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Is a Dirty Swab a "Visually Clean" Failure?

The purpose of visual examination as part of a cleaning validation protocol is to confirm that the equipment, when used for manufacture, is compliant with 21 CFR 211.67(b)(6). It is a reasonable expectation that if equipment should be visually clean at the beginning of manufacture, it should also be visually clean at the end of cleaning. This inspection, of course, involves inspection of equipment surfaces for visual cleanness.

One question that sometimes comes up during the execution of a cleaning validation protocol is "What does it mean if the inspected surface is visually clean, but a swab of the same surface is not visually clean? Is this a failure of the protocol?"

To answer that question, one must understand what happens to residues on the surface when they are transferred to a swab in a swabbing procedure. If the swab head itself has a total surface area of 2 cm^2, and the swabbed surface has a surface area of 100 cm^2, then all the residue that was originally present on a larger surface area becomes "concentrated' on a much smaller surface area. Using the surface areas mentioned, a surface might contain a residue at an average level of 0.5 $\mu g/cm^2$. At this level, most people would expect the surface to be visually clean under most circumstances. If that entire residue were transferred to a swab, the average residue level on the swab would be 25 $\mu g/cm^2$, a level that most people would say is readily visible. (Note: This does leave out the aspect of the swab being wet and hence the residue being not as readily visible, but basically that does not undermine this argument.) This is an argument for saying that a "dirty" swab does not necessarily cause a protocol to be a failure provided the swabbed surface itself was visually clean before it was swabbed. Of course, once the surface is swabbed, there is no way to go back and check whether the surface really was clean. This only underscores the importance of having two people do a visual inspection of the each surface that is visually examined.

A visually "dirty" swab can have other implications for manufacturing, however. In some cases when the swab head is dirty but the swabbed surface is clean, it is due to rouge on stainless steel equipment surfaces. The rouge is not readily visible on the equipment surfaces, but becomes readily visible as a brown/black deposit when concentrated on the swab head. If the residue on the swab head can be analyzed as iron (ferric and ferrous) and if the other measured residues are within their acceptance limits, this can usually confirm rouge as the source. Even this is not a cause for a cleaning validation failure. However, it might be suggestive for the need for derouging/passivation of stainless steel surfaces in the near future.

One can go one step further in this analysis and ask "What if there is rouge on the equipment surfaces that is readily visible? Does this constitute a cleaning validation failure?" Even in this case it should be apparent that unless the rouge is directly related to the specific cleaning event as part of the protocol, the presence of readily visible rouge on equipment surfaces should not constitute a cleaning validation failure. If the visible residue on the surface can be definitely be determined to be rouge, this is a case in which an argument can be made that the specific cleaning validation run is not valid. The cause of the visible residue was not an ineffective cleaning process. Rather, the cause of the visible residue was ineffective preventive maintenance (that is, lack of an appropriate derouging/passivation program). The solution is not to revise the cleaning procedure and begin a new protocol; rather the action called for is to derouge and passivate the system prior to continuing with the previous protocol.

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This last situation points to the importance of doing a "baseline" visual examination on all equipment surfaces that are to be visually examined during the cleaning validation protocol. If those surfaces are not clean prior to protocol execution, then one cannot reasonably expect that they will be clean after protocol execution.

As with other Cleaning Memos, this one is not designed to prescribe certain practices or to proscribe certain practices. Rather the intent is to help scientists involved in cleaning validation to understand more fully what is involved in various practices.

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