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Revalidation

The 1993 FDA cleaning validation guidance document calls for validation procedures to address "when revalidation will be required". What, then, are the appropriate conditions for revalidation of a previously validated cleaning process?

As a general rule, the requirements for revalidation for cleaning processes should follow the same principles as revalidation for general process manufacture. After all, cleaning validation is just a subset (albeit a highly specialized subset) of manufacturing process validation. How does this ordinarily work out?

First is the general principle that revalidation should be done on any significant change in the cleaning process. What is a "significant" change and what is a minor change is open to some interpretation, but there are certainly a large group of changes that most people would agree are significant, such as a change from a static spray device to a dynamic spray device or a change from solvent-based cleaning to aqueous-based cleaning. In such cases one is typically going to perform three cleaning validation runs as part of the protocol execution for this "new" cleaning process (although there typically would be a variety of prequalification studies performed to confirm "validatability" of the new cleaning process). Based on previous studies, it may be possible to reduce the number of swab sampling locations for the revalidation protocol. In one sense, with a "significant" change, one is not *re-validating* an existing cleaning process, but rather validating *for the first time* what is a new cleaning process

There is probably another group of changes which most people would consider minor, and would be handled by a change control procedure. This may include a small change in cleaning agent concentration, an increase in cleaning time, or a change in the supplier of manual cleaning brushes or wipes. Such changes may be done with a simple evaluation and documentation of the changes, but may include lab evaluations and perhaps even one confirmatory validation run (again, perhaps with a reduced number of swab sampling locations).

I'm sure there are certain changes where reasonable scientists would disagree as to the significance. Part of this may be due to the experience base of those making the decision, and part may be due to the specific circumstances in which the change is being evaluated. However, whether a change is viewed as significant or minor, in both cases the effect on the cleaning process is going to be evaluated and documented. And, in cases of both minor and significant changes, training or retraining may be needed.

The second type of "revalidation" is a periodic review, typically called a "cleaning review". This may be done every year, for example, and it could be either a part of the annual product review or could be a separate review. The "cleaning review" includes an evaluation of relevant data from the review period that may be an indication of whether or not the cleaning process is in a "state of control". Data reviewed may include:

- Routine monitoring
- Change control
- Deviations
- Corrective and preventive actions
- Equipment maintenance

- Training records
- Product quality records

If a review of this data demonstrates that the cleaning process is still in a state of control, then the data should be summarized with a conclusion that the cleaning process is still in a state of control and that the cleaning process is still validated. On the other hand, if a review of the data indicates that the cleaning process is not or may not be in a state of control, an investigation into the cleaning process should be done. Corrective and/or preventive actions should be taken to bring the cleaning process back into a state of control. This may involve execution of one or more cleaning validation runs.

One exception to this may be fully manual cleaning processes. Since one of the main issues with consistency of such manual cleaning processes is consistency of the cleaning operator, it may be appropriate to repeat one cleaning validation run on a yearly basis. It should be noted, however, that if one manual process is used to clean several different products, and if cleaning validation of those different products has been done separately, a yearly challenge using that manual cleaning process on *only one* of the products should be adequate to demonstrate "revalidation" of the cleaning process for each of the products cleaned. In such a case, however, it would be prudent to choose a different product for the "validation confirmation" each year.

That said, there is nothing that prevents a company from performing one or more validation runs on each cleaning process every year or on a less frequent basis (every two years, every three years, and so on). However, provided that the regular cleaning reviews provide adequate evidence of the process being in a "state of control", there are probably more effective ways to improve the quality and consistency of manufactured products other than repeating a cleaning validation protocol.