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Pharmaceutical Characterization meets Forensics Science: What Happened to Our Product?!

Andrew D. Vogt, John R. Roth, Maurice J. Pheil, and Joseph P. Neilly

AbbVie, Inc., NCE Analytical R&D, North Chicago, IL, USA

Forensic science based methods in the pharmaceutical industry are applied to many activities, including the identification (ID) of unknown materials, complaint testing, failure analysis, investigations, patent infringement support, reverse engineering studies, authenticity (counterfeit) testing and product tampering. The testing carried out is highly dependent on the specific need. In most cases, a systematic approach is followed, starting with visual and microscopy characterization and continuing with spectroscopic examination [1]. For ID of unknown materials, initial testing is used help determine chemical identity, followed by locating possible sources and comparison testing. This testing may determine that the material was incidental contamination, the product was tampered with, and or the material was not authentic [2]. Two case studies are presented below.

Case Study 1. Initially treated as a product complaint, we received Creon® capsules that contained unknown blue-green cylindrical-shaped particles to identify the particles. Creon® capsules normally contain only cream-colored pellets as shown in Figure 1. Physical measurements of dimensions of multiple capsules from each the complaint sample and the control sample did not indicate any significant differences, but variances in the weights of multiple complaint capsules were greater than those of the control capsules. The capsules were examined by optical microscopy and their contents by a combination of optical and scanning electron microscopy (SEM) and spectroscopy. There were no visual differences between capsule shells of the complainant or the control samples. The cream-colored pellets in both the complaints capsules and the control capsules were morphologically similar by optical microscopy and SEM. Energy dispersive x-ray spectroscopy (EDS), Fourier transform infrared spectroscopy (FT-IR) and Raman spectroscopy of the cream-colored pellets from the complaint and control capsules were similar. The blue-green particles were morphologically similar to a rodenticide by optical microscopy and SEM. The blue-green material had a composition consistent with at least carbohydrate and silicate and similar to d-CON®, also shown in Figure 1. These results indicate that the Creon® capsules were tampered with.

Case Study 2. Labels on pharmaceutical products identify brand and product details. In addition to the container and the product itself, the secondary packaging, including labels are counterfeited. Labels are often printed by thermal direct printing or thermal transfer printing. In the latter case, it is critical that ink properly adhere to the label substrate so as to not give a false appearance or misrepresent the product. In one such example, labels affixed to containers were observed to have incomplete printing of the ink, indicating that the ink did not completely adhere to the label. To understand the issue, two types of labels, one with varnish containing benzophenone and one without, were examined. By digital microscopy and SEM, scratch marks were observed along the length of both label types, but scratch marks in random directions and pits were also observed on the labels with benzophenone-containing varnish. Ink did not appear to be in intimate contact with the labels in all areas. Using the "Scotch™ tape" test, where tape was adhered to both labels over the ink and removed, more ink was removed from the labels containing the benzophenone-containing varnish than labels without benzophenone-containing varnish (Figure 2). Also, the thickness of the ink on the benzophenone-containing label appeared thin relative to the label without varnish. The composition by FT-IR and EDS of varnish-free areas on labels with and without benzophenone-containing varnish was primarily polyethylene with titanium dioxide and other minor inorganic components. Particulate and inclusions were observed on all labels in the varnish-free areas. The results suggest that the benzophenone-containing varnish might infiltrate the ink causing it to weaken its bonding to the substrate.

References:

[1] A Vogt, *et al*, Microscopy and Microanalysis Proceedings (2010) pp. 1584-1585.
[2] N Talaty, *et al*, Microscopy and Microanalysis Proceedings (2014) pp. 1412-1413.

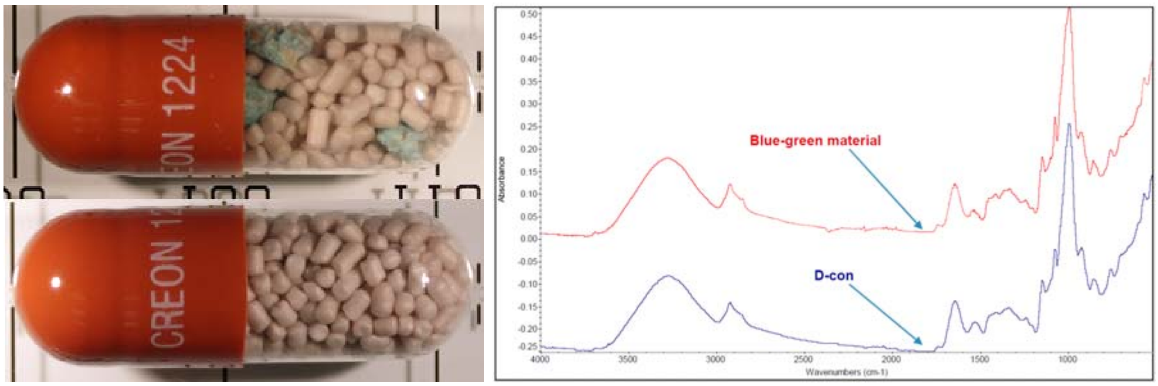
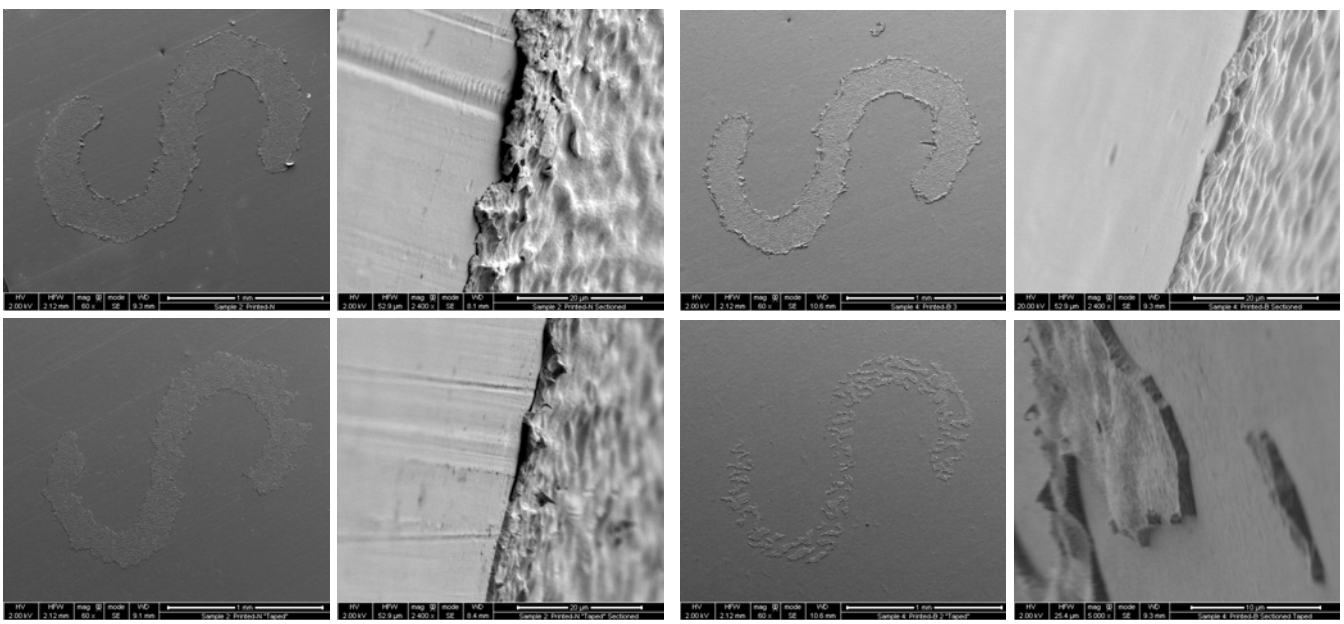


Figure 1. Left panel: Image of a complaint capsule containing blue-green material (top) and a “control” capsule (bottom). Right panel: FT-IR spectra of blue-green material (top) and d-CON® (bottom).



Without Benzophenone-Containing Varnish **With Benzophenone-Containing Varnish**

Figure 2. SEM images of labels with and without benzophenone-containing varnish, before (top row) and after (bottom row) applying and then removing scotch tape.

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