



## Measurement of Counterfeit Pharmaceuticals Using the Spotlight Imaging System

### Introduction

Counterfeiting of pharmaceuticals and the proliferation of substandard drugs constitute a serious health risk for the world population, including both industrialized and developing countries.

The manufacturing, sale and distribution of counterfeit drugs are not only serious crimes, but also lead to failed treatment, disability, and even death.

Loss of revenue for the pharmaceutical industry and potential exposure to huge damage claims will push up the price of legitimate pharmaceutical products.

The World Health Organization (WHO) defines counterfeit drugs as “deliberately and fraudulently mislabelled with respect to identity and/or source” and that “counterfeiting can apply to both branded and generic products and may include products with correct ingredients, with wrong ingredients, without active ingredients, with insufficient quantity of active ingredient or with fake packaging.”

### The Scale of the Problem

It is estimated that five to eight percent of the world’s total pharmaceutical sales are counterfeit or of dubious quality (this is an average figure as pharmaceutical counterfeiting varies tremendously from country to country).

## Technologies

Of the several types of counterfeiting defined by the WHO, this application note covers the case where the counterfeit is chemically very similar to the genuine product, containing active ingredient and excipients in the correct concentrations. Traditional techniques such as HPLC and NIR spectroscopy could not differentiate the genuine and counterfeit products. They both work at the macro level, so would show only that the concentrations of ingredients were very similar.

In many cases, counterfeit products use stolen or illicitly obtained packaging materials, so again detection of the counterfeit product could not be based on identification of fake packaging.

This type of counterfeiting, where the counterfeit has identical packaging and chemically very similar or identical chemical composition, is clearly difficult to differentiate with traditional macro techniques.

This application note discusses the identification of counterfeit drugs based on differences in the distribution of ingredients within the product. This may be caused by different blending processes, or differences in the ingredients, which could be in fine powder, fine crystalline or coarse crystalline form.

The microscale distribution of ingredients in a powder was determined using the Spotlight™ FT-NIR Imaging System and then compared with reflectance analysis of the bulk sample using a conventional non-imaging FT-NIR spectrometer.

## Method

The samples were a proprietary analgesic capsule containing 5% w/w caffeine, and a second analgesic capsule with no caffeine. The latter was adulterated with 5% caffeine, representing a counterfeit copy.

The capsules were opened and the contents poured into a stainless steel cup. The top was leveled to ensure that the sample surface was regular and flat.

## Imaging Method

Spectra were collected on the Spotlight between 7800 and 4000  $\text{cm}^{-1}$ , using 16- $\text{cm}^{-1}$  spectral resolution, 25- $\mu\text{m}$  pixel resolution, and 2 scans per pixel. Image size was approximately 800 x 1200  $\mu\text{m}$ . Image acquisition took less than two minutes.

## NIRA Method

Spectra were recorded using a Spectrum™ FT-NIR Spectrometer with Tablet Autosampler. Spectra were recorded in reflectance mode between 7800 and 4000  $\text{cm}^{-1}$  with 16- $\text{cm}^{-1}$  spectral resolution at one minute per scan.

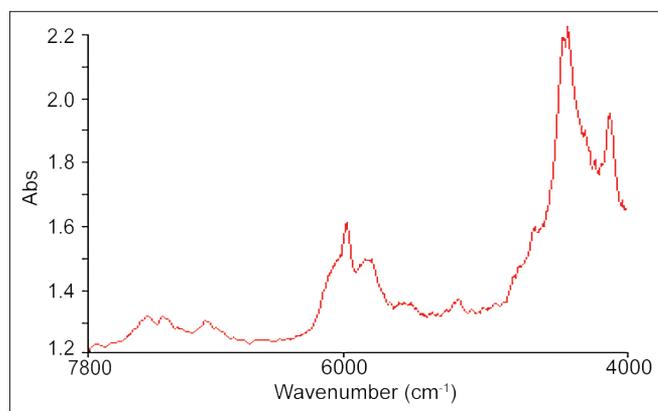


Figure 1. Caffeine reference spectrum.

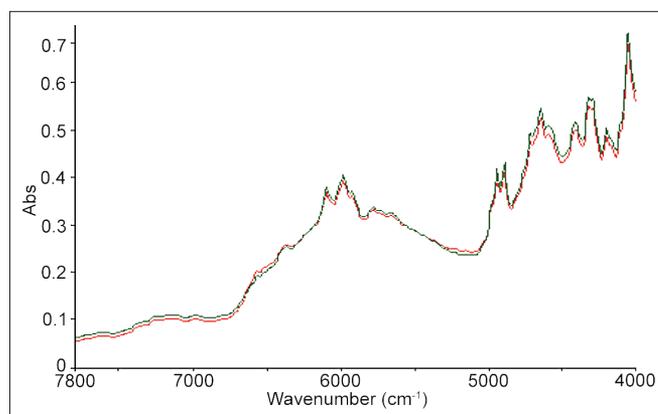


Figure 2. Genuine (green) and counterfeit (red) products measured using the NIRA system – macro sampling.

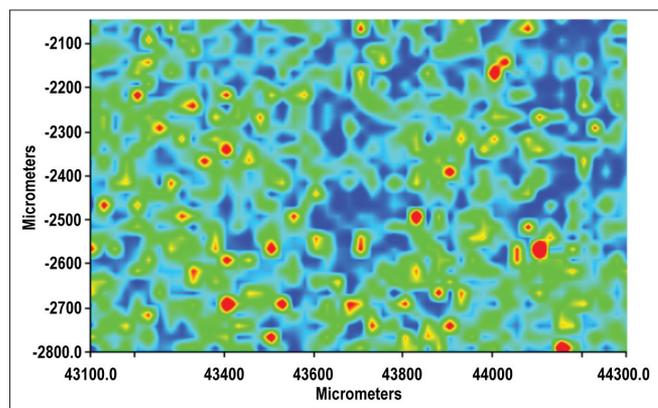


Figure 3. Band ratio image 4300/6072  $\text{cm}^{-1}$  for the genuine product.

## Results

The caffeine reference spectrum, collected using the Spotlight, is shown in Figure 1.

Figure 2 shows the NIRA absorbance spectra for the genuine and counterfeited blend. Differences between the two spectra were minimal, and could be due to differences in excipients: the concentrations of many of these were not stated for either product.

Figures 3 and 4 show the band ratio images for the genuine and counterfeited products respectively.

The distribution of caffeine is clearly homogeneous in the genuine product, but very localized in the counterfeit, reflecting different manufacturing processes. Note that both images are ratios, and are auto-expanded in terms of the ratio axis. The absorbance ratio in the counterfeit sample image is much higher than in the genuine sample image: the absolute amount of caffeine in each sample is the same.

## Conclusions

The Spotlight FT-NIR Imaging System is ideally suited to the rapid identification of counterfeit drugs based on the distribution of ingredients. Traditional techniques cannot perform this task as they report only the overall chemical composition of the sample.

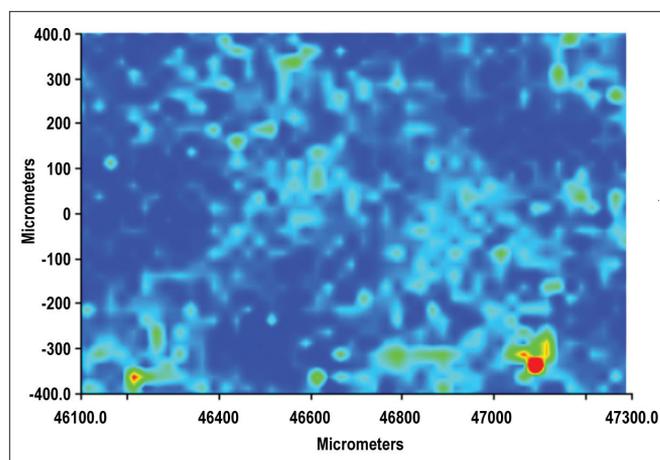


Figure 4. Band ratio image 4300/6072  $\text{cm}^{-1}$  for the counterfeit blend.