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Adequate "Documented Evidence" for Cleaning Validation

A short definition of cleaning validation is "documented evidence with a high degree of assurance that a cleaning process will consistently produce equipment and products meeting predetermined quality specifications." In an internal audit or regulatory investigation, a key is reviewing that "documented evidence". What could be included with that documented evidence?

One usually first thinks of the cleaning validation summary report. This is an important item. However, there is much more to the "documented evidence" than just this summary report. The consistency of the cleaning process is not demonstrated just by the three validation runs. I don't want to get into semantics, but it may be useful to think of the three validation runs as "confirming" the consistency of the cleaning process. Other documents that could be considered part of the relevant "documented evidence" include the following:

- Cleaning validation master plan or high level policy
- Cleaning validation procedure
- Cleaning procedure or cleaning instruction
- Cleaning process development report or technology transfer report
- Cleaning validation protocol
- Analytical procedure
- Sampling procedure
- Report on rationale for selection of sampling locations
- Report on rationale for challenges (e.g., worst cases) to the cleaning process
- Analytical method validation
- Analytical/sampling method recovery
- Limits calculation report
- Deviation investigation report
- Training records
- Change control report
- Monitoring records and/or trend reports
- Revalidation report and/or annual cleaning review report

Certainly under the new FDA investigation program, a key point to consider is the cleaning validation master plan or high level cleaning validation policy. While not absolutely necessary (although I believe it is a practical necessity), this higher-level document ties together most of the items listed above. One would question, for example, whether a cleaning process can be considered validated (beyond the initial validation protocol) if it is not covered under a change control policy/procedure. Supporting the higher-level policy may be a more specific cleaning validation procedure document.

Another important document is the cleaning process procedure or instruction (or whatever the detailed cleaning process followed by the cleaning operator is called in your facility). One may have excellent validation data (all the swab and rinse samples meet the properly calculated acceptance criteria), but the cleaning process may be inadequately detailed and controlled such that there is no reasonable assurance that the cleaning process will produce the same data if carried out in the future.

The rationale for a cleaning process development report is twofold. One is just to provide future scientists in your company with a good rationale on how the cleaning process and the various parameters (cleaning agent, cleaning agent concentration, times, temperature, hold times, etc.) were selected (and while not critical to the validation investigation, regulatory authorities may also ask for this information). A second reason is to provide assurance that the cleaning validation will be successful once the protocol is executed. The execution of the cleaning validation protocol should not be viewed as an experiment to test whether the cleaning process is effective or not; rather the "experiments" should be performed before the execution of the protocol, in order to have a high degree of assurance that the cleaning process will be successfully validated when the cleaning validation protocol is executed.

Other protocol related documents, such as the cleaning validation protocol itself, analytical procedure(s), sampling procedure(s), a report on the rationale for selection of sampling locations, a report on rationale for challenges (e.g., worst cases) to the cleaning process, analytical method validation, sampling/sampling method recovery, limits calculation report, training records, and any protocol deviation investigation report, may exist as "stand alone" documents (e.g., analytical method validation), but some may also just be incorporated into the cleaning validation protocol (e.g., justification for sampling locations).

Other documents related to demonstrating consistency after initial validation include the training records (particularly for retraining and for operators in manual cleaning processes), monitoring/trending after protocol execution, process related deviations/investigations, change control, and revalidation.

The purpose of this Cleaning Memo is not to proscribe certain ways to document cleaning validation, but rather to consider all the evidence that can be part of the assurance of consistency of a cleaning process. This Cleaning Memo also serves as a reminder that any of these documents may be requested as part of an audit or investigation of cleaning validation for a process or a facility.