Cleaning Memo for December 2019
Issues in Rinsing – Part 2

This Cleaning Memo is a follow-up to the November 2019 Cleaning Memo, and focuses on the impact of an understanding of rinse sampling and its effect on rinse sampling *recovery studies*. Please read this only after reviewing Part 1. In that first part we discussed that the objective of the washing step in an *ideal world* was to remove all residues from equipment surfaces such that they could be readily removed from the equipment in the rinsing step. If that were the case, then the only residue remaining on equipment surfaces would be due to final rinse solution left in the equipment before drying. But, we also discussed that there may be situations where soils which initially were captured by the washing solution were redeposited during the rinsing step. And, I should add that there probably are situations where we have designed our cleaning processes with the goal of capturing all soils in the washing solution, but we have missed items like dead legs, have misjudged the levels of soil in certain equipment locations, or could not meet acceptance criteria adequately (with a *reasonable* margin of safety) with that cleaning process. So, what does mean for sampling recovery studies?

Typically, sampling recovery studies are designed to *simulate* in some way the rinsing process. They may involve spiking a coupon, suspending it above a clean collection vessel, and then passing a fixed amount of rinse solution across the coupon to collect it in the vessel below. Or, they may involve spiking the bottom of a clean vessel, adding rinse solution to it, and then mildly agitating it to simulate time and flow of the final rinse. There certainly are other possibilities. But most involve application of spiked residues *in solution* to a surface, *drying* the spiked solution on the coupon, and then *approximating* a rinse situation. The question arises "In what way does *drying* the residue on the surface simulate the rinse situation?"

Let's consider the answer to that question in situations where the cleaning process involves a CIP system, and the rinse sample is the final portion of the final *process rinse*. In what sense is doing a recovery study on *dried* residues applicable? The best that could be said is that in most situations a rinse recovery percentage on dried spiked residue represents a *worst case* (a lower recovery percentage) as compared to the actual sampling conditions. I can live with that. In addition, since the value of the residue measured in the rinse sample taken in this manner represents a possible worst case as compared to a separate rinse sample taken after the process rinse is complete, that provides additional support for doing a rinse recovery using dried residue. If I tried to do a rinse recovery with a spiked coupon that was *not* dried, I am open to the objection that my rinse recovery procedure might not pick up residue that was *not* adequately captured by the washing solution.

Let's move on to the situation where I'm performing a separate sampling rinse (SSR) *after completion of the process rinse*. In this situation, I will generally choose to perform my visual inspection and swab sampling before I perform my SSR. Since ordinarily I prefer to do a visual inspection on dried surfaces and since generally I prefer to do swab sampling on dried surfaces, the equipment will be dried before I perform my SSR.

Therefore, a rinse sampling recovery on dried spiked residue should be applicable. Let me bring up a few caveats in this particular situation. One is that I want to make sure the swab sampling and/or visual inspection do not interfere with the integrity for that type of rinse sampling. Secondly, if I swab the surface I will remove residues that could have been picked up by the SSR. However, providing my swab sample passes, this should not affect the validity of the rinse sample (provided that rinse sample also passes). Assuming the rinse sample limit was based on the same L3 value ($\mu g/cm^2$) as the swab limit, and assuming the swabbed area is small as compared to the rinsed area, it should not affect the validity of a protocol using this approach.

Here is a *second* situation for use of a SSR. What if I choose to *not* perform swab sampling? Could I then choose *not* to dry the equipment before the SSR? In other words, I would complete the process rinse, and then *immediately* begin the SSR. In that situation, could I do a recovery study on residue that was not dried? I would tend to doubt it, for the objection previously discussed (that my rinse recovery procedure might not pick up residue that was not adequately captured by the washing solution) comes into play. Furthermore, the idea of omitting the drying between the process rinse and the SSR causes problems with my visual inspection. If I were to dry the equipment after the SSR and then perform my visual inspection, what have I proved, particularly if my SSR recovery percentage was very high? Of course, even if my cleaning process was not fully effective, I could expect the equipment to be cleaner after that SSR; again, what have I proved? Of course if the equipment is *not* visually clean after the SSR, I clearly have done something wrong (either in the cleaning process or in the SSR).

Where does this leave us with rinse recovery studies? I wish I could say that rinse recovery studies were not necessary, or that rinse recovery studies could be done on non-dried residues. However, I don't think we are at that point in terms of having data that support those practices, or even deciding what data should be developed to possibly support those practices. It may be that if we can determine that swab residue values are consistently well below calculated limits in worst-case swab locations, and if we were to include in those worst-case swab locations swab surfaces where a final rinse was likely to pool, perhaps that might help. The complicating factor is that it is hard to generalize from one product to another product, from one cleaning process to another cleaning process, and from one manufacturer to another manufacturer. Furthermore, the way to develop consistent data is certainly more than just three protocol runs (remember the importance of *design and development* in a life cycle approach), and I may not want to omit rinse sampling in the early stages of validation for fear my swab data alone will not support my desired conclusion. Or, perhaps my objective may not be trying to reduce rinse sampling, but rather trying to eliminate swab sampling.

I fully realize the result of this discussion may not bring us to a clear path forward. However, I hope this two-part series helps us to better understand what is involved in rinsing, rinse sampling, and recovery studies for rinse sampling.