May 2008
More on Floors and Walls

I am hearing more and more about regulators asking questions about measuring residues for non-product surfaces such as floors and walls. Is that an appropriate question to ask for a cleaning validation program? My answer is "No". Is that an appropriate question to ask a pharmaceutical manufacturer? My answer is "Yes, under certain circumstances".

Why I say that it is not part of a cleaning validation program is the answer that the PIC/S guidance (PI 006-03) gives: that cleaning validation normally applies to product contact surfaces. Things like floors and walls are not (or should not be) product contact surfaces (any product that contacts floor or wall is not saleable product). Yes, there are equipment surfaces that are not product contact, which generally should be considered as part of a cleaning validation program. For example, lyophilizer shelves for vial freeze drying are not product contact surfaces, yet it is common practice to include those shelves as part of a cleaning validation program. The reason is possible product spillage onto the shelves and its close proximity to open product, giving rise to the possibility (albeit minimal after cleaning) of airborne transport from the shelves to the vials. Another example would be the walls of ovens used for tray drying. Product from previous run may somehow adhere to the walls, and then perhaps flake off during the next production run. In either case, for multiproduct equipment there is a concern about cross contamination. Let me add here that when limits are set for such "critical" non-product contact surfaces (sometimes I call them "indirect product contact surfaces"), there are several options discussed in my Cleaning Memo of October 2006. Furthermore, I should emphasize that the surface area of the indirect product contact surface is not included in any MAC (MACO) calculation for setting limits.

Okay, how do floors and walls differ from the case of lyophilizer shelves? Basically there are two differences. One is that floors and walls are not in close proximity to product. The second is that they are not in close proximity to open product. That is, for most manufacturing situations, there is little risk of transfer of residues from walls to the manufactured product. The route would have to be by an airborne route or by mechanical transfer, such as from the gloves of an operator. Are those possible routes?

For mechanical transfer by an operator, it may be possible, but it should be something that can be addressed by training operators not to touch walls (and floors!), and to wash hands and change gloves if such touching occurs accidentally.

What about airborne transfer? It is possible, but only possible if the product is open to the environment at some time in its manufacture. Of course, that said, if the previous product/active becomes airborne, this also becomes a potential problem for operator safety (for inhalation or for skin contact). This brings up a possible way to address the possibility of product contamination by leveraging data that has been developed for occupational exposure. For example, if data has been developed on airborne levels of an active during its manufacture, it is a reasonable extrapolation that the levels of that same active that would be present in the air during manufacture of the next product would be the same or (more likely) lower. If those measured values are acceptable values (using some model of transfer from the air to the product), it is possible to overcome any questions about the need for cleaning validation for floors and walls.

Of course, if that data is not available or if the analysis is inadequate, then it is possible to perform conclusive

(or what I think would be conclusive) studies to demonstrate the lack of airborne transport to the next product. In this case, the relevant study would be to manufacture Product A, and following that manufacture clean the equipment and the room as usual. Then make a placebo batch of the next product. During that placebo manufacture, measure airborne levels of the active of Product A. Following manufacture of the placebo, measure levels of the active of Product A in the manufactured placebo. What one would like to establish is that the active of Product A is not detected in the air and that levels of the active of Product A in the placebo is below the acceptance criteria (what I typically call the L1 value) calculated by traditional methods . Note that in this case, it is possible to measure some level of the active in the placebo due to transfer from cleaned equipment surfaces (and hopefully not from airborne transfer from walls and floors).

I would not encourage every company to do such a study. However, if enough companies performed such studies and published the results, it might go a long way to confirm whether this concern about transfer from floors and walls is a significant issue or not.