An Introduction to IPAC-RS

What the industry group does for its member companies and for you

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IPAC-RS

After the United States Food and Drug Administration released its 1998 draft guidance on metered dose inhalers and dry powder drug products, a group of developers, manufacturers, and marketers of orally inhaled and nasal drug products (OINDP) joined together to provide a response. This ad hoc group developed a consensus response to the proposed guidance in 1999. After two years of collaborative OINDP industry efforts to address concerns with the state of regulatory guidance, changes in the regulatory environment, as well as the global focus of the Consortium's member companies, led to a broader scope of activities. In order to fully address their needs, the ad hoc group formed an industry association, the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS).

How IPAC-RS works

Thirteen companies currently participate in the consortium, with each making a substantial financial contribution to fund its activities. Each company selects two individuals to serve as representatives on the board of directors, an experienced and dynamic group of individuals with CMC (chemistry manufacturing and controls), clinical, and regulatory experience in the pharmaceutical industry. The board meets face to face for a day and half at a time at least three times per year. If necessary, the board conducts teleconferences a few times a year to discuss issues or make decisions between the meetings. Member companies in warm weather locations are often selected to host the February meetings, and the June meeting is often held at one of the member companies in Europe; this year's board meeting was held in England and hosted by GlaxoSmithKline, and the 2006 meeting was hosted by Boehringer Ingelheim in Germany.

The October meeting is typically held at the Washington, DC or Chicago offices of Drinker Biddle & Reath, a law firm that serves as secretariat and legal counsel to the consortium. The secretariat provides all necessary administrative support, including capturing the minutes at meetings and preparing draft slides for the working group presenters. The organization and support of the secretariat ensures that the pace of development of the consortium is rapid, in contrast to some other industry organizations that lack this type of support and rely solely on the members to advance their initiatives.

The board distributes its responsibilities among a number of committees and working groups. A planning committee, made up of the board chair and vice chair, along with 6 members elected to 2-year terms, meets monthly via teleconference. The planning committee does not make decisions itself, but it discusses and proposes topics for discussion at the board meetings and reviews the final agenda, which typically includes highlights and discussion of each of the working group efforts, a discussion of the 1- and 3-year strategic plans, prioritization and allocation of resources to each effort, review of the budget, a roundtable discussion of emerging regulatory issues and potential topics for new working group efforts. The committee also reviews the efforts of the working groups in between board meetings to ensure that they are in synchrony and that information is communicated across groups.

Although IPAC-RS was formed to serve its members' interests, its activities also benefit companies and organizations that cannot afford membership in an industry association. From the earliest days of its collaboration, IPAC-RS members have sought to advance scientifically driven approaches to enhancing the quality of inhaled and intranasal drug products. The board has defined four goals:

1. "Provide information and services to enable member companies to achieve their current and future product development and regulatory goals.

2. Advance OINDP regulatory and manufacturing science through discussion, research, and publication.

3. Increase outreach to the broader OINDP industry, OINDP suppliers, regulatory authorities, and other stakeholders, and participate in regulatory and scientific collaborations.

4. Be a constructive, effective and well-respected advocate for the OINDP industry."

The consortium aims to facilitate the industry's efforts to develop high-quality OINDP, develop new approaches to product development and lifecycle

management in line with the current regulatory thinking, and to implement Quality-by-Design concepts to their fullest extent.

Regulatory activities

IPAC-RS achieves its primary focus on allowing its members to reach their development and regulatory goals by commenting on regulations and guidances and by promoting clear and harmonized international regulatory expectations for OINDP. The consortium works with regulatory agencies worldwide, such as Health Canada, the US FDA and the European Medicines Agency (EMEA), to develop coherent and effective guidelines for inhaled and nasal drugs and monitors the progress and output of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

The consortium has collaborated with a number of organizations, including the Inhalation Technology Focus Group of the American Association of Pharmaceutical Scientists, the European Pharmaceutical Aerosol Group (EPAG), pharmacopoeias in the US, Europe, and Japan, and the International Organization for Standardization (ISO). The consortium has also provided active support to scientific collaborations such as the Product Quality Research Institute (PQRI). PQRI efforts affecting the inhaled and nasal drug industry have included working groups on leachables and extractables testing, particle size distribution mass balance, and particle size distribution profile comparisons.

Several technical reports, published articles, and comprehensive, detailed comments to draft regulatory guidances have been submitted to US and international regulators by IPAC-RS. The consortium's Supplier Quality Control (SQC) working group, comprised of pharmaceutical manufacturers and container closure system and device component suppliers, drafted and published a good manufacturing practices (GMP) guideline for suppliers of OINDP device components that regulatory authorities have highlighted as a good example of consensus industry standards and best practices. The SQC working group's supplier members, Valois, Rexam, West Pharmaceutical Services, and Bespak, are affiliate members of IPAC-RS and have played an important role in promoting understanding between manufacturers and suppliers.

One of IPAC-RS's working groups prepared an overview of the technical aspects and challenges of foreign particles testing for OINDP and a paper on best practices and clinical relevance regarding foreign particles in OINDP both of which were published in Pharmaceutical Research [1, 2]. Another working group completed a thorough and systematic assessment of a statistical method for determination of in-vitro equivalence of particle size distribution profiles obtained from cascade impactor testing. The working group's findings are reported in several papers published and accepted for publication in AAPS PharmSciTech [3, 4 ,5]. IPAC-RS members led PQRI's Leachables and Extractables (L&E) initiative, which included scientists from FDA, industry and academia. The L&E initiative developed recommendations that provide safety and analytical thresholds for leachables and extractables in OINDP and best practices for the analytical and safety evaluation of OINDP extractables and leachables. Recently, a great deal of attention has been focused on the FDA's Quality by Design initiative, and two new working groups are examining the role of QbD in product development and analytical methods.

Educational activities

Members of IPAC-RS seek to disseminate their expertise in the manufacture of inhaled and nasal pharmaceuticals by holding workshops, by presenting papers at conferences and, as of last year, by holding its own conference. The IPAC-RS public website, which contains public scientific position papers relating to OINDPs, is accessed by many non-IPAC-RS members, and IPAC-RS has become a source of information and leadership for the OINDP industry. IPAC-RS activities or positions have been highlighted in a number of scientific or regulatory journals, including The Gold Sheet, Pharmaceutical Research, the DIA Journal, The Journal of Aerosol Medicine, the Proceedings of Respiratory Drug Delivery, and American Pharmaceutical Review. Articles for peer-reviewed journals and a book on the development of safety thresholds are currently in preparation [6, 7].

Members of IPAC-RS

Abbott
Aradigm
AstraZeneca
Boehringer Ingelheim
GlaxoSmithKline
Nektar Therapeutics
Novartis
Novo Nordisk
Pfizer
sanofi-aventis
Schering-Plough
Teva
3M

The consortium sponsors workshops to progress dialogue among manufacturers, suppliers and regulators, and to train suppliers using its GMP Guideline for Suppliers of OINDP Devices [8]. The supplier workshop is open not only to manufacturers of device components but also to resin and rubber manufacturers who provide materials to the device companies. In addition, PQRI offers an annual two-day workshop, open to the public, based on the best practices for leachables and extractables developed with IPAC-RS. Over the course of the workshop, a series of speakers provide instruction on topics like selection of container/closure system components and control strategies for quality. IPAC-RS representatives have also been asked to provide instruction for workshops held by other organizations, including the FDA, the Barnett Educational Series, Pharmaceutical Education Associates, and the Management Forum.

Conferences provide another valuable means of conveying information to the industry. In recognition of the value of IPAC-RS' work, its board members and working group chairs have been invited to participate in numerous scientific conferences and meetings such as Respiratory Drug Delivery (RDD), the AAPS annual conference, the Society of Toxicology conference, and Drug Delivery to the Lungs. Presentations have included both papers and posters on highlights of IPAC-RS activities and conclusions reached by the working groups.

In November, 2006, IPAC-RS held its inaugural conference on regulatory and scientific approaches for orally inhaled and nasal drug products. The conference, titled "Inhalation and Nasal Drugs: The Regulatory Landscape," was open to the public and was attended by close to 200 industry, academic, and regulatory representatives. Besides promoting best practices and fostering communication between industry and regulators, the conference also sought to focus on the ways in which the Quality by Design paradigm applies to inhaled and nasal drugs, to generate recommendations on that topic, and to deliver those recommendations to the FDA. The second public conference will be held on September 22-24, 2008 in Bethesda, MD, and IPAC-RS intends to follow with additional conferences in even-numbered years.

Examples of IPAC-RS working groups

Supplier Quality Control (SQC)
International Industry Coordinating Group
Model OINDP
OINDP Materials
Leachables & Extractables
Profile Comparisons
Risk Management

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