Cleaning Memo for August 2019
What's a Visual Limit?

"Visual Limit" (VL) is a term dealing with amounts of residue which could be on a surface that are detectable (or not detectable) by visual examination. We all know that the visual detectability of a residue on a surface will depend on such factors as the viewing distance, the lighting, the angle of viewing, the contrast between the residue and surface and the eyesight of the person who is the viewer. However, those parameters will *not* be the focus of this Cleaning Memo. Instead we will focus on how to define and determine the VL. For clarification, this approach is typically used when we want to know whether the VL is a more stringent (as compared to a *calculated* carryover limit) assessment to determine whether the surface is acceptably clean. In other words, the VL is used to determine whether a visually clean surface has residue below the *calculated* carryover limit.

There appear to be at least two general approaches to defining the VL. Both are related to spiking studies (also called spotting studies) in which fixed amounts of residue are placed on a surface, typically as a solvent solution. The spiking is done over a certain surface area (typically a round area based on the solvent spreading across the surface to form a circular shape). Based on the amount of residue spiked and the surface area it is applied to, we are able to determine the concentration of the residue on the surface in terms of mass per area, such as micrograms per square centimeter (mcg/cm^2). Upon evaporation of the solvent, the spiked surface can then be viewed.

In one approach the VL is the *lowest* spiked level in which *any* amount of residue is seen on the spiked surface. That is, at high spiked levels the residue may be visible across the *entire* spiked surface. Then, at lower spiked levels there may be residue visible only on *certain portions* of the spiked area. Eventually we get to a point where there is *no residue at all* seen on the spiked surface (that is, the surface is visually clean under the defined viewing conditions). The lowest spiked level where there is at least some residue visible is considered the VL.

Now with this approach you might *first* ask why isn't the highest level at which the surface is *completely* visually clean the VL. The answer to that question is based on the objective of this spiking study. Remember that the objective is to say that a visually clean surface in a protocol has a residue level below the *calculated* carryover limit. Let's suppose I spike at 0.5, 1.0, 1.5 and 2.0 mcg/cm^2, and that 0.5 mcg/cm^2 is visually clean and 1.0 mcg/cm^2 is the lowest level at which I can see *any* residue on the spiked surface. Depending on the calculated carryover limit, I can't necessarily say that a VL of 0.5 mcg/cm^2 is appropriate. For example, suppose my calculated limit is 0.8 mcg/cm^2 (note that I have deliberately chosen this limit to illustrate the point.) In that case, if I had spiked at 0.75 mcg/cm^2, I might have seen some residue on the spiked surface, and I could not be assured that a VL of 0.5 mcg/cm^2 (as defined based on the highest level which is *completely* visually clean) means that I am assured of being below a calculated limit of 0.8 mcg/cm^2.

Now, you might also ask why I would only see residue on a *portion* of the spiked surfaced. The likely reason is that as the solvent evaporates, it does not *evenly* evaporate at the same rate across the entire spiked surface. For example, evaporation may be faster at the edges as opposed to the center of the spiked area. This results in unevenness of dried residue across the surface. In any case, my concern with this approach is related to this issue of uneven appearance of residues on the dried surface. If I spike at a level of 1.0 mcg/cm^2, and see some residue on the surface, does this mean that if 1.0 mcg/cm^2 were spread *evenly* across the surface, that I could *clearly* see it as visible residue. My answer is "No"; the reason is that the small amount of visible residue on the spiked surface probably represents a value of residue in that specific location (and not across the entire spiked surface) of a value *higher* than 1.0 mcg/cm^2. This is due to uneven evaporation, which will cause parts of the surface to be values *higher* than 1.0 mcg/cm^2 and other parts to be *lower* than 1.0 mcg/cm^2.

This brings me to a second approach for defining the VL (and this is the one I prefer). In that approach, it is still possible to spike coupons at different levels. However, the VL is the *lowest* spiked level where residue is seen across the *entire* spiked surface. Using the same spiking levels given in the previous example, let's suppose that 0.5 mcg/cm^2 is visually clean, 1.0 mcg/cm^2 is the lowest level at which I can see any residue, and 1.5 mcg/cm^2 is the lowest level where I can see residue across the entire spiked surface. In this last case of a spiked level of 1.5 mcg/cm^2 I suspect that portions of the spiked surface are slightly above a value of 1.5 mcg/cm^2 and portions might be slightly below a value of 1.5 mcg/cm^2. But in either case, I would have confidence that any surface observed (again under the same viewing conditions) to be visually clean would have residue values below 1.5 mcg/cm^2. So as long as my calculated carryover limit was 1.5 mcg/cm^2 (or higher), I could readily use a visual examination (again considering equivalent viewing conditions) to determine that the target residue was below that carryover value. Note further that I am not stating the actual value of residue on the surface visually clean surface; I am merely using a visually clean assessment to determine (in a pass/fail test) that I am meeting my calculated carryover limit.

I typically like to take this one step further. Rather than spiking at multiple levels, a simpler approach is just to spike *at the carryover limit*. For example, if my carryover limit is 2.0 mcg/cm^2, I spike *only* at that level of 2.0 mcg/cm^2. I suspect that because of unevenness of evaporation, that portions of the spiked surface will be at levels below 2.0 mcg/cm^2 and that portions will be above 2.0 mcg/cm^2. But, if I can see residue across the entire spiked surface, then I can have assurance that any surface viewed as visually clean (again considering equivalent viewing conditions) would have target residue values below 2.0 mcg/cm^2. How much below I can't say, since this is a pass/fail test.

That said, to show the robustness of my visual assessment, for this latter approach I might spike at a level somewhat below my calculated limit (such as 20% or 40% below) to show the "robustness" of such a visual assessment. The robustness of the assessment might also be addressed by having the viewing conditions in the spiking study to be more "stringent" than the conditions of visual observation in the plant operations. By more "stringent", I mean under conditions that are more likely to result in higher values for the

VL. For example, lower light levels and longer distances will result in higher VL values. This clarification of the meaning of "more stringent" is necessary because *lower* light levels and *longer* distances are more stringent in the lab study involving spiking studies to determine the VL, but *brighter* light levels and *shorter* distances are more stringent in a protocol evaluation for plant equipment. In the ideal world, the viewing conditions in spiking studies would be exactly the same as conditions on the factory floor, but we don't live in an ideal world. (Probably the closest you can get to having the viewing conditions exactly the same is to place the spiked coupons in the equipment itself, but this has other concerns such that it may not be practical).