

## Cleaning Verification using the D3 Klarite® SERS technology

### Application Note



#### INTRODUCTION

Cleaning verification is an important factor in pharmaceutical production. Stringent cleaning protocols are essential for regulatory conformance and contamination control, while rapid turnaround times are desirable to minimise production downtime.

Klarite® SERS substrates offer a revolution in sampling times and specificity. Rapid analysis and feedback on contaminant levels and identity can be achieved with minimal sample preparation. Specific improvements on existing technologies like HPLC are contained within an easy-to-use analysis protocol. In particular:

- Significantly improved sample response times prevent a measurement backlog, common amongst HPLC users, meaning production downtime is minimised.
- Reduced production downtime from days to hours allows companies to significantly increase production volumes.
- In contrast to HPLC, all components in an analyte mixture will be detected and displayed simultaneously – no need to ‘search’ for contaminants.
- Identification of molecular functional groups allows end users to apply targeted cleaning procedures.
- Ease of use allows routine SERS detection technology to be used by non-experts.
- Flexible technology enables the use of a wide range of instrumentation.

#### WHAT IS SERS?

Surface Enhanced Raman Spectroscopy (SERS) is an extremely powerful analytical technique capable of detecting trace quantities of analytes to parts-per-billion levels. Combining the fast, non-invasive compositional analysis capabilities of Raman spectroscopy with Klarite® micropatterned surfaces increases sensitivity levels by many orders of magnitude, providing consistent and reproducible trace analysis solutions. SERS experiments are fast, cost effective and simple to run.

Due to the high signal enhancement, SERS can provide the following benefits:

- Small sample volumes ( $\mu\text{L}$  and below)
- High degree of specificity
- Real time response
- Qualitative and quantitative analysis
- Simultaneous multi-component detection



#### KLARITE® SERS SUBSTRATES

Klarite® SERS substrates are manufactured using a unique combination of photonic crystal design and semiconductor fabrication techniques. Alongside outstanding sensitivity and performance, Klarite® offers unparalleled reproducibility between measurements, bringing SERS analysis to new levels of reliability.

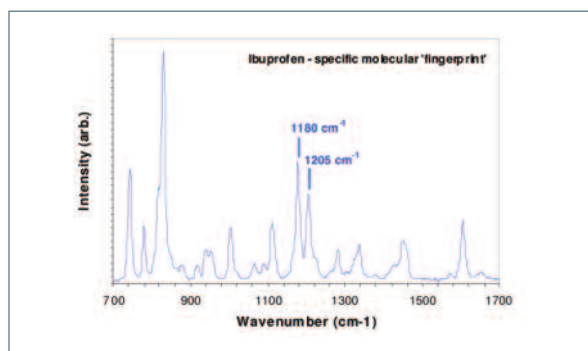


Figure 1 – Ibuprofen molecular fingerprint

#### MOLECULAR FINGERPRINT

The SERS spectrum is specific for the particular analyte measured (see sample ibuprofen spectrum above). Analyte mixtures can be differentiated by their unique spectral shape (see over).

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## ANALYSIS OF MIXTURES

Figure 2 shows the SERS spectrum taken from a mixture of ibuprofen (16 µg/ml) and warfarin (243 µg/ml). The spectrum from the mixture (top) perfectly overlays features from both reference spectra, allowing a quantitative multicomponent analysis.

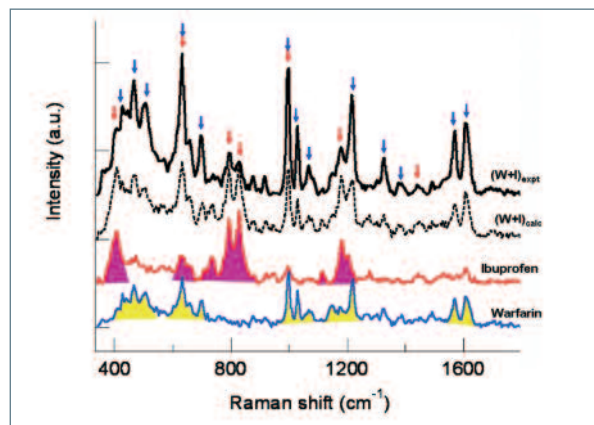


Figure 2 – SERS spectrum from an Ibuprofen/Warfarin mixture, with reference spectra from each

For more complex mixtures, multivariate statistical analysis, applied using commercially available software, can generate detailed qualitative and quantitative information.

## QUANTIFICATION

Quantification of known analytes can be achieved through the construction of calibration curves, standard in analytical chemistry.

Figure 3 shows spectra from a series of solutions of ibuprofen in methanol, ranging from 10<sup>-3</sup>M (206 ppm) to 10<sup>-6</sup>M (0.2 ppm). The results show how the SERS signal intensity varies as a function of concentration, allowing a robust calibration curve to be plotted.

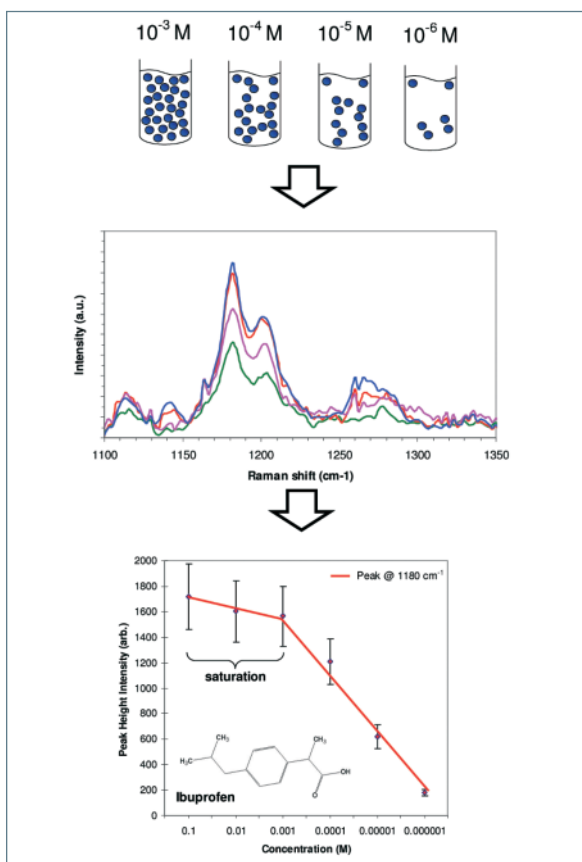


Figure 3 – Schematic of quantification protocol applied to Ibuprofen solutions in methanol

Figures 2 and 3 show that the identification and quantification of unknown molecules can be achieved. Compound libraries can also be generated.

Cleaning methodologies can be developed based on the molecular structure information generated in every SERS spectrum.

## TRANSFERABLE TECHNOLOGY SOLUTIONS

Klarite<sup>®</sup> and SERS can deliver real improvements in the cleaning verification sector. The results shown here illustrate the advantages of Klarite<sup>®</sup> based protocols, in terms of chemical identification, quantification and mixture analysis.

In addition to Klarite<sup>®</sup> substrate technology, D3 Technologies offers research programs tailored to customer specific needs. A research program can deliver appropriate sample preparation methods, ideal experimental and instrumental parameters and targeted analysis of analytes/contaminants, with protocols individually developed to the customer's requirements.



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