IPEC-Americas Representatives Provide Oral Testimony at FDA OTC Monograph Hearing

On March, 26, 2014, IPEC-Americas representative David R. Schoneker, Vice Chair for Maker and Distributor Relations attended the FDA OTC Monograph Hearing to provide testimony on behalf of IPEC-Americas. Priscilla Zawislak, Vice Chair for Harmonization and Compendial Monographs and Katherine Ulman, Vice Chair for Science and Regulatory Policy participated in the meeting through a webcast.

During his remarks, Mr. Schoneker provided background about how many excipients are used as an “active ingredient” in OTC drug products. These materials are frequently referred to as atypical actives and in certain cases, may be the only ingredient in an OTC product. Although atypical actives are seen commonly in OTC drug products they are also present in generics and even in some branded prescription products. Many OTC formulations existed long before ICH Q7 was developed as the GMP guideline for APIs and in most cases, supplying excipients manufactured to ICH Q7 for these OTC applications is not feasible nor is there any supplier available who currently produces these atypical actives manufactured to ICH Q7 GMPs.

Unlike traditional APIs, “atypical actives” usually have a physical effect rather than a purely pharmacological effect. Because of their long history of safe use in many applications, it is common that excipient manufacturers may not be aware of how their material is being used. In several cases their use as an “active” has not been communicated to them by their customer or through distributors. It’s also important to recognize that atypical actives are not limited to excipients; food additives and personal care ingredients have also been listed as actives in OTC drug products.

Mr. Schoneker explained to FDA why it is not possible to expect that atypical actives will be produced using ICH Q7 GMPs and that IPEC-Americas believes that there must be flexibility in determining the appropriate type and level of GMPs to be used for these materials.

If FDA requires compliance to ICH Q7 GMPs for atypical actives there may be significant negative implications to the industry and to patients who depend on these products. Many OTC and generic drugs depend on atypical actives for which suppliers meeting ICH Q7 GMPs don’t exist. In some cases, upgrading supplier facilities to achieve ICH Q7 would require significant investment and would typically not be an option. Reformulating the OTC drug may not be feasible, especially if the active ingredient is the drug (e.g. rubbing alcohol). Withdrawal of the OTC drug product from the market could result, which could also lead to possible drug shortages for common OTC Drugs and cause significant impact to patients and consumers.
Since appropriate GMPs can satisfy safety and risk concerns for use of excipients, food additives or personal care ingredients for the **bulk** of a drug product, what is the real risk to patient safety if these GMPs are used for atypical actives? A realistic balanced regulatory approach based on risk must be developed to provide flexibility for the use of atypical actives in OTC drug products.

GMPs aligned with the IPEC-PQG Excipient GMPs or other appropriate GMPs should be acceptable for existing atypical actives. Some additional technical considerations may be necessary for use in some OTC products; not a higher level of GMP, for example:

- Composition and potential variability
- Tighter specifications (when needed)
- Stability
- Cleaning / environmental controls
- Change control and customer notification procedures

Viable approaches to controlling “atypical active” quality and appropriate GMPs are needed between industry and regulators. Appropriate guidance is needed to clarify regulator expectations for existing OTC products and separate guidance may be needed for new products. IPEC-Americas provided similar information to FDA during GDUFA discussions on the generic uses of atypical actives, however, clear guidance regarding the expected level of GMP or technical information is still needed to support their continued use.

In his testimony, Mr. Schoneker stated that IPEC-Americas is requesting FDA to carefully consider these issues when assessing how best to improve the OTC Monograph system and provide a clear, pragmatic guidance for the manufacture and handling of “atypical actives.” Unfortunately, FDA inspectors have been showing up at excipient manufacturing plants expecting ICH Q7 API GMPs. This is causing significant issues. These FDA Inspectors should be informed of potential issues of trying to apply ICH Q7 GMPs at these facilities and provided guidance on how to appropriately audit an atypical active manufacturing facility. They should not use ICH Q7 API GMP!

IPEC-Americas will be submitting written comments to the FDA docket which will provide a detailed proposal with recommendations for how flexibility could be provided for atypical actives going forward. Hopefully through this flexibility the industry will continue to maintain adequate GMP controls for patient safety and minimize the potential for OTC drug shortages in the future.