The USP Excipients Stakeholder Forum Meeting #2 for 2010-2015

Wednesday, June 18, 2014

Development and Utilization of a Global Spectral Library for Excipients

Steven Wolfgang, Ph.D.

Associate Director, Risk Science, Intelligence and Prioritization (Acting)

CDER, US FDA

Bei Ma, M.Sc.

Manager, International Business Development

USP

Pharmaceutical Globalization

- It is typical for drugs to be manufactured by multinational firms for multiple markets
- A significant portion of the supply of ingredients comes from outside US and a large share of that is used at foreign manufacturing sites
- Fine line between excipient and industrial grade ingredient
- Various intermediaries make up a typical supply chain with
  - varying, often lesser degree of personal interaction
  - multiple transactions of ownership & transfers in possession
  - transportation over long distances by common carriers

Why Consider a Library for Excipients?

- Certain excipients are very common to drug products
- Potential for unrecognized infiltration of unsuitable excipients into the pharmaceutical supply chain (substandard, falsified)
- Heavy reliance upon ID testing as gateway for acceptance of shipments arriving at finished dosage manufacturing sites
- Qualified excipient suppliers are tied to drug approval and continuity of drug quality and availability throughout lifecycle
- Common excipients show up in all FDA regulated products (food, cosmetic, animal drug, device, tobacco)

How Can a Library Benefit Stakeholders?

- Manufacturers of excipients
  - Chance to secure global distribution networks against infiltration of falsely portrayed substitutes
- Users of excipients
  - Identification and authentication of excipients
  - Rapid screen for anomalies
- Parties involved in compendial development/revision
  - Possible solution to the difficult task of excipient monograph ID test modernization
- Regulatory agencies
  - Tool for less invasive and time-consuming processes

Global Scan: Where are Libraries being Developed?

- Global regulatory agencies
  - US FDA; China FDA; NAFDAC; RZN etc.
  - CBP; Forensic Labs
- Multinational pharmaceutical manufacturers
- Analytical instrumentation providers
- Informatics solution providers
- Digital publishing houses
- Standard setting bodies
- Academia and research institutes

Libraries in Existence are Products of Disjointed Efforts

- Instrument and software solution providers seized the opportunity
  - Individual pharmaceutical manufacturers chose to work with certain solution providers
  - Library development by solution providers in absence of recognized, agreed-upon standards
- There is no protocol dictating sample collection for building libraries
- Thus. the quality/robustness of each library is variable depending on solution provider's perception of required discriminatory power and adequacy of training sets*

*based on discussion with certain solution providers and studies by FDA labs

Challenges in Development and Implementation

- Acquisition of representative, adequate number of samples for each excipient
- Equivalency of multiple master instruments if multiple labs are involved in building the library and among users
- Differentiation of excipients from different manufacturers
- Managing the quality of the library through the excipient lifecycle
- Establishing standards for building and using library (e.g., instrument design and data processing)
- Hosting the library and managing the input and access of spectral- and meta-data on an ongoing basis
- Although we conceive this to be a public library, we still might need to consider limited access to excipient clients where security or IP becomes a concern

Collaboration is Key to Success

- Excipient manufacturers with global presence
  - Ongoing support to provide representative samples
- Laboratories to participate in building library
  - Firms intending to use spectroscopic ID & screening
  - Global participation
- Solution providers and standard developing organizations
  - Standards for instrumentation, software and creation of algorithms
- Host for library
  - Web portal, possibly a single access point for genuine pharmaceutical excipients

Primary Candidates

- Excipients used in solid, oral dosage forms (appear to comprise >80% of excipient production volume)
- Among these, there is a short list of widely-used excipients in each of the main functional categories
  - Fillers and binders
  - Lubricants and flow aids
  - Disintegrants
  - Release rate modifying excipients
- Among the most widely used, ID and assay testing is often non-specific or non-existent
- Excipients in which falsified botanical source might be a safety risk
  - E.g., oils used as vehicles in injectable drugs which, if substituted, might contain allergenic proteins