July 2006
FTIR with Fiberoptic Sampling

Last month I mentioned two new analytical techniques that have been promoted for pharmaceutical cleaning validation in the last five years. "Ion mobility" was discussed in last month's Cleaning Memo. The other "new" technology is FTIR with a fiberoptic probe. In one sense this is just a novel combination of two technologies, "conventional" infrared analysis and a fiberoptic probe. The exciting part about this development is the sampling aspect, and not necessarily the infrared aspect.

The major player in this field is Remspec Corporation, which offers its "Spot-View" instrumentation for pharmaceutical applications. For measurement of residues on surfaces, the Spot-View has a grazing angle probe which can be placed on flat surfaces for analysis. The grazing angle probe utilizes attenuated total reflection (ATR) to be able to measure at low residue levels. To further increase the detection levels, the technique generally does not utilize a single peak, but rather analyzes the spectrum over a wider range (generally over about 1000 wave numbers). The grazing angle probe is connected to the infrared unit by a fiberoptic cable, which carries the light from the unit to the probe. The grazing angle probe also contains a detector to capture the reflected light. Readout can either be directly on the probe or an electrical signal can be sent back to a conventional infrared spectrophotometer for analysis and recording.

The grazing angle probe is handheld, and weighs about 1 kilogram. The surface area measured by the unit is about 1.25 cm. by 11.5 cm. The standard fiberoptic cable is about 3 meters long, but it can be customized in lengths as long as 5 meters.

Use of this technology has all the features (and limitations) of infrared analytical techniques. A suitable range of wave numbers must be selected for calibration. Calibration curves must be established using known standards. Possible other substances that might be present on the surfaces after cleaning must be evaluated to make sure they don't interfere.

The major feature of this technology is that it is a "direct" sampling of surfaces. Note that when I use the term "direct sampling" here, I am not using it in the same way as in the FDA cleaning validation guidance. In the FDA guidance, "direct" sampling refers to swab sampling. This new technology is "direct" sampling in that residues are not removed from the surfaces as they are in rinse or swab sampling. This direct surface sampling eliminates the need for sampling recovery studies (although in another sense, I might say that "recovery" is an integral part of the analytical method validation). It also provides for the possibility of an "immediate" result. Note that a calibration curve will be required for each surface analyzed; the calibration must be done for each surface type, such as stainless or glass.

This is certainly an exciting prospect for pharmaceutical cleaning validation and verification. However, before we get too excited, there are limitations for implementation in pharmaceutical manufacturing. One limitation is the length of the fiber optic probe. A second limitation is that the grazing angle probe must be held in place by a person.

Several other concerns are being addressed by Remspec. One issue is variability of the surface quality in terms of roughness and directionality. This has been addressed in a recent publication, and requires that the

calibration be done on a series of surface types which represent the range of variability of the actual surface to be sampled. Analysis of curved surfaces can be handled by adjusting and controlling the focal point of the grazing angle probe. Note that this applies only to curvature in one direction, such as on the sidewall of a round tank. In the specific case of a round vertical tank, the probe must be held vertically. Finally, analysis of various organic polymer surfaces can be done, because the technique relies not on absorption at a specific wave number, but rather a chemometric analysis based on absorption over a range of approximately 1000 wave numbers.

As with ion mobility, this is certainly a technique that should be considered by pharmaceutical manufacturers to see if the technology, with its benefits and limitations, can be successfully utilized in specific situations.

In the interest of full disclosure, I should state that I am not now nor have I been in the past a consultant to Remspec.