Published on *IPEC-AMERICAS* (http://ipecamericas.org)

IPEC Federation Publishes Position Paper on EU Risk Assessment Guidelines for Excipients (2015/C 95/02

IPEC Federation Position Paper on EU Risk Assessment Guidelines for Excipients (2015/C 95/02)

Problem statement

The IPEC Federation (IPEC) acknowledges and welcomes the risk-based approach of the EU Guidelines1 following the principles of Quality Risk management according to ICH Q92. However, IPEC members acknowledges the limited jurisdiction of the EU Guidelines and recognizes that other Regulatory Agencies may view the specifics expressed in the EU Guidelines on Risk Assessment for Excipients differently. Therefore, this position paper applies only to the community regulated under the EU Risk Assessment Guidelines and is not intended to be commentary on risk assessment for other regions or in general. IPEC reserves the right to make additional or different comments on other laws, guidance, and publications as appropriate. The general principles are to properly control and track the quality and safety of excipients, throughout the entire supply chain, by appropriate means of quality management. This involves ensuring that Good Manufacturing Practices (GMPs) and Good Distribution Practices (GDPs) are implemented, in alignment with IPEC's objectives and related guides and standards3. IPEC appreciates that many comments on the draft guidelines made by IPEC members have been considered in the final version.
IPEC is convinced that the application of appropriate GMP and GDP throughout the entire pharmaceutical excipient supply chain will enhance patient safety. This can however only be achieved if the risk-based approach is always scientifically sound and risks are evaluated in collaboration with all relevant parties in the supply chain.

IPEC is concerned that there is not enough time to complete risk assessments for all excipients by the 21 March, 2016 deadline, and that incomplete assessments may jeopardize the availability of high quality excipients that have been in use for many years.

Points to consider

The 'excipient industry' does not exist as such because the ingredients produced are not only targeted for use in pharmaceuticals but also in food, cosmetics, or as general chemicals. The supply of ingredients for use as pharmaceutical excipients is often minor compared to their use in

other applications; however, the availability of the ingredients for use in the manufacture of medicinal products may be essential to the performance and delivery of a drug product.
Quality systems applied during the manufacture of pharmaceutical excipients are diverse and usually based on their use in a specific application, thus – by necessity – they often already include risk-management principles.
Adjusting current quality systems to "pharmaceutical quality systems" according to 2.6 (i) of the guidelines may be difficult and conflict with other requirements. Furthermore, specific criteria has not yet been defined for what is a pharmaceutical quality system; therefore, additional clarification of the specific expectations by the regulators is necessary. IPEC is happy to provide experts to collaborate with regulators as they work to develop and define future requirements. Inappropriate requirements could jeopardize the availability of high quality excipients that have been used for many years and potentially lead to drug shortages.

Many elements of GMP and GDP were implemented by excipient manufacturers and suppliers, prior to the existence of the EU GMP Guidelines Part I and II; these are the only references given in this new EU guideline. Historically, other voluntary GMP guides and standards have been available and use by excipient suppliers to facilitate implementation of excipient GMPs3. IPEC believes these guides and standards have appropriately defined and support pharmaceutical GMP requirements for excipients according to the EU regulation.

The EU guidelines set out a number of high level GMP principles for excipients that excipient suppliers will be required to comply with. Historically a significant number of these principles have not been embraced and implemented by excipient suppliers for the reasons outlined above. As a consequence, Manufacturing Authorisation Holders (MAHs) may conclude that an excipient supplier and their excipient(s) are "high-risk". When mitigation measures are not possible, the control will be for the MAH to cease using that excipient supplier. This action will result in the shortages or lack of availability of existing medicines which - until the publication of these guidelines - were accepted by all as safe and effective.

Position

IPEC will contribute to the implementation of the risk management and GMP principles of the EU guidelines and related article 46f of Directive 2001/83/EC as amended by Directive 2011/82/EU. In that context, IPEC would like to put forward some points for consideration by the key stakeholders.

- The assessment of all associated risks of an excipient and its suppliers can only be achieved by the MAH through open communication, collaboration and flow of information between all parties in the excipient supply chain.
- The risk-assessment application process, as described in the guidelines, could lead to situations in which an excipient from a single manufacturer could be classified by different MAHs into different risk classes (low, medium, high), depending for example on its intended use and application. This could result in differing expectations relating to the appropriate GMPs necessary in the manufacture of the same excipient. It would be impossible to comply with these different expectations in one quality system unless the highest level of GMP were to be implemented. IPEC sees this as a major concern and topic for further discussion between excipient users, excipient suppliers and authorities.

- As the evaluation of the "supply chain complexity" is required in 2.3 (viii) of the EU guidelines, communication, collaboration and cooperation along the entire supply chain is critical to avoiding gaps in a holistic risk-assessment process.
- IPEC views third-party auditing and certification schemes like EXCiPACT™ and national standards such as NSF/IPEC/ANSI 363-2014 as playing an essential role to achieve compliance with new requirements for the qualification of excipients and their suppliers. Without additional information concerning GMP and GDP compliance of the excipient supply chain through independent third-party audits, it will be nearly impossible for MAHs on their own to gather all the necessary data required. IPEC is committed to developing a document which traces the links between the EU guidelines and IPEC's own recommended good practices.

Rationale

Considerable effort will be required by the industry in order to complete all excipients risk assessments by 21 March 2016, as required by the EU guidelines.

The implementation of appropriate excipient GMPs by suppliers will require more than a year, and may be difficult to achieve for manufacturers of certain substances not typically produced as pharmaceutical excipients. MAHs may need to collaboratively establish realistic timelines with their suppliers to achieve the appropriate level and timing for implementation.
IPEC will share their views with the EC on the challenges to complying with the current compliance timeline and request collaboration with them to help establish more realistic goals and timelines.

1. Guidelines on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use
2. ICH guideline Q9 on quality risk management
3. EXCiPACT™, NSF/IPEC/ANSI 363 2014; IPEC PQG GMP Guide 2006 and IPEC GDP Guide 2006

About IPEC Federation:
Created in 2010, the IPEC Federation is a global organization that promotes quality in pharmaceutical excipients. The IPEC Federation represents the four existing regional International Pharmaceutical Excipient Councils (IPECs) – IPEC-Americas, IPEC Europe, IPEC Japan and IPEC China - and provides a unified voice to promote the best use of excipients in medicines as a means of improving patient treatment and safety. Its global membership extends to more than 200 companies.

Source URL (modified on 2015-05-06 14:13): http://ipecamericas.org/content/ipec-federation-publishes-position-paper-eu-risk-assessment-guidelines-excipients-2015c-9502