

FDA Form 483: Irregularities in the handling of personnel and changing of clothes in aseptic production - Class A/B environment, exposed skin, combing hair

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2023.10.12-20 FDA Investigator Justin Boyd audits Indian pharmaceutical company for 10 days and shares results.

- It was found that the operator was working barefoot in the filling area, combing his hair in the Class B area, not wearing protective clothing or gloves, and exposing his skin to Class A/B conditions on more than one occasion. Confirmed, this is their standard practice? The problem is clearly systemic.
- The (main) source of pollution comes from people (operators), which account for about 75%. In order to manage, two points must be implemented
 - Correct gowning procedures and training, and demonstrate the main mistakes that operators (probably) make in a cleanroom.
 - Persons (entering the A/B zone) shall be confirmed (qualified) and/or disqualified (unqualified) twice a year (at least).
- Most of the observations related to the operator who performed the (intervention), so the (poor) gowning procedure, or the error that should not have been performed.
- For sterility assurance, in addition to process and cleanliness assurance, it is particularly important to observe and control behavior. CCTV is often used, and the behavior is supervised by the production supervisor and QA, but it is difficult to ensure that they are watching. There is a new technology to use, (probably) Google Glass.

OBSERVATION 1

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written and followed.

Specifically, during setup, aseptic filling, transfer of equipment and components, and line disassembly/cleaning in the Grade A area of xxx cap and bottle lines, xxx and xxx used to aseptically fill U.S. marketed drug products, the following instances of improper aseptic processing technique were observed:

1. On October 12, 2023, and October 17, 2023, operators working in the grade A area of xxx performing line set up, aseptic filling and equipment transfer and cleaning, were not wearing goggles resulting in skin exposure to the Grade A area.
2. Operators working in the Grade A area on October 12, 2023, were observed to have exposed skin on their nose throughout the entire aseptic filling process on xxx during the filling of xxx . Batch # xxx These operators repeatedly performed xxx interventions that included leaning over the filling line and open sterile bottles.
3. On filling line xxx during the aseptic filling of xxx. Batch # xxx an operator was observed standing outside of the filling line in the extended Grade A LAF scooping sterile empty bottles from an open non-sterile bag into a shoot, extending outside of the filling line. that feeds into the bottle xxx On October 19. 2023, this operator was observed bent over a bag of sterile bottles, reaching his gloved hand into the bag holding the sterile bottles. taking scoops of bottles out and placing them into the xxx 96 times in 24 minutes.

4. On October 19, 2023, an operator was observed performing continuous interventions in the (b)(4) using the non-sterile xxx and xxx, for 10 minutes and 15 minutes consecutively on xxx during the aseptic filling of xxx. Batch xxx. They were also observed placing a partially filled bag of extra caps onto the filling and the cap xxx where the bag extended upward line between the xxx blocking/interfering with first pass air to the surrounding area.
5. On October 12, 2023, on filling line xxx, during the aseptic filling of xxx Batch xxx, an operator was observed reaching over and around the Grade A filling line xxx holding the sterile xxx used to cap bottles of aseptically filled xxx drug products. The operator's gowned forearm and elbow was observed brushing up against the inside of the xxx and the sterile xxx. This same operator was also observed bumping the inside of the (b) (4) with their non-sterile gown.
6. An operator, working on filling line xxx. xxx Batch xxx, on 10/12/2023 was observed leaning over open sterile bottles on the filling line and reaching over the xxx b) (4) where their head and torso were inside the Grade A filling area, and where they used a blue cloth to wipe the entire area of the xxx holding the filling and xxx. The blue cloth was observed brushing up against the filling and xxx.
7. Operators were observed taking bags of sterile components which were stacked up against the wall of the Grade B area outside of xxx and placing them into the Grade A area without disinfecting them, then opening them and pouring their contents into one of the xxx where the outer part of the plastic bag they were packed in touched the inside of the xxx and the sterile component that was poured into that xxx This was observed on October 12, 2023 during the aseptic filling of xxx, Batch xxx and on October 19, 2023, during the aseptic filling xxx , Batch xxx.
8. Operators were observed stopping the filling machine and wiping the bottle conveyer and surrounding area of the Grade A filling line on xxx during the aseptic filling of xxx. Batch xxx, using both hands, while reaching over open sterile unfilled bottles. The bottles were then permitted to remain on the line and progress through filling and capping.
9. An operator was observed using a non-sterile xxx to stand up open, prefilled, fallen bottles on filling line xxx during the aseptic filling of xxx Batch xxx and xxx, Batch #(b) (4). The bottles were permitted to remain on the line for filling despite falling over where the top of the bottle came in contact with the conveyer.
10. During the setup of the aseptic filling line, xxx, an operator was observed using his gloved hands to manipulate the xxx that hangs inside the bottle xxx and comes in direct contact with the sterile bottles in which the aseptic xxx is filled into.
11. An operator was observed reaching over the area near the filling xxx and filling line on xxx to place an environmental monitoring stand on the line. their entire head, torso and right arm were observed to be in the Grade A filling area.
12. The xxx enclosing the extended LAF Grade A area of xxx was observed to have brown residue at the top where the xxx connects to the HEPA filtration system. The xxx surrounding the extended LAF Grade A area of xxx was observed to be disconnected from where it was xxx creating a gap allowing free air passage from the Grade B area to the Grade A area of the extended LAF. This was observed during an xxx intervention.
13. Operators were observed reaching over open bottles with the non-sterile xxx to perform interventions at the incoming bottle xxx to pick up fallen bottles, push jammed bottles, or change environmental monitoring plates during aseptic filling on xxx. Similar interventions were observed being performed on bottles following the placement of the sterile (b)(4) before the final cap was affixed.
14. On October 16, 2023, an operator working in the Grade B area, surrounding the aseptic filling line. xxx. was found not wearing a nose mask under their Grade B gowning. Per procedure

KHIL/RB/PD/048, entitled, "Entry and Exit Procedure for xxx Filling Area, September 21, 2022, operators are to don a nose mask prior to gowning xxx e Grade B area.

15. Per procedure KHIL/RB/PD/049, entitled, "Entry and Exit Procedure for xxx Manufacturing Area, August 13, 2023, personnel are required to remove company uniform and don headgear, shirt, trouser, booties, hand gloves and footwear prior to entering the Grade C area. Review of the CCTV footage from October 3 and 4t, 2023, showed personnel working in the Grade C xxx area where materials are passed into the Grade B filling area. Operators did not wear the specified gowning, gloves, and were working barefoot as they transferred materials into the Grade B area for filling line xxx The deputy manager of production confirmed that this is their standard practice.

16. Additionally, this room has a Grade A LAF hood for washing small filling machine parts. An operator was observed standing in the hood and another operator was observed taking his hat off and brushing his hair while in the hood.

17. Upon arrival at the entrance to the Grade C area for xxx on October 13, 2023, there were gloves in wet trays. Production personnel reported the gloves had been washed

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