SCHOOL OF PHARMACY

DEPARTMENT OF
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TO: Dockets Management Branch
Food and Drug Administration
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RE: docket number 2003N-0361

This communication concerns docket number 2003N-0361 and relates to the activities of the Counterfeit Drug Task Force.

As you know, the FDA has indicated that a multipronged strategy is required to combat drug counterfeiting, including the Agency working with manufacturers, distributors, and practitioners. A suggestion is described below, and relies on near infrared (NIR) spectroscopy and the Agency's SUPAC guidelines to achieve a collaborative effort.

NIR spectroscopy is able quantify levels of drug and excipient in final dosage forms. Additionally, NIR is sensitive to subtle physical attributes of a dosage form (e.g. hardness, particle size). Additional attributes of NIR as an analytical methods include its non-invasiveness, potential for low detection limits, and rapidity of analysis (approximately seconds), including minimal or no sample preparation. The vast majority of components in pharmaceutical products can be accurately quantified using NIR spectroscopy.

Through Agency initiatives such as the SUPAC guidances, the Agency allows for minor formulation changes, without submission of a prior approval supplement.

NIR and current regulatory policy can be combined as a method to evade and detect counterfeiting. A manufacturer who wishes a product to not be counterfeited could vary the composition in the dosage form, for example batch-to-batch, to provide a unique NIR spectral signature for each batch of product. Components of an oral solid dosage forms (e.g. tablets or capsules) include the fillers, disintegrants, binders, lubricants, glidants, and coating materials. One or more of the component levels can be modified to yield a unique NIR spectra for the batch. Only the manufacturer (or collaborators of the manufacturer, such as the Agency) will know the composition and NIR spectra of products from a particular batch. A suspect product can be subjected to NIR analysis and cross-referenced against the authentic NIR spectra. The association between authentic

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product's batch number and its NIR spectra, along with the easy of measuring NIR spectra, provides a basis to combat counterfeit drugs, including the use of Agency field agents. Of added benefit, the association between NIR spectra and batch number(s) need not be provided to regulatory agencies or enforcement officials or health care providers, who could still perform field sampling and relay NIR spectra to the manufacturer. Furthermore, past compositions (i.e. past NIR spectra) of previous batches would not be indicative of future compositions (i.e. future NIR spectra). Hence, a counterfeit effort would have no target product to counterfeit, without detection.

This new approach to combat counterfeiting relies on the availability of several formulas for the marketed product. Fortunately, FDA allows for a range of component and composition changes in the manufacturing of products, without onerous regulatory requirements. In the case of immediate release and modified release oral solid dosage forms, changes are denoted Level 1, Level 2, and Level 3 type changes (1,2). Level 1 changes are those that are unlikely to have any detectable impact on formulation quality and performance; regulatory filing documentation of a Level 1 change is limited to the Annual Report.

This approach avoids the use of a taggant that is fixed, or is one which is included in the formulation for the sole purpose as a taggant. The approach above uses the formulation's components themselves as a taggant effort, and does so in a more subtle fashion, such that this taggant approach is less detectable and less susceptible to being counterfeited.