbone Analyses, ...) - resulting often from lacking process knowledge

What is a GOOD Quality Culture ?

- Advanced Aseptic Processing Facilities
- Good Supplier Management in place
- Recognition of shop-floor staff by management (QA and Management presence/ information/ Bonus salary/ ..)
- Long time employees
- Open-minded conversation culture and teamwork (show deviations/ CAPAs)
- Motivation (Awards as e.g. “Employee of the Month”)
- Effective Training Tools:
  - In-house illustrative videos, or purchased training videos
  - VR- Training, e.g. www.innerspace.eu

What is a GOOD Quality Culture ?

- Convincing Training sessions (e.g. impact of WL on the company /individual)
- KPI´s (Key Performance Indicators) established and displayed about aseptic working practices (EM –Trending and Deviations/ Behaviors/ Audit Findings/ ..)
- Production/ QA/ QC/ Engineering are “Partners”
- Physical presence of QA in production building (including batch record review)
- Systematic execution of Proactive- Risk analyses by a QRM team (e.g. “my” Risk Analysis, published at PDA in 2011)

What is a GOOD Quality Culture ?

- Tell the cleanroom operators they are really important !
- Interactive Training with demos and tests
- Periodic Shop Floor presence also by the upper management
- Involve personnel &request feedback – they are the experts!
- Environment within cleanroom and gowning must be convenient
- Bonus salaries for good, qualified individuals
- Motivation by recognizing their good and hard work

Experiences of Shop Floor Oversight and Mentoring (including isolators)

- Shop Floor Reports
- Benefits of a Third Party Shop Floor Oversight... *Fresh eyes often helpful*
- Structure and Topics of Report :
  - *Cleanliness/ Maintenance*
  - *Gowning of operators*
  - *Performance of Environmental Monitoring*
  - *Aseptic Operations Practices*
  - *Specific Topics for detailed review*
  - *Summarize overall impression and provide „numbers“*
- Include Pictures (in agreement with individuals, but without compromising individuals, work council agreement)
- Prepare your own videos as effective Training tools (but: legal clarification required)
- Awards for „very positive“ observations and practices executed by individuals
- Trending and display of positive, but also negative findings in a positive way
- Examples of reports are presented

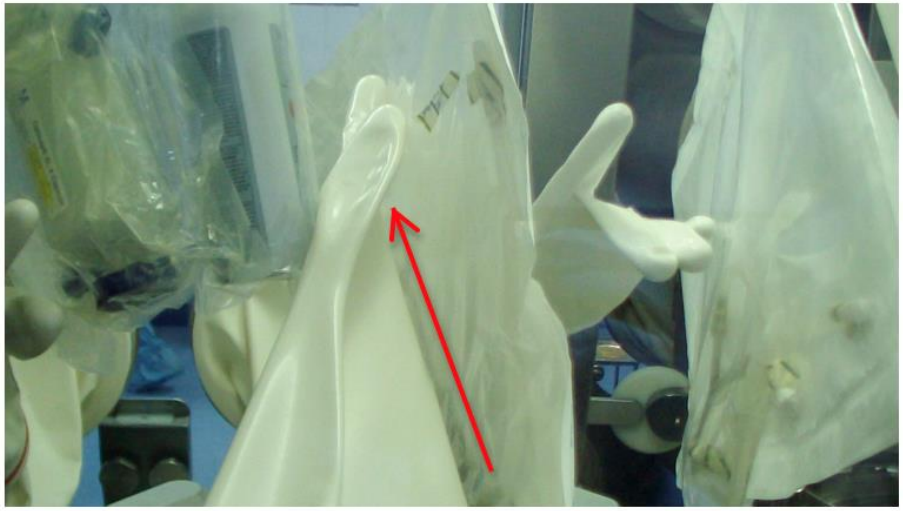
Example Shop Floor Mentoring Report: include pictures (2017)

2.5. Specific Topics in Focus of the Shop-Floor Visit (varying):

VHP Decontamination cycle

- The cycle printout has been reviewed and parameters are according to the SOP xxx. ☑
- During the VHP cycle some movable equipment parts (e.g. conveyor belts) have been moving to allow access for decontamination. Some gloves have (close) contact to bags, which have been hanging in the isolator. This could prevent sufficient access of VHP and may compromise the surface decontamination. ←
  Solution: It is already planned to use the new glove extension systems (will be reviewed in the next week during a VHP cycle)

Pictures 2: Isolator inside during the aeration cycle



Example Shop Floor Mentoring Report: conclusions

3. Overall Impressions of the Shop Floor Mentoring No. 5:

Set- Up practices of filling line is simple; disinfection procedure of isolator gloves within LF zone; passive air monitoring is now performed "in operation"; usage of disinfectant dispensers instead of contacting the spray flasks;

Review speed of isolator glove movements if "deliberately slow" enough; during filling there should be no spraying of disinfectants inside the isolator; SOP(s) require more details (and pictures) about the set-up activities of the filling line

3.1. Number of "Items for Improvements"

3 ←←←

Selected Findings of Shop Floor visits (from different sites)

- Not clearly defined & trained Hand-washing and Hand/ Glove Disinfection procedure (includes the glove disinfection before entering isolator gloves)
- Glove disinfections by operators has not been done in the same way **(critical in audits !) – prepare TRAINING VIDEOS !**

Selected Findings during Shop Floor visits (different sites)

- Cleanliness of Floors
- Maintenance of Floors and e.g. rusty door frames
- Curtains in LF Zones “worn out”
- Incorrect used “Three Bucket Method”
- No detergents used for (dirty) floors
- Rapid Movements of operators !

- **ISOLATOR:**

- No Verification of RTP (Rapid Transfer Ports) Integrity
- No Requalification of welding device for equipment packaging
- Contact of gloves with bags during VHP cycle
- Rapid movements of isolator gloves during manipulations
- Spraying of disinfectants during filling
- EM- samples within isolator not labeled

- Wrong sequence of Surface Monitoring (surfaces/ gloves)
- Insufficient number of surface monitoring samples within grade C
- Settle plates exposed under static conditions and not in operation

Effective Training – Lessons learnt

- My experiences from the past

The Auditorium : Their Expectations

Practical Lively Training in Classroom (with volunteers & demonstrations)

Prepare your own Training Videos

- With voluntary "actors“ (if legally allowed)
- Simulate correct activities and behaviors
- Simulate incorrect activities and behaviors
- Perform written tests (e.g. was this activity shown in the video correct ?)

Tell them about the Risks of NON-STERILITY and NON-COMPLIANCE

Impact of Non-sterile Product on the Market

- QC controls for release are not sufficient to assure sterility of the whole batch (sterility testing)
- May lead to adverse reactions and death of patients
- These patients may be my family members, and/or You too
- Dramatic effect on my company
  - Ban product on the market
  - FDA Warning Letter / MHRA/ Local Agencies
  - Consent Decree
- Finally also loose their job

Impact of a “poor” FDA Audit

- Inspectors might walk – several hours- through the plant
- Observe operators at the shop-floor and may do interviews
- You have to live these behaviors and incorporate
- Dramatic effect on my company
  - Ban product on the market
  - FDA Warning Letter / MHRA/ Local Agencies
  - Consent Decree
- Finally also loose their job

Tell them about : General Microbiology

- Microorganisms cannot be seen with the naked eye!
  - Visible only as a mass (colony = millions of individual cells)
  - Or with magnification by a microscope

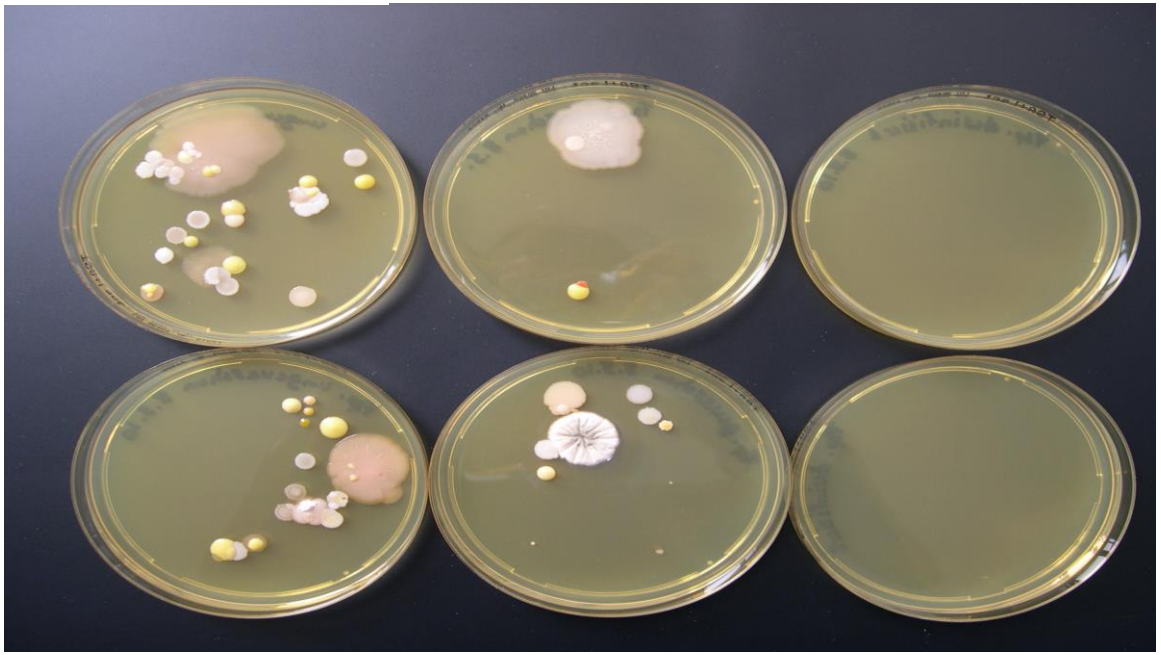
Hygiene and Disinfection

Fingerprint on Agar Plates

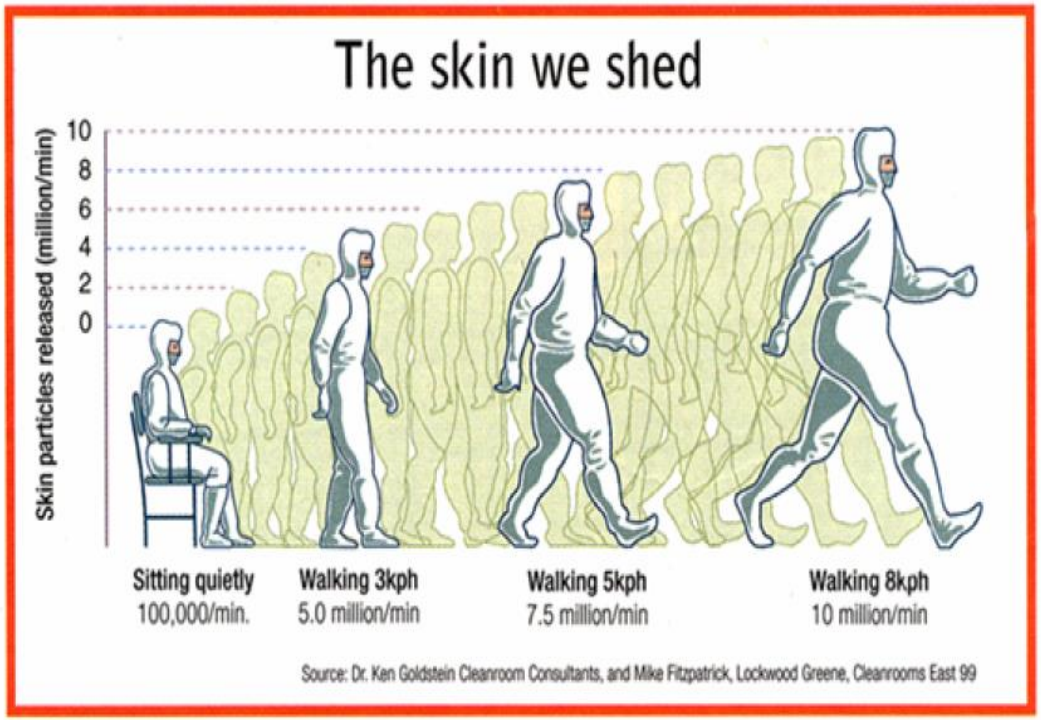
Fingers **not washed**

Fingers **washed**

Fingers **washed** and **disinfected**



Personnel … WE SHED SKIN (and BACTERIA)



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