Cleaning Validation: On-Site Trials of SpotView®

REMSPEC CORPORATION

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SpotView is a portable system for real-time, in-situ surface analysis using grazing-angle infrared spectroscopy. Organic films and coatings on metal and glass surfaces can be measured and identified in seconds. The system, which was originally developed for use in the aerospace industry, is particularly useful for cleaning validation in the pharmaceutical and food industries.

On-Site Trials at Pharmaceutical Plants

Background

During a series of visits to pharmaceutical and fine chemical plants, a SpotView system was used to develop preliminary calibrations for various APIs, excipients, and cleaning materials. The calibrations were based on sets of spectra collected from standard coupons. In the first case, the calibration was challenged with a set of samples that had been independently prepared, some spiked with an additional contaminant. In two other cases, the calibrations were tested using data collected from reactors before and after cleaning.

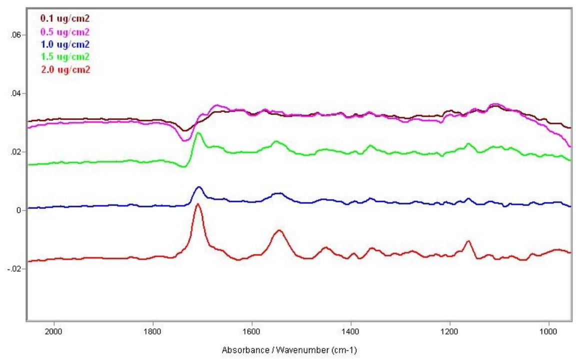
Calibration samples for SpotView are prepared using coupons of the material that is to be checked for cleanliness. Stainless steel and glass-lined reactors are commonly encountered in the pharmaceutical industry, and both materials were used in the trials described here. Extensive studies have been published[1,2] on the results from glass and

1 *Grazing-angle fiber-optic IR reflection-absorption spectrometry (IRRAS) for in situ cleaning validation.* Hamilton et al., *Org. Process Res. & Devel.*, **9**(3), 337-343, 2005

2 *Grazing-Angle Fiber-Optic Fourier Transform Infrared Reflection-Absorption Spectroscopy for the in Situ Detection and Quantification of Two Active Pharmaceutical Ingredients on Glass*. Perston et al., *Analytical Chem.*, **79**(3), 1231-1236, 2007.

steel and on the effect of varying surface roughness on SpotView measurements[3 4]. There are different methods for preparing the calibration coupons, including a simple smear method using a measured quantity of a standard solution, and a spray method that requires a secondary analysis tool such as UV/Vis spectroscopy. The simple smear method was used during these trials.

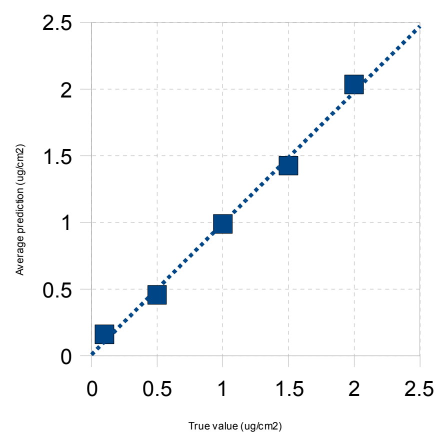
Trial 1: Undisclosed API on Stainless Steel Surfaces



The SpotView spectra collected from the five coupons coated with 0.1-2.0 μg/cm^2 API are shown.

It is hard to interpret the spectra by eye below about 1.0 μg/cm^2, but it is clear that there are features in the region between 1800 and 1000 cm^{-1} that vary in intensity as the surface concentration changes.

When a PLS1 calibration was built using commercial chemometrics software, a cross-validation test gave R^2=97.5 and the RMS error was 0.11, suggesting a Limit of Quantitation (LOQ) at about 0.3 μg/cm^2. A graph of the average predicted surface concentration against the true value is shown here.



3 *Fiber-optic infrared reflection absorption spectroscopy for trace analysis on surfaces of varying roughness: sodium dodecyl sulfate on stainless steel.* Hamilton et al., *Appl. Spectroscopy*, **60**(5), 516-520, 2006.

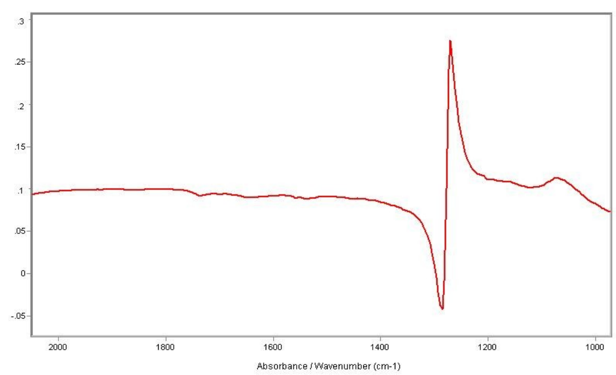
4 *Fiber-optic infrared reflection absorption spectroscopy for trace analysis on surfaces of varying roughness. Part II: acetaminophen on stainless steel.* Perston et al., *Appl. Spectroscopy*, **62**(3), 312-318, 2008.

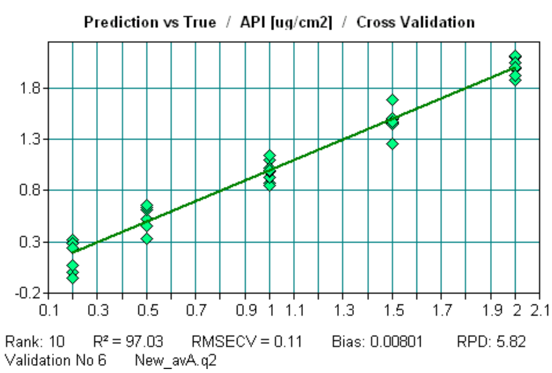
File	Description	Prediction	Units
test.43	detergent 0.2% in water	-0.95	ug/cm2
test.44	detergent 0.2% in water	-1.13	ug/cm2
test.45	detergent 0.2% in water	-0.91	ug/cm2
test.46	mixture API and detergent	0.9	ug/cm2
test.47	mixture API and detergent	0.57	ug/cm2
test.48	mixture API and detergent	0.47	ug/cm2

The calibration was tested further by collecting SpotView spectra from a small set of coupons spiked with a detergent and with a mixture of the API and a detergent. As the results at the left show, realistic results were obtained from the coupons that included API, but not from the ones treated only with detergent. It has already been shown[2 5] that calibrations can be built using multiple compounds, including detergents and excipients.

Trial 2: Undisclosed API on Glass Surfaces

The second trial, which used a different API from the first, involved a glass-lined steel reactor where the glass surfaces had to be examined. Mid-IR reflectance spectra from glass substrates are typically inverted and include a strong Si-O peak from the glass at about 1230 cm^{-1}. An example from the present trial is shown at the right.





A preliminary calibration built using spectra from five glass coupons spiked with different levels of the API is shown at the left. The RMS error of 0.11 $\mu g/cm^2$ suggests an LOQ of about 0.3 $\mu g/cm^2$.

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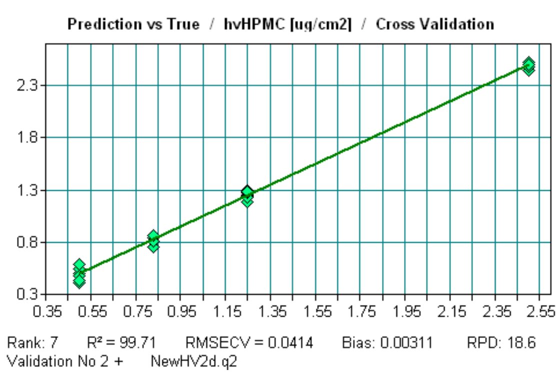
5 *Quantifiction of Active pharmaceutical Ingredients on Metal Surfaces Usnig a Mid-IR Grazing-Angle Fiber Optics Probe* Teelucksingh et al., *Spectroscopy,* October 2005

The SpotView was then used to obtain spectra from the surfaces of a glass-lined steel reactor before and after cleaning. Each spectrum was collected for 12 seconds. The results are shown at the right. Even using the very limited calibration from this demonstration, it was possible to distinguish surfaces that required cleaning.

File	Description	Prediction	Units
test.0	inside reactor	4.51	ug/cm2
test.1	inside reactor	6.96	ug/cm2
test.2	inside reactor	1.6	ug/cm2
test.3	inside reactor cover	0.37	ug/cm2
test.4	inside reactor cover	0.78	ug/cm2
test.5	inside reactor cover	1.11	ug/cm2
testB.0	inside reactor after cleaning	1.76	ug/cm2
testB.1	inside reactor after cleaning	1.56	ug/cm2
testB.2	inside reactor after cleaning	1.28	ug/cm2

Trial 3: Cellulose Derivative on Glass Surfaces



The third trial involved detection of a cellulose derivative on the surfaces of a glass-lined reactor. Calibration coupons were prepared using aqueous suspensions of the material and a preliminary calibration was built from the resulting spectra.

Spectra collected from inside a glass-lined reactor before and after cleaning clearly show a difference between cleaned and uncleaned surfaces.

Location	Average Prediction	Units
inside reactor before cleaning (site A)	23.78	ug/cm2
inside reactor before cleaning (site B)	8.15	ug/cm2
inside reactor cover before cleaning	10.85	ug/cm2
inside reactor after cleaning	2.94	ug/cm2
inside reactor cover after cleaning	2.92	ug/cm2

The trials described here, although limited in nature and scope, demonstrate clearly the potential of the grazing-angle mid-IR method for real-life cleaning validation.

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