Cleaning Memo for October 2018
Timing for Swab Sampling in a Protocol?

In performing swabbing *for chemical residues* after completion of a cleaning process in a cleaning validation protocol, is the timing for taking the swab sample critical? In the tradition of being a consultant paid by the hour, the *correct* answer is "It depends."

When I do swab sampling at the end of a cleaning process, I will usually wait until the equipment is dry. One reason for this is that I may also do a visual examination at the same time, and a visual examination under dry conditions is usually the more stringent. Another reason for waiting until equipment is dry before starting swabbing is that recovery studies are usually done on dry coupons, so I would want my swab sampling in a protocol to reflect that same condition.

Another issue that may cause a delay in swab sampling of the surface is the traditional conflict from people who are doing swabbing for microbiological purposes and those who are doing swabbing for chemical residues. This conflict revolves around which is done first. The argument for doing microbiological sampling first is that it is that the people swabbing for chemical residues may not be aware of microbiological contamination issues. The argument for doing swabbing for chemical residues first usually involves use of TOC as the analytical method. If after microbiological sampling the surface is "cleaned" with an alcohol/water blend, the air in the environment around the sampling location may have levels of the volatile alcohol which could cause high TOC values in the swab sampling. The purpose of this Cleaning Memo is not to resolve this "conflict", except to say that proper training and proper procedures should help resolve those concerns.

In general, the issue of the timing of swab sampling for chemical residues should be that sampling should be as soon as practical. For example, it is always appropriate from an operator safety perspective for equipment rinsed at elevated temperatures to wait until the equipment cools down considerably. In addition, swabbing as soon as practical avoids the situation where, despite all the warning placards about the validation status, the equipment is used for product manufacture *before* swab sampling is performed.

This brings us to the main reason for this Cleaning Memo. It is possible that residues on surfaces may degrade considerably due to exposure to such elements as light or air. If such degradation *after* completion of the cleaning process is real, we are now talking about a real concern. That concern is more valid if the analytical method used is a specific one, such as HPLC. The longer we wait to swab sample the surface, the lower our analytical values might be. The end result may be that we pass the acceptance criterion when it would have failed if we had swabbed earlier. Now it might be countered that if we sample immediately after the cleaning process, the active will still degrade on the equipment before the next use. And then we will have to evaluate the safety of that degradant.

For the vast majority of cases, it is probably the case that this degradation issue does not apply. So, let's return to the main issue. And the answer is that we probably already have data showing the maximum acceptable delay time for swabbing for chemical residues. When a swab recovery study is done, there is usually an interval between the time of spiking the chemical material and the time of swabbing the coupon. That time could be the starting point for setting a maximum "hold time" for sampling. Some may record the end of the cleaning process as the time at the end of draining of the equipment, some might record it as the end of an airblow, and some might record it as the end of drying. Obviously, if in a sampling recovery study the chemical material is spiked with a volatile organic solvent, the time from spiking until dryness is minor as compared to spiking with an aqueous solution. In any case, the time between dryness on the coupon and initiation of swabbing in a recovery study provides a reasonable estimate of the maximum time that should be allowed for swab sampling in a cleaning validation protocol for the cleaning process itself. That is, if I allow coupons to dry 18 hours in a recovery study, then in a cleaning validation protocol I should perform swab sampling within 18 hours.

There may be other considerations, such as whether the equipment is maintained under nitrogen after cleaning, thus reducing the likelihood of any degradation. Furthermore, if I have concerns about degradation on surfaces after cleaning, I might use TOC as my analytical method (assuming the chemical species does not degrade all the way to CO_2). Finally, I might decide to do formal studies and evaluate residues on a spiked surface as a function of time. In such a study, I could either prepare replicates at an L3 (amount per surface area) level, and swab different replicates over a certain time (such as over four days). Such a formal study may be useful to provide additional support for my maximum "hold time" before swabbing.

Note that this issue of degradation after completion of the cleaning process does not apply to rinse sampling if the sample is the last portion of the final process rinse. However, if the rinse sample is a separate sampling rinse after completion of the process rinse, then similar principles are generally applicable.