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Manual Cleaning Issues – Part 1

As recognized in both the FDA and PIC/S guides on cleaning validation, there are special considerations which should be taken into account for cleaning validation of a manual cleaning process. This Cleaning Memo will address issues related to the definition of manual cleaning, as well as issues related to obtaining consistency in manual cleaning.

The first issue to clarify is that contrary to a common misconception, manual cleaning is not the opposite of CIP cleaning. For clarification, there are two major elements which can be used to describe a cleaning method. One element is the extent of automation. There are fully automated processes (well, almost fully automated because generally an operator is still required to select a cycle and push a button), and there are fully manual processes (where all parts of the cleaning procedure are performed by an "operator"). Of course, there are some semi-automated procedures (I assume we could technically call these "semi-manual", but that term is generally not used) in between the extremes of this continuum, such as use of a "portable" CIP skid, where some (but not all) important tasks are done manually.

The second element involves whether the equipment is cleaned in place, or alternatively moved to a different location to be cleaned out of place. (Note that I make a distinction between "cleaning in place" and "CIP"; the latter term specifically refers to an automated process involving spray devices, recirculation pumps, etc. Something can be "cleaned in place" without the use of a CIP skid.) Usually when equipment is cleaned out of place, there is a degree of disassembly involved. Unlike the automation/manual continuum, there is no continuum involved here. However, it should be noted that for some equipment, some parts may be cleaned in place and some parts may be cleaned out of place. For example, with a tablet press, some parts may be disassembled and moved to a sink or parts washer for cleaning, while the major portion of the tablet press may be cleaned in place (in its location for manufacturing).

For clarification, we can then combine the elements of degree of automation with the element of "in place" vs. "out of place" cleaning to have a variety of cleaning methods, as indicated below (with examples).

Automated clean in place (a CIP skid for a bioreactor)
Manual clean in place (manually operated spray hose for a mixing vessel)
Automated cleaning out of place (automated parts washer for disassembled small parts)
Manual cleaning out of place (manually brushing disassembled small parts in a sink)

These four methods are given as extremes, remembering that the element of automation may be a continuum.

The above discussion is one reason why I usually like to clarify the definition of manual cleaning. Manual cleaning is a cleaning process where a significant (or high) degree of operator skill and technique are required to assure the consistency of the cleaning procedure. (Note: This is not to say that operators for automated processes are not highly skilled; it just that pushing a button to start a fully automated cycle is generally not the major issue in the consistency of a fully automated process.)

This leads to the second issue for clarification, which involves what I consider the major concerns in obtaining consistency in a manual cleaning process. Those concerns are initial design of the cleaning process, detail in the procedural steps in the cleaning SOP, and training (and retraining) of the manual cleaning operators. For

the first concern (design), it is important to include the operators in the design phase in order to make sure that the designed cleaning process is something that is implementable. A second reason for including the operators is that the operators may be aware of certain issues in cleaning that the person responsible for designing the cleaning process is not aware of.

For the second concern (the SOP itself), there should be adequate detail in the SOP such that each different operator can carry it out the same. For example, “brush each part with 1% Detergent ABC” may not be adequate. It may be necessary to specify things like “overlapping strokes” and/or to give a time or number of strokes required to make sure that the part is adequately cleaned. (Note here that I am not a big fan of “brush until no residue is visible”; “no visible residue” at the end of the washing step may be a necessary condition for the part to be adequately cleaned, but it is not a sufficient condition. During the detergent brushing step, a part may look visually clean and still be visually clean after the rinse step, but on drying it appears visually dirty. So if after brushing in a defined manner for a time or number of stokes, the part is visually dirty, then clearly something is wrong; however, just specifying brushing until visually clean may not be enough.)

The third concern for consistency of manual cleaning is training and retraining. Training may include a “qualification” step whereby the operator actually cleans a part and residues on that part are measured and compared to an acceptance criterion for that qualification procedure. That is a possibility; however, my preference is to spend that time on training to assure that the operators are performing the process correctly (as compared to measuring residues once to assure they are performing the process correctly). Retraining may be done based on an event (such as a clarification of language in the SOP) or based on time (such as yearly retaining). If yearly retraining is done, it is not necessary to repeat all elements of the initial training. However, if there is a video of the "correct” cleaning procedure (which may have been used in initial training), it is helpful to view that video. This yearly training should probably focus on those elements of the cleaning procedure where “procedural drift” is most likely. It is also a time to help ensure that ideas for improving the cleaning process (hopefully without major validation efforts) are expressed. (And, if ideas are rejected because they require major validation efforts, the reason should be clearly communicated and the operator praised for proposing improvements. You don’t want to discourage possible suggestions for improvements in the future. Furthermore, those improvement ideas, even if rejected, should be captured somewhere in case significant validation efforts are required in the future.)

The purpose of the Cleaning Memo is to help clarify some key issues in manual cleaning processes and their validation.