January 2004
Monitoring a Validated Cleaning Process

In discussing monitoring for cleaning validation, it is important to carefully define what one means by "monitoring". As used here, the term "monitoring" refers to the routine measurements taken on the cleaning process that serve as indicators of whether the process is in a state of control (or considered from the opposite point of view, serve as indicators that the process either is not or may not be in a state of control). The purpose of monitoring is not to have clear evidence that the surfaces are acceptably clean. To do that, one would have to sample the surfaces (much as one would do in a cleaning validation protocol). Monitoring as discussed here refers to monitoring of an already validated cleaning process.

Now, monitoring *may* include some of the same rinse and swab samples that are done during a validation protocol, but those are not necessary parts of a monitoring program. As stated in PIC/S document PI 006-1, one of the purposes of having cleaning validation is so that "analytical monitoring may be omitted or reduced to a minimum in the routine phase". This is supported by the FDA's Second Quarter 2001 Human Drug CGMP Notes, which states that "once cleaned by a validated procedure, a firm generally should not be expected to analytically examine equipment surfaces to demonstrate cleanliness" and that "usually, visual inspection of equipment surfaces, including hard to clean nooks and crannies, along with rinse water testing would suffice".

In other words, if you want to perform swab sampling on a routine basis for an already validated cleaning process, you may. But, it is not necessary. The place for repeating any such swab sampling, however, is in revalidation (see the December 2003 Cleaning Memo).

What then should be monitored routinely? The answer is that you should monitor those parameters of the process which (1) are indicative of process control and (2) which can be readily accomplished without disrupting the cleaned system. The second item is added because it makes no sense for routine monitoring to use a monitoring technique (such as extensive equipment disassembly) which will require that the equipment be recleaned following the monitoring process.

For automated processes, monitoring should include items which are probably already measured as part of the process automation. These parameters include times (of the various steps), temperatures, flow rates, pressures, and concentration of cleaning agent. It may also include measurement of TOC, conductivity, and/or bioburden of the final rinse water. It includes visual examination of the cleaned equipment. Alarms tied to various steps or parameters are also part of the monitoring process.

For manual cleaning, there are fewer options for routine monitoring. Parameters that may be monitored include times, temperatures, and concentration of the cleaning agent. Visual examination during manual cleaning is also important. If (and this is a big "if" in manual cleaning) a parameter of the final rinse water can be appropriately and conveniently measured, this should also be considered.

How should action and alert levels be established for the monitoring techniques? In some cases, they are determined by the process design parameters themselves. Certainly if a spray device has a specified pressure range, the change in pressure outside that range should be a cause for action. In the case of visual examination,

the presence of any visual residue, whether it be from a "failure" in the cleaning process or from a failure in a preventive maintenance process (e.g., rouge), should be a cause for action. In the case of rinse water conductivity, TOC or bioburden, action/alert levels can be set on the process capability (based on trends). Any value for an alert level should be below any response that would constitute a failure in a validation protocol, and any value for an action level should be no higher than any response that would constitute a failure in a validation protocol. This can be initially set based on data obtained during any prevalidation runs. However, as routine monitoring data is accumulated, action/alert levels should be reevaluated.

Is monitoring the only thing that gives one assurance of control for an already validated cleaning process? NO! It is only part of a package which includes appropriate preventive maintenance, good change control procedures, and adequate training. However, it is an important part of this continuing assurance of control, and can certainly provide early evidence of a process that may be going out of control. For those reasons, it is important to carefully select monitoring parameters which are indicative of a "state of control".