IPQ INTERNATIONAL PHARMACEUTICAL QUALITY
Inside the Global Regulatory Dialogue

ICH Q3D Process Opens the Door to Broader Participation; USP Announces Possibly Delaying Heavy Metal Chapter Deadlines

The development and implementation of the ICH Q3D guideline on elemental impurities could provide a model for a more inclusive ICH process.

In addition to the three agency and three association members from the US, Europe and Japan, several other stakeholders have played an important role in addressing the challenging issues involved and assuring the broad viability of Q3D as it emerges from the ICH pipeline. Prominent among them have been the International Pharmaceutical Excipients Council (IPEC), the US, European and Japanese Pharmacopeias, and regulatory agencies from China, Taipei, Korea, Canada, and Switzerland. Health Canada and Swiss Medic are voting members on the ICH steering committee.

> **At a PQRI conference on "evolving product quality" in mid-September in Washington, D.C., Novartis Analytical Science and Technology Group Quality Operations Global Head Mark Schweitzer – the industry rapporteur for ICH Q3D through Step 2 – highlighted the broad stakeholder involvement in the Q3D expert working group (EWG) and the benefits of that participation.**

"I think it worked," he said, "because we got a better view of the issues and global concerns" the guideline addresses as well as the significant challenges in its implementation.

Implementation Challenges

In addressing a session on international harmonization at the PQRI conference, Schweitzer discussed the development of ICH Q3D and provided an update on the implementation phase and what ICH has in mind in assisting in that process.

A "recurring theme" in the questions that the Q3D EWG has received on implementing the guideline has been interpreting how to conduct the risk assessments it calls for. Of concern are where to start the risk assessment, how far back it needs to go, what level of detail is expected and what level of data, and the potential sources that should be considered.

The questions have prompted the EWG to put together a concept paper recommending to the ICH steering committee the formation of an implementation working group (IWG) that would produce training materials and help industry through the implementation challenges.

> **One of the relevant issues has been the interface of how Q3D implementation interfaces with the new USP chapter on heavy metals *(IPQ October 17, 2013)*.**

On October 24, USP announced that its Elemental Impurities Expert Panel had met the previous week and approved a recommendation that the <232> limits "be revised to align with the ICH Q3D Step 4 document to the extent possible."

In addition, USP is considering adjustments to the elemental impurities implementation timeline "based on developments related to the anticipated ICH Q3D Step 4 document," and "is engaging in ongoing dialogue with representatives of industry and FDA on this topic."

Potentially influencing the USP committee's discussions was a letter from the Coalition for Rational Implementation of the USP Elemental Impurities Requirements, of which IPEC is a member.

The coalition letter expressed concerns over the global implications of the USP 2015 date, noting that the EP is targeting 2017. Of concern is that although FDA would not be required to enforce the 2015 date, other regulatory agencies that key off of USP may proceed with that date, significantly complicating ICH Q3D implementation. It also indicated the importance of harmonizing the heavy metal limits as well.

The Product Quality Research Institute (PQRI) – of which FDA is a member – is planning a workshop at USP headquarters on March 31 and April 1 on the next steps in implementing the elemental impurities requirements. The meeting will include presentations by key participants in the process and breakout groups to address key topic areas. The output is anticipated to be a white paper that will help provide help to industry in solving implementation challenges.

The workshop may include an update from ICH on its implementation process and participant feedback on the implementation issues to ICH on issues warranting further consideration.

[A full review of Schweitzer's presentation and the discussions that ensued at the PQRI conference session appeared in the October 2014 IPQ Monthly Update. By special arrangement, excerpts of IPQ's extensive coverage of the September PQRI/FDA conference are being made available to the PQRI community. IPQ provides in-depth coverage of emerging drug and biotech CMC and GMP issues and developments with a mission of helping advance and harmonize the quality regulatory process globally. For information on how to take advantage of IPQ's introductory company/organization license fees for 2015, contact Wayne Rhodes (rhodes@IPQPubs.com, (202) 841-9720) or Julia Zimmerman (zimmerman@IPQpubs.com). For more on IPQ, visit our website at www.IPQpubs.com.]