IPEC AMERICAS insider

IPEC-Americas Presents Two Key Excipient Topics at FDA GDUFA Meeting
Part I of 2-Part Series – Novel Excipients Topic

On June 15, 2015, FDA held a public meeting to seek input on the reauthorization of the Generic Drug User Fee Amendments of 2012 (GDUFA). IPEC-Americas representative, David R. Schoneker, Director, Global Regulatory Affairs, Colorcon, IPEC-Americas Past Chairman and current Vice-Chair for User and Maker Relations, presented comments during the meeting.

There were two key issues on which the presentation and comments centered:

1) The need for an independent FDA safety review and qualification process for novel excipients outside of a drug application; and
2) Improvements needed in the inactive ingredient database (IID) and policies on how families of related excipients can be referenced in abbreviated new drug applications (ANDAs).

This is the first of two articles on this meeting and addresses the topic of novel excipients as presented in the recent GDUFA meeting.

Novel excipients may be an important key to drug product development. They may address the following issues:

- development of high-quality drug products – through, for example, improving the solubility of poorly soluble APIs
- patient compliance – through, for example, advancement of formulation of more patient friendly dosage forms
- advancement of manufacturing science for drug products – through, for example, enabling or facilitation of continuous manufacturing for drug products

Currently neither pharmaceutical companies (as excipient users) nor excipient manufacturers have incentives to use or develop novel excipients which can produce all three potential improvements discussed above.

Pharmaceutical companies are generally not willing to risk the use of novel excipients because of the uncertainty of the current regulatory process to get them approved in their formulation which can result in delays in approval of their application. This is especially problematic for generic companies where cost (including speed to market) is critical.

In the case of excipient manufacturers, it follows that if their customers are unwilling to risk using novel excipients, there is little incentive to develop them. This can, and in some cases does result in stagnating market growth and innovation.

In the current state of affairs, there is no mechanism for evaluation of excipients alone – they are only evaluated as part of drug products in NDAs and ANDAs.

This results in sometimes developing drug products which are “good enough” but may not be optimal. This is not aligned with the concepts of quality by design.

IPEC-Americas has proposed to FDA that it adopt a new regulatory review process for excipients which provides for stand-alone (independent) review and qualification of excipients by the agency to mitigate the uncertainty associated with novel excipient use.

It is important to note that IPEC-Americas has not suggested that novel excipients would or should be “approved” outside of the drug approval process, but rather that there could be preliminary safety and qualification assessments independent of the drug that could be based on the intended route(s) of administration and intended use level(s).

Currently the only mechanisms that exist for excipient manufacturers to present excipient specific information to the agency independent of a drug application are in Type IV (Excipient, Colorant, Flavor, Essence, or Material Used in Their Preparation) or Type V (FDA Accepted Reference Information) drug master files (DMFs). However, DMFs are only intended to be reviewed by the agency in conjunction with a drug application and there is no consistent approach to DMFs which may result in delays of the application.

FDA toxicologists have referred IPEC-Americas to the Biomarker Qualification Program (BQP) as a possible model process for novel excipients. IPEC-Americas believes that there are many important, relevant concepts in the program and with modification could provide a foundation for engaging FDA on modernizing novel excipient development.

IPEC-Americas has presented some additional options to FDA for consideration, again emphasizing that independent FDA safety assessment of novel excipients is needed outside drug applications. They do not expect “approval” per se, but rather safety evaluation and qualification in the intended route(s) of exposure and exposure level(s). Following are some of the additional options presented.

- Novel excipient safety information, including studies and bridging arguments which would be provided in Type IV or V DMFs
- Implementation of a GDUFA / PDUFA (Prescription Drug User Fee Act) –type user fee system to fund FDA resources to perform independent safety assessments/qualifications
- Development and publication of a list of excipients “qualified” for specific intended uses and levels in pharmaceutical products

IPEC-Americas intends to include the relevant BQP procedures and to collaborate with FDA on any additional needs for such a process.