October 2006
CV for General Room Surfaces?

I am hearing questions more frequently, particularly from pharmaceutical manufacturers in Europe, about regulators and/or auditors who are asking for cleaning validation for surfaces such as floors, walls and external surfaces of process vessels. This month's Cleaning Memo addresses some of the issues related to such cleaning validation, and particularly addressing why, in general, it is not a value added task and why requests for such validation should be resisted.

First, let me make it clear that I am not talking about activities related to cleaning of surfaces and environmental monitoring of surfaces in cleanrooms and controlled environments. While I am hearing more and more people refer to qualification of disinfectants and disinfection procedures in cleanrooms as "cleaning validation", I believe this is an inappropriate use (and confusing use) of the term "cleaning validation". There are perfectly good terms, such as "disinfectant qualification" and "environmental monitoring" that refer to these activities for cleanrooms.

An example of how confusion arises is a recent Pharmaceutical Microbiological Forum discussion about microbiological limits for cleaning validation. Some of the postings to that forum suggest making analogies between limits for process equipment cleaning validation and environmental monitoring in cleanrooms. While both involve enumeration of bioburden on surfaces, for cleaning validation for process equipment product contact surfaces, limits are set; if the limits are exceeded, the validation fails. For environmental monitoring of cleanroom surfaces, action and alert levels (not limits) are typically set; exceeding those levels does not result in failure, bur rather an investigation, with possible corrective action. For the reasons of clarity and specificity of terminology, it is preferable to limit the term "cleaning validation" to product contact surfaces of process equipment.

Let's get back to the issue of cleaning validation for floors, walls, and external surfaces of process equipment. As I suggested during my digression on cleanrooms, the term "cleaning validation" is usually reserved for product contact surfaces of process equipment. The PIC/S guidance PI 006-2 makes this explicit when it states in Section 7.3.1 that "Normally only cleaning procedures for product contact surfaces of the equipment need to be validated". Of course, the key word in this PIC/S quote is the word "normally". Are there "abnormal" cases of non-product contact surfaces where cleaning validation is (or should be) required? The answer to that question is "yes". For example, lyophilizer shelves are not product contact surfaces, but it is a current expectation that the cleaning of lyophilizer shelves be validated. Some may argue that product spilling onto shelves makes it a product contact surface. While in one sense that is true, in the context of cleaning validation "product contact" means that "good" product could contact those surfaces. In the case of a broken or spilled vial, the resultant product that actually contacts the shelf is not considered usable product.

Do floors, walls and the outside of process vessels fit within the same category ("abnormal" cases which require cleaning validation)? I would argue that the answer is a definite "no".

It is clear that we should have cleaning procedures for such surfaces. This is just good housekeeping and good CGMP. However, the risk of manufactured product contamination from residues on floors, walls, and the outsides of equipment is a negligible risk. The risk of soil, product, cleaning agent or bioburden entering the

manufacturing vessel to potentially contaminate the manufactured product is small (if the risk were significant, it should probably be addressed by engineering controls rather than by cleaning validation). Furthermore, how would limits for residues on such surfaces be established? Is visually clean adequate? The answer is that even though a surface like a floor could be visually clean immediately after cleaning, there is no expectation that the floor should remain visually clean, particularly after foot traffic. The other ironic thing about this issue is that for residues on non-product contact surfaces, the most likely scenario for potential manufactured product contamination is an airborne route. Those residues most likely to become airborne are those residues which loosely adhere to the surface. And, it is precisely these residues which are easy to clean. Any tightly adherent residue, which is more difficult to clean, is not likely to become airborne, and therefore the probability of that tightly adherent residue contaminating the manufactured product is small. In other words, for such non-product contact surfaces, it is those residues which are easiest to clean which are most likely to potentially contaminate the next manufactured product.

If these are some of the reasons for not doing cleaning validation on floors, walls, and the outsides of process vessels, then what should be done? First, we should have cleaning procedures (SOPs) for these surfaces. Second, we should consider that at the end of each cleaning procedure, the surfaces be examined to determine they are visually clean (in a sense, this is like cleaning verification, but without a protocol). But as a reminder, there is not necessarily an expectation that the surfaces will remain visually clean, particularly for floors. Third, we should document our rationale for not performing cleaning validation on floors, walls, and the outside of process vessels. As part of that evaluation, we should identify any "non-product contact surfaces" which do require cleaning validation and provide the rationale. Doing these three things will put a pharmaceutical manufacturer in a better position to defend a program that excluded floors, walls and the outside of process vessels from formal cleaning validation studies.