

November 2003
Correlation of TOC with a Specific Analytical Method?

Sometimes the question is asked, “Do I have to correlate my TOC method for my active with a specific method, such as HPLC, during the analytical method validation?” As with other questions of this nature, it depends on what you mean by “correlate”. If by “correlate” you mean run side by side full validation of both analytical methods, then the answer is “no”. If I were required to perform full validation on the specific HPLC procedure, I would probably choose to use that method for my cleaning validation residue measurement of the active. As I have discussed many times, other things being equal, it is much easier to be below my acceptance limit if I utilize a specific method as opposed to a non-specific method [I do realize that other things are **not always equal**, and therefore TOC may be the preferred analytical technique in many situations].

On the other hand, there is a sense (or should be a sense) in which TOC should be “correlated” with a specific method. When you run a TOC method validation, you run linearity, precision, accuracy, etc. with known concentrations of the active. How else do you know what those known concentrations are unless you perform analysis with a specific method? For example, you might have a precise assay of the active agent by an HPLC procedure. You then prepare the standard solutions by weighing out accurately a fixed amount of the active and diluting it volumetrically to a known concentration. Finally, that stock solution is serially diluted to prepare standards for your accuracy, precision, and linearity studies. While you don’t have to (and might not be able to) run those diluted standards by your specific HPLC method, those diluted standards are prepared from the stock solution which has been measured by the specific HPLC procedure. If this is what is meant by “correlation” of the two methods, then the two methods are “correlated”.

However, I would prefer not to use this terminology in referring to my TOC method validation. I would prefer to say something like “My TOC method validation involves use of standards prepared from a sample of the active analyzed as to activity by a specific method.”, or some other similar description of what has been done. The important point is that when I do my validation using TOC, I use standards of known concentration or activity. That known concentration or activity can come either from analysis by a specific method or by certificates of analysis from purchased standards (or even from purchased cleaning agents).

The purpose of this Cleaning Memo is to neither promote nor discourage the use of specific or non-specific methods. Rather the purpose is to point out proper method validation for non-specific analytical techniques, and to help avoid unnecessary analytical work in the method validation of non-specific methods.