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Issues in Cleaning Validation for Parts Washers

There are certainly lots of possible issues to talk about for parts washers. However, I am going to limit this Cleaning Memo to a discussion of issues related to cleaning different products in the same parts washer, either in sequential loads or in the same load.

For clarification, a parts washer is usually considered as an automated cabinet washer for cleaning disassembled parts. Think of it as being like a very expensive home dishwashing machine. In one sense, a "parts washer" could also refer to a tunnel washer, an ultrasonic tank, or a more primitive "COP" parts washers. My discussion about different products may apply to those situations, but my illustrations will be with a cabinet washer. The cabinet washer is an enclosure with racks for holding parts, and with nozzles or spindles to direct a cleaning solution or rinse solution into or onto various parts that require cleaning. The cabinet washer complete cycle may involve a ambient temperature water pre-rinse, a washing step with an alkaline detergent, a water rinse, an acidic detergent or acid wash step, a series of rinses ending with a rinse of higher purity water, and a drying step. In certain cases some of those steps, such as the acidic detergent or acid wash step, may be omitted.

The question of different products in a given machine is related to the fact that most parts washers are designed to direct solutions into or onto the parts being cleaned. They are not necessarily (but they might be) designed to ensure that any soils and/or detergents are also rinsed from the parts washer's internal surfaces (that is, the internal surfaces of the enclosure). The concern is that residues of the previous product or of detergent might be adequately removed from the parts being washed, but that somehow soils and/or detergent might splash onto the equipment walls and not be adequately rinsed, and that those residues could conceivably transfer to the parts that are washed in the subsequent cycle. That is, in cycle #1 parts dedicated to Product A and soiled with Product A are washed. Is it possible that residues of Product A might remain on the washer surfaces and somehow contaminate parts dedicated to Product B, which are cleaning in cycle #2?

I must confess that I have never seen a company sample the internal walls of a parts washer, although I have seen companies comment that internal surfaces of a parts washer were not visibly clean. However, in a well designed cycle, I believe the risk for cross-contamination is low. Why? Let's suppose that somehow, during the washing of parts dedicated to Product A, some residue of that product remains on the walls of the parts washer at the end of the cycle. I then initiate a second washing cycle with parts dedicated to Product B in that same washer.

How do those residues of Product A get transferred to the parts in that second cycle? Well, if the parts washer uses a sump for recirculation of the cleaning/rinse solutions, those solutions could contact the walls, dissolve/ emulsify/disperse the soil, and then transfer it to the items being washed. Another possibility is that cleaning/ rinse solutions contact the wall, dissolve/emulsify/disperse the soil, and then ricochet back onto the parts to possibly redeposit soils onto the parts being cleaned. However, if the cleaning/rinse solutions from that cycle are able to dissolve/emulsify/disperse the residues from Product A, then it is not likely those residues from Product A would survive on the surfaces of the various parts through multiple steps that might include multiple sequential steps (pre-rinse, alkaline detergent wash, rinse, acid detergent wash, final rinses). For there to be any significant residues would involve either a poorly designed parts washer, a poorly designed cleaning cycle,

a failure of the washer, or a rather unusual soil (in the latter case, one would assume that alternatives to a parts washer cleaning cycle would be considered). It would be fairly easy to design an experiment (such as by artificially applying a given residue to walls prior to initiation of a cycle, and then measuring that residue on parts cleaned in a cycle. However, most companies don't want to artificially soil equipment to perform these experiments. Furthermore, if something goes wrong (including the fact that my hypothesis might be wrong), such experiments are generally seen as a lower priority in the various things that are required to safely produce drug products.

If a given company is still concerned about the possibility of cross-contamination of cleaned equipment from this scenario, there are two other options. One is to not only measure residues of Product B in a cleaning validation protocol for the cleaning of parts soiled with product B, but in that same protocol also measure residues of the previous product (Product A) on the cleaned parts. Note that this won't work if you are biotech, because in each case (measuring residues of Product and of Product B) you will use TOC as an analytical method. So, you can't distinguish from which product the residues came. The second alternative is to always perform a empty chamber wash cycle between the washing of any two different products. That empty chamber wash cycle would provide additional assurance that residues from Product A were not present on the washing chamber walls just waiting (somehow) to transfer to parts in the next cycle.

Okay, the next situation is this. I want to wash parts soiled with Product A with parts soiled with Product B in the same wash cycle. The issue is fundamentally the same whether parts are dedicated or not dedicated to one product. Well, I guess I will have residues from both products on all equipment items. This is true. Provided that the cleaning cycle is designed correctly (such that "all" soils are either dissolved, emulsified, or dispersed in the cleaning detergent), I can expect to have more or less the same levels of either residue on parts from Product A manufacture or on parts from Product B manufacture. The exception to this involves situations where there is an unusual reaction between soils from Product A and soils from Product B to leave an insoluble residue that is not removed by the cleaning detergent (if that were true, it should be something I should have learned in my development work). The question then becomes, when I then manufacture Product A with cleaned equipment, are residues of Product B on the parts at an acceptable level? And vice versa for making Product B. This assumes limits for the cross-contaminating residue can be established and measured in a cleaning validation protocol.

For those in biotech, where measurement of residues of the previous product is performed by TOC, this can be viewed as a problem. How can I determine which residues come from Product A and which from Product B? That can be answered somewhat by appealing to the (probable) degradation of the active protein in the cleaning cycle (and also during any autoclave cycle, if the small parts are subsequently steam sterilized). Suppose I were to process a full load of parts soiled only with Product A, and measure residue at a certain value (for example, X mcg of TOC per cm2). Then I process a mixed load of parts soiled with Product A and parts soiled with Product B. If I obtain essentially the same level of TOC residue with the mixed load, am I more concerned because the degraded fragments are now a mixture of degraded Product A and degraded Product B. If I am, then I would take steps to wash parts in separate cycles or in separate parts washers. If I am not, then the parts should be acceptably clean to be used for subsequent manufacture of either product.

This type of evaluation can be expanded to cover situations involving more than just two products. However, the key (can I emphasize this enough?) is to have an adequate understanding of the cleaning process and possible transfer of residues to equipment parts.