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Understanding and Applying "Visually Clean"

I have recently published a paper on the use of a "visually clean" standard as the sole acceptance criterion in cleaning validation protocols. That publication was based on a presentation at the December 2000 PDA meeting in Washington, D.C. and a similar presentation at the February 2001 Japan PDA meeting in Kyoto, Japan. Since that time I have a slightly different approach to the use of "visually clean" in this manner. This new framework does not invalidate what I have published (and presented numerous times), but rather modifies the framework in which it is presented.

Previously, "visually clean" was presented as an alternative residue limit to the standard dose-based limit (0.001 of the minimum dose of the residue active in a maximum dose of the next manufactured product). On further reflection, I would not present "visually clean" as an alternative residue limit. Rather, the residue limit is still based on the dose-based calculation. Visual examination then becomes the analytical technique to determine that the examined surface has residues below that of the dose-based limit. In essence, this still emphasizes the importance of a dose-based limit, but what changes is the measurement technique. Instead of analyzing a swab or rinse sample by a technique such as HPLC or TOC, a visual examination is used.

This more accurately reflects how visual examination can be used in validation protocols, and particularly emphasizes the fact that when used as a "sole criteria", a determination of "visually clean" must clearly demonstrate that the residue on the surface is below that level allowed in a dose-based calculation.

This really doesn't change the steps that one must go through to utilize "visually clean" as the sole acceptance criteria. One still calculates the dose-based surface limit (typically in $\mu g/cm^2$), and then determines by appropriate lab studies that the residue is clearly visible at or below the dose-based residue limit. Note that this doesn't mean that one has to exactly determine the lowest level at which the residue is clearly visible (this is also a change from my published paper). For example, if a dose-based limit is calculated as 6.2 $\mu g/cm^2$, and it can be determined that the target residue is clearly visible on the same surface under equivalent viewing conditions at levels of 3.0, 4.0, 5.0 or even 6.0 $\mu g/cm^2$, then any determination that a viewed surface was visually clean (under equivalent viewing conditions) would constitute evidence that the residue on the surface was less than 6.2 $\mu g/cm^2$.

Other conditions for utilizing "visually clean" as the sole acceptance criteria still apply:
1. Critical surfaces must be available for visual examination.
2. The conditions of viewing the cleaned equipment surfaces must be the same or better than the conditions used for the laboratory "visually dirty" studies.
3. Visual examination must be performed under an appropriately detailed SOP.
4. Viewers must be appropriately trained.