Discussion of NIPTE Excipient Database 31st March 2011

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Chair IPEC QbD Committee

NIPTE is developing an excipient database on behalf of the FDA, hosted on pharmaHUB.org. It is open access (read-only), containing data on commonly used excipients, from literature and commissioned academic research studies. An update meeting was held on 31st March, in the Kurz Purdue Technology Center, West Lafayette, IN.

The database is the first step in developing an excipient information management system that can be used to guide formulation development. There is some flexibility in how the data is organized to provide a structure that can grow into a full information management system. To start the process it was decided to focus on direct compression (DC) excipients, and once the database structure is defined other classes of excipients will be added. Microcrystalline cellulose (MCC) was chosen as the lead excipient for further database development, as it is the most commonly used, high-volume, continuously produced DC excipient.

The key features of the database include:

1. Traceability of information to a test method, equipment and person or organization that supplied the data. It is hoped that the structured entry of information into the database will help to standardize test methods, which will facilitate comparisons.
2. The database is structured around the listing of compendial excipients, products containing those excipients and data on selected lots of excipients.
3. One has the ability to easily find key characters or attributes of an excipient and compare by excipient type, different grades or products and functional categories.

At the March 31, 2011 meeting/teleconference at Purdue, an online demonstration highlighted the key features of the database. Discussions addressed features, ease of use, incorporation of pre-existing user/supplier databases, and possible mechanism to fund the future development of the database.

A key discussion point was that many excipient-related effects on finished product performance are a function of the specific application (formula, process, scale). In other words there may be no general correlation between a specific excipient attribute and finished product performance. However in certain circumstances the variability of the same excipient attribute may be highly significant to finished product performance.

Data on excipient attributes combined with finished product performance data in the NIPTE database would enable multivariate data mining to identify such ephemeral interactions and guide research into their mechanisms. It was noted that PQRI is also looking at this area and the NIPTE database could be the ideal clearing house for such a data meld. On the excipient side this would require access to supplier data, which may raise problems of confidentiality, but

the database can be configured in such a way to allow the blinded incorporation of such data, if eventually made available.

For continuous-production high-volume excipients (e.g. MCC) a finer level of scrutiny is required beyond Certificate of Analysis (CoA) data, which tends to average out underlying variability. The traceability of a particular excipient needs to link user reference numbers, through supplier "batch" numbers, to intra-"batch" references. As MCC "batches" may represent hundreds to thousands of tones, over weeks to months of continuous manufacture, access to the most relevant in-process data will give a more accurate assessment of the impact of the excipient variability on finished product performance. One way of doing this is sequential numbering of containers within a given "batch".

There is sufficient flexibility in the structure of the database to link to pre-existing databases or simply import data via spreadsheets.

The database initiative is currently funded by FDA and in the future it is likely that such monies will switch more to scientific research on excipients, rather than maintenance of the database itself. NIPTE cannot solicit commercial funds directly so one idea would be for NIPTE to partner with IPEC on future database development.

Prabir Basu of NIPTE proposed:

- Further discussion* at the 24th May IPEC QbD meeting in Washington DC.
- A subsequent meeting with FDA, with representation from the IPEC QbD Committee.
- A two-day workshop on excipients for 2012 in collaboration with FDA/AAPS.

*Prior evaluation of the live database online at pharmaHUB.org is recommended to maximize committee discussion time. If enough people are interested NIPTE would be willing to host a demonstration interactive webinar before the 24th May IPEC QbD Committee meeting.