CROSS-INDUSTRY Organizations

An IPAC-RS update: Delivery Systems, L&E and GRRO

Ilse Peterson, Svetlana Lyapustina and Lee Nagao
On behalf of the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS)

The International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS) is an association committed to advancing consensus-based, scientifically-driven standards and regulations for orally inhaled and nasal drug products. The Consortium provides periodic updates on its activities to *Inhalation*. In this issue, the IPAC-RS Device, Materials, Leachables and Extractables Development Paradigm, and Global Regulatory Review and Outreach Working Groups are featured.

Device Working Group

In 2010, in response to concerns about variability in management of device changes throughout the product lifecycle, IPAC-RS conducted a survey to establish a baseline of current practices for typical scenarios that may be encountered throughout a "combination product" lifecycle. The survey's objective was to assess attitudes toward device changes to establish a view on the "as is" situation in relation to device changes; facilitate a move toward consensus on appropriateness of *in vivo* and *in vitro* testing; and highlight areas where regulatory requirements may differ from what is perceived to be technically required.

It was evident from the survey results, presented at a conference organized by IPAC-RS and the International Society for Aerosols in Medicine (ISAM), that there was extensive variance in the ways respondents managed the change process and notified regulatory authorities of changes. It was further concluded that risk management, as defined by the International Conference on Harmonisation (ICH), did not appear to consistently inform decision making. These results suggested that development of guidance utilizing a risk-based management approach to evaluate and manage device changes for orally inhaled and nasal drug products (OINDPs) could be of significant value to all stakeholders (i.e., patients, regulators and industry).

In response to this need, the IPAC-RS Device Working Group developed a framework for management of device changes for the product lifecycle. This is based upon the ICH Q8, Q9 and Q10 definition of risk-based approach to product development. It includes all combination products post the start of pivotal clinical studies and does not distinguish between innovator and generic products. The framework is conceptualized in terms of a decision tree that addresses potential effects of post pivotal clinical changes with an emphasis on critical quality attributes. Those attributes are defined as aspects of the drug product that determine:

- the safety and/or efficacy of the combination product;
- physiological changes that would not be detectable by standard *in vitro* test methods; and
- the ways the target population and/or patient or health care professional may interact with the device.

Later this year, IPAC-RS plans to publish a paper on its website describing this framework and is working with member companies and other organizations to encourage adoption.

Materials Working Group

The IPAC-RS Materials Working Group recently finished a webinar series on materials quality. Presentations are available on the IPAC-RS website and the group is translating these presentations into Mandarin. The recently-developed Baseline Materials Requirements will be presented as part of an ACS Rubber Division Workshop to be held in conjunction with the October 2013 Advanced Materials in Healthcare Conference. The group recently presented and published a proceedings paper on risk management approaches to materials quality at the May 2013 Smithers Rapra Extractables & Leachables Conference and is developing a risk management tool based on elements of its publication, feedback from the Smithers Rapra Conference and IPAC-RS member input. Group members have also co-authored posters on the rationalized approach to materials quality and risk management thinking applied to materials quality, presented at Inhalation Asia.

L&E Development Paradigm Working Group

The Leachables and Extractables Development Paradigm Working

Group (L&E) has developed a systematic approach for evaluating the linkage of process parameters to extractables profiles and, ultimately, to the critical quality attribute of leachables. The group is drafting a paper based on its experimental work that demonstrates this approach by linking identified process parameters for component molding to the component extractables profile. The investigation has involved:

- identification of critical molding process parameters;
- development of a molding design of experiments (DOE);
- analytical assessment of molded components; and
- statistical and non-statistical evaluation of the extractables profiles from the molding DOE.

The interim results of this work were published in a proceedings paper and presented at the May 2012 Smithers Rapra Extractables & Leachables Conference.

GRRO Working Group

The IPAC-RS Global Regulatory Review and Outreach Group (GRRO) continues to monitor and work with IPAC-RS working groups to respond to current and emerging global regulatory issues and to liaise with other organizations that have mutual and complementary interests. The working group has two subteams, one focused on outreach to Brazil and the other on China. These groups are monitoring relevant regulatory topics and establishing contacts with appropriate in-country organizations and government agencies. Representatives from the China sub-team were scheduled to attend the Inhalation Asia Conference to present posters. Participants are also providing input for the IPAC-RS/University of Florida 2014 Conference.

Additional updates

The book *Good Cascade Impactor Practices, AIM and EDA for Orally Inhaled Products* was published in May by the Cascade Impaction Working Group to introduce a new, simpler, more effective way to interpret pharmaceutical aerosol particle size data from orally inhaled products.

IPAC-RS is also holding a workshop with the AAPS INTFG, USP and FDA entitled Inhaled Drug Products: Current Practices and the Future of *In Vitro* Testing Technologies and Regulation, September 9-10, 2013 and planning the Orlando Inhalation Conference—Approaches in International Regulation with the University of Florida to be held March 18-20, 2014.

For more information on IPAC-RS activities, visit www.ipacrs.com.