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Campaigns and Dedicated Equipment

Campaigns and dedicated equipment may get special treatment in cleaning validation. For clarification, dedicated equipment is equipment used to make only one product. A campaign is a series of consecutive batches of the same product manufactured in a piece or train of equipment. In a sense, "dedicated equipment" is just a special case of a campaign (it's just one continuous campaign). When considering campaigns, it's usually the case that when you end one campaign and begin another, cleaning validation is required to prevent cross-contamination of different products. What is of interest, however, is what has to be done for cleaning and cleaning validation between batches (lots) of the same product within a given campaign.

Here's what regulatory documents say about this issue. The FDA cleaning validation guidelines specify that when cleaning "between lots of the same product", visually clean is enough, and furthermore that "validation" is not required. There are two possible interpretations of this. First, cleaning validation is not required, but if you choose to do cleaning validation, visually clean is sufficient as an acceptance criterion. A second interpretation is that cleaning validation is not required, but that a visual examination, similar to that required before use in 21CFR 211.67(b)(6), should be performed after each cleaning.

The proposed European guidelines discuss cleaning in "batch-to-batch" production, but do not echo the FDA guidelines about whether validation is required. Rather, proposed Annex 15 states that "it is not necessary to clean after every batch", but that "cleaning intervals and methods should be determined".

Regardless of these regulatory guidelines, for cleaning between lots (batches) of the same product, manufacturers would be prudent to evaluate these two issues: (1) the need to validate, and (2) the use of only visual examination if validation is performed. These will be covered in the reverse order.

Here are possible things to consider in campaigns that might indicate the need for more than just visual examination between lots of the same product for validation purposes:

1. Are the worst case ("hardest to clean") locations accessible for visual examination? If not, one should consider other means of evaluation, such as rinse sampling.
2. Is there documented evidence or concerns about build-up of microbial residues? If so, one should consider microbial sampling as part of the cleaning assessment.
3. Is there documented evidence or concern about build-up of unacceptable degradation products, which could be present at objectionable levels but still not be visible to the eye? If so, one should consider sampling for those degradation products.

If any of these concerns are documented and valid, then it makes sense to consider a formal cleaning validation protocol to demonstrate that the cleaning procedure is a good one.

The other issue is whether cleaning validation is required at all. The rationale for why it should not be considered is that cross-contamination of actives is not an issue. In such a case, cleaning may not be a critical processing step. However, the concerns raised previously (such as possible microbial contamination, contamination from the cleaning agent in inaccessible locations, and/or unacceptable degradation products)

may cause one to reclassify the cleaning process as a critical process.

In addition to these concerns, some companies may choose to validate cleaning in campaigns for internal reasons, such as having one quality standard for all products. If "visually clean" is the main residue acceptance criterion, then a cleaning validation protocol is simplified considerably. This is not to say that life will be simple with just visual examination. The two most time-consuming tasks in cleaning validation are designing the cleaning SOP and the sampling/analysis of residues. Using a "visually clean" acceptance criterion reduces the workload for analytical/sampling, but offers only a slight reduction in effort for designing the cleaning process. And, as proposed Annex 15 suggests, it is still necessary to design an adequate cleaning process.