

August 2002 Selecting Swab Sampling Sites

If sampling is designed to identify potential residues on cleaned equipment surfaces that might be transferred to the next manufactured batch, then it is necessary to select swab sample sites that can appropriately provide that information. This Cleaning Memo will cover selection of sampling sites for swab sampling (next month's will cover an equivalent subject for rinse sampling).

There are generally five types of sampling sites (or sampling locations) that can be considered for cleaning validation protocols. They are:

1. **Most difficult to clean locations:** This is one type of a "worst case" location. Certain locations in the manufacturing equipment may be more difficult to clean, and therefore more likely to show residues first if cleaning is inadequate. For example, if a lower than specified concentration of cleaning agent were to be used for cleaning, certain locations may still be acceptably clean, but there might be other locations (the most-difficult-to-clean locations) where residues are at unacceptable levels.

How does one select these locations? They can be selected based on good scientific (typically engineering) judgment. For example, any junction of two materials is probably more difficult to clean than a flat expanse of one material. Another example might be the underside of the lip at the top of a vessel. A second method of selecting these locations is prior experience. This prior experience may be anecdotal (the cleaning operators tell you the bottom of the agitator blade is always most difficult to clean). Prior experience may also include information one learns from prequalification studies either that resulted in a failure or that had been designed (by making them less stringent) to identify the "first-to-fail" locations.

2. **Locations that are likely to produce non-uniform contamination of the next batch:** This is also a worst case. The non-uniformity referred to is NOT non-uniform contamination of the process equipment prior to cleaning; rather it deals with the possibility that with certain equipment surfaces, residues on those surfaces may preferentially transfer to only a limited portion of the next batch. This may occur on items such as filling needles and discharge chutes.
3. **Representative functional locations:** These are not necessarily worst-case locations. However, it is prudent to select "representative" functional locations in the equipment for sampling. This might include, for example, vessel sidewalls, vessel dome or lid, ports, valves, and agitator blades. At least one sample from each representative functional location should be considered. This can be particularly helpful in addressing any cleaning validation failures.
4. **Representative materials of construction:** These are also not necessarily worst-case locations. However, it is prudent to select different materials that are present in the equipment, such as stainless steel, glass, and/or various plastics or elastomers.
5. **Most likely to be recontaminated locations:** This only applies to the cleaned equipment hold time (CEHT) studies. In sampling at the end of the "storage" or "holding" time of cleaned equipment, one should consider how the equipment can become recontaminated, and where that contamination is most

likely to be. These sites are not necessarily the most-difficult-to-clean sites (as given in case #1 above).

Note that in many cases certain categories may overlap. For example, an agitator blade may represent both a “most-difficult-to-clean” location and a representative functional location.

While the specific swab sampling locations should be specified in the cleaning validation protocol, it is preferable to have a separate document justifying the selection of those specific swab sampling locations for that protocol or for a given piece of equipment.

This Cleaning Memo is designed to stimulate thought on the proper selection of swab sampling sites for pharmaceutical cleaning validation protocols. It is the responsibility of each facility to select sample sites that provide appropriate information in determining the cleanliness of the cleaned equipment.