



**INTERNATIONAL PHARMACEUTICAL AEROSOL
CONSORTIUM ON REGULATION AND SCIENCE**

**STRATEGIC PLAN &
2007 INITIATIVES**

**STRATEGIC PLAN & 2007 INITIATIVES
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I. INTRODUCTION

The Board of Directors of the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS) has developed this 2007 Strategic Plan to articulate the Consortium's key objectives and identify priority activities to support these objectives. This Strategic Plan, which is available publicly on the IPAC-RS website and has been shared with a number of interested parties, identifies a clear and forward-looking three-year strategic vision, and sets forth initiatives that will execute that vision in 2007. We hope that the plan set forth in this document as well as the activities described provide a clear picture of IPAC-RS, its mission and how it seeks to contribute to addressing important scientific and regulatory issues facing OINDP.

II. BACKGROUND

During the 1990s, regulation of the OINDP industry grew progressively more stringent; however, little regulatory guidance specific to OINDP existed. The publication of draft Guidances and guidelines on OINDP led to active public comment and discussion, and robust scientific dialogue regarding the regulatory expectations for these important drug products. These discussions prompted collective responses from the OINDP industry and directly led to the formation of IPAC-RS in 2001. Current IPAC-RS members include: Abbott, Aradigm, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Nektar Therapeutics, Novartis, Novo Nordisk, Pfizer, sanofi-aventis, Schering-Plough, Teva and 3M.

In a relatively short time, IPAC-RS has become a leading pharmaceutical industry group for inhaled drug product manufacturers. While the Consortium initially focused on responding to and commenting on guidances, its scope has expanded as its effectiveness and recognition have grown, and as the regulatory environment has changed. In recent years, IPAC-RS has developed technical reports, comments and best practices recommendations for submission to regulatory agencies and standard-setting bodies in the EU, US, Canada and internationally. IPAC-RS currently engages a broad range of OINDP companies, Consortium members and non-members alike, in scientific and regulatory discussions of critical importance to the OINDP industry. The Consortium also collaborates closely with many other industry and scientific organizations.

IPAC-RS activities or positions have been highlighted in a number of scientific or regulatory journals, such as *The Gold Sheet*, *Pharmaceutical Research*, *the DIA Journal*, *The Journal of Aerosol Medicine*, *the Proceedings of Respiratory Drug Delivery*, and *American Pharmaceutical Review*. IPAC-RS has been invited to participate in numerous scientific

conferences and meetings, such as Respiratory Drug Delivery (RDD), AAPS annual conferences, the annual conference of the Society of Toxicology, Drug Delivery to the Lungs, Barnett Educational Series, Pharmaceutical Education Associates, Management Forum, FDA internal educational sessions, and others. IPAC-RS organized and hosted a 2006 conference addressing pressing issues in OINDP regulation and science, and is organizing another conference for 2008. The IPAC-RS public website, which contains public scientific position papers relating to OINDP, is accessed by many non-IPAC-RS members, and has become a source of important information for the OINDP industry.

III. RECENT ACCOMPLISHMENTS

IPAC-RS Working Groups have made significant contributions to achieving IPAC-RS' mission of advancing scientifically driven approaches to enhancing product quality of inhaled and intranasal drug products. Following are recent highlights from some of these Working Groups:

- The Supplier Quality Control Working Group finalized its supplier GMP guideline and made a number of public presentations on the guideline. Regulatory authorities have highlighted the IPAC-RS guideline as a good example of industry standards and best practices. The Working Group sponsored a manufacturer-supplier forum to launch the guideline in the US and has held multiple training sessions for suppliers.
- The OINDP Materials Working Group continues to foster a better understanding among OINDP suppliers of extractables, their sources, and expectations for testing and control. The group has organized several symposia on extractables for OINDP suppliers and manufacturers.
- The Foreign Particles Working Group prepared a best practices/clinical paper that was published in *Pharmaceutical Research*. The Working Group also made podium and poster presentations at conferences and workshops, e.g., Respiratory Drug Delivery X and NIST. The Working Group completed its objectives in late 2006.
- IPAC-RS formed an International Industry Coordinating Group comprised of industry representatives of IPAC-RS, EPAG, EFPIA, and PhRMA to stay abreast of the evolving international regulatory landscape and identify opportunities for collaboration.
- The PQRI Leachables & Extractables (L&E) initiative, led by IPAC-RS members, finalized its PQRI recommendations, which have been hailed as a significant PQRI deliverable. The Working Group has organized several successful and well-attended L&E training sessions and is preparing several articles for peer-reviewed journals.
- The Mass Balance Working Group prepared a scientific evaluation of cascade impactor (CI) mass balance specification limits that will be published in the *Journal of Aerosol Medicine*. In finalizing its PQRI recommendations in early 2007, the Working Group completed its primary objectives.

- The USP Working Group published in the Pharmacopeial Forum a stimulus article about microbiological testing of OINDP. The group also reviewed and prepared responses to the public comments on the stimulus article. USP will incorporate the approaches recommended in the article into an appropriate USP chapter. The Working Group completed its objectives in 2006.
- The Profile Comparisons Working Group completed assessment of a statistical method for determination of equivalence of CI profiles and reported its findings in interim and final reports, which have been accepted for publication in *AAPS PharmSciTech*.
- The IPAC-RS Conference Organizing Committee organized and hosted the Consortium's first public Conference, a premier OINDP regulatory and scientific event in November 2006 (See <http://www.ipacrs.com/conf2006.html>). Over 180 people from 40 companies and multiple regulatory agencies attended the Conference. IPAC-RS will host its second public Conference in September 2008.

IV. STRATEGIC PLAN

This section presents the elements of the IPAC-RS Strategic Plan. The initial part of this Plan reiterates IPAC-RS' vision and mission. The second part of the Plan proposes four central strategic objectives for IPAC-RS over the next three years, followed by an organizational chart that describes IPAC-RS initiatives that support these objectives. The objectives of these specific IPAC-RS initiatives are described in more detail in Section V, "IPAC-RS Initiatives – 2007."

Vision

IPAC-RS is and will remain the leading resource and advocate of the OINDP industry.

Mission

To advance scientifically driven approaches to enhancing product quality of inhaled and intranasal drug products.

Strategic Objectives

1. Provide information and services to enable member companies to achieve their current and future product development and regulatory goals
 - Serve as a resource for sound analyses of OINDP regulatory requirements.
 - Engage in initiatives and develop tools to facilitate current and future OINDP product development processes (e.g., facilitation of the manufacturer-supplier relationship through collaborative scientific and

regulatory dialogue; creation of a range of tools to help member companies understand the application of Quality by Design to OINDP).

2. **Advance OINDP regulatory and manufacturing science through discussion, research, and publication**
 - Develop and publish IPAC-RS best practices for OINDP.
 - Identify and address key questions for OINDP under a Quality by Design framework, and aspects of the implementation of new regulatory initiatives that require clarification.
3. **Increase outreach to the broader OINDP industry, OINDP suppliers, regulatory authorities, and other stakeholders, and participate in regulatory and scientific collaborations**
 - Strengthen relationships with regulatory authorities and standard-setting bodies (e.g., FDA, Health Canada, EMEA and other international bodies).
 - Provide educational and training workshops and conferences for the OINDP industry, suppliers, and regulators, as appropriate, on current and emerging scientific and regulatory topics relevant to OINDP.
 - Contribute actively to scientific and regulatory discussions among industry, government, and standard-setting bodies (e.g., PQRI, ISO).
4. **Be a constructive, effective and well-respected advocate for the OINDP industry**
 - Actively comment on regulations and guidances that impact OINDP and promote clear and harmonized international regulatory expectations for OINDP.
 - Engage regulatory authorities in constructive discussion and sharing of ideas on OINDP best practices and the application of Quality by Design to OINDP.

International Pharmaceutical Aerosol Consortium on Regulation and Science

VISION

IPAC-RS is and will remain the leading resource and advocate of the OINDP Industry.

MISSION

To advance scientifically driven approaches to enhancing product quality of inhaled and intranasal drug products.

STRATEGIC OBJECTIVES 2007-2009

Objective 1

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

- Regular reporting and monitoring of OINDP regulatory developments
- Input to regulatory agencies and standard setting bodies on OINDP issues
- International Industry Coordinating Group

Objective 2

Advance OINDP regulatory and manufacturing science through discussions, research and publication.

- QbD Initiatives**
- Model OINDP Combination Products
 - Supplier Initiatives (SQC, Elastomers, etc.)
 - Feasibility Study Groups
 - Risk Management
 - QbD Methodology
 - QbD Correlations

Objective 3

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

- Supplier Initiatives (SQC, Elastomers, etc.)
- L&E
- International Industry Coordinating Group
- ISO
- PQRI
- IPAC-RS Workshops & Conferences

Objective 4

Be constructive, effective, well respected advocate for OINDP industry.

- FDA, Health Canada, EMEA
- EurPh, USP, JP
- ISO, ICH
- PQRI
- EFPIA, EPAG, PhRMA

2007 TACTICAL INITIATIVES

V. IPAC-RS INITIATIVES - 2007

All IPAC-RS Working Groups and extramural efforts are described here. They are arranged under the headings, “QbD Initiatives,” “International Outreach Activities,” and “Legacy IPAC-RS Initiatives.”

QbD INITIATIVES

A. OINDP MATERIALS WORKING GROUP

Objectives

To improve materials quality and integrity, and reduce supply chain problems by optimizing control strategies, through:

- Scientific, peer-reviewed publication(s) on the improvements in OINDP quality and control strategies, and
- Education and training of all parties involved with the supply chain for OINDP materials.

Activities

- Held US and European symposia on extractables for OINDP suppliers and manufacturers.
- Publish articles on materials and process quality, safety assessment, analytical techniques and practical capabilities.
- Develop additional tools for IPAC-RS member companies that would address OINDP materials selection and quality under a QbD framework.

B. MODEL OINDP WORKING GROUP

Objectives

- To consider and explain how initiatives such as Quality by Design may be applied to OINDP. The focus of this group will be two-fold: internal, through industry discussion and education, and external, through dialogue with regulatory authorities and standard-setting bodies.

Activities

- Developed *P2 Points to Consider* document providing guidance on content of P2 section of CTD for OINDP under a QbD paradigm.

C. QbD ANALYTICAL METHOD DEVELOPMENT WORKING GROUP

Objectives:

- To understand and stimulate public discussion on the topic “QbD of methods for OINDP” through preparation and publication of a concept paper.

Activities

- Review information in the public domain about how to study method variability and how to fit that knowledge into a manufacturing process.
- Publish paper on application of QbD to OINDP method development and its relationship to process development.
- Prepare a *Points to Consider* paper addressing key questions regarding characterization of current capabilities of control methods for APSD and DDU.

D. QbD CORRELATIONS WORKING GROUP

Objectives

- Explore the possibility of designing clinical trials that could address questions about links between clinical safety and efficacy and key quality parameters of OINDP, e.g., APSD, fine particle dose. The focus is not on academic understanding of fundamental principles but on pragmatical considerations for establishing a QbD design space.

Activities

- Conduct due diligence, including contacting several outside clinicians to gather information and explore the feasibility of designing a clinical study.

E. RISK MANAGEMENT WORKING GROUP

Objectives

- To better understand the use of Risk Management in a Quality by Design paradigm and its application to OINDP design, development, and performance; and to identify risk areas common to OINDP, with the end goal of facilitating harmonization of regulatory approaches to OINDP.

Activities

- Undertake OINDP Risk Identification and Analysis.
- Review Medical Device Global Harmonization Task Force (GHTF) concepts and other relevant materials and articulate essential Risk Management principles for design, performance and safe use of OINDP.

- Identify and share best industry practices (including examples) on Risk Management and evolving approaches to OINDP quality assurance.

F. QBD LEACHABLES & EXTRACTABLES FEASIBILITY GROUP

Objectives

- Consider feasibility of an IPAC-RS effort on how OINDP extractables and leachables can be addressed under a QbD paradigm.

Activities

- Developing proposal for review by IPAC-RS Board of Directors.

G. SHELF LIFE STABILITY WORKING GROUP (through PQRI)

Objectives and Activities

- Review current ICH guidelines and best practices in the estimation of shelf life or retest period for stability indicating quality attributes of pharmaceutical products.
- Investigate alternative statistical approaches for estimating shelf life.
- Develop statistical methodologies for QbD discussions on shelf life estimation.

H. SUPPLIER QC WORKING GROUP

Objectives

- To encourage quality through design rather than through testing and to enable the provision of consistently high quality components by promoting the implementation of robust quality systems by OINDP component manufacturers. The focus of this Working Group going forward is external, i.e., promoting acceptance and use of the IPAC-RS Guideline, and engaging suppliers, regulators, and other stakeholders.

Activities

- Conduct workshops on the IPAC-RS Supplier GMP Guideline for OINDP manufacturers and suppliers, and increase supplier involvement in the Working Group, including recruitment of additional n-1 suppliers and potentially n-2 suppliers.
- Incorporate guideline into a public standard, and consider need for further supplier-related guidelines.
- Monitor activities with regard to DMF system reforms and consider a workshop on this topic.

I. CASCADE IMPACTION WORKING GROUP

Objectives

- To determine and publicize best scientific approaches for developing CI method for OINDP.

Activities for 2007

- Publish a paper about minimizing variability of CI test method.
- Publish a paper about quantification of sources of variability in a CI method, e.g., as part of method validation, diagnostic, etc. Paper will include general guidance and recommendations for a statistical study design for understanding and separating sources of variability.

INTERNATIONAL OUTREACH ACTIVITIES

J. INTERNATIONAL INDUSTRY COORDINATING GROUP

Objectives

- To assess the evolving international regulatory landscape for OINDP, conduct risk assessment of worldwide regulatory developments, and, as appropriate, participate in relevant efforts (e.g., EPAG, EFPIA, PhRMA, ISO, Ph. Eur., USP, JP) with respect to OINDP issues.

Activities

- Develop global OINDP regulatory grid that includes links to pertinent regulations and notes key regional differences. This grid will serve as “roadmap” to help companies navigate the regulatory and development process for a given product depending on the target geographical region(s).
- As necessary, coordinate joint efforts to comment on regulatory and standard-setting documents and meet with regulatory authorities on OINDP issues.
- Monitor, regularly assess and discuss emerging OINDP regulatory issues around the world and identify opportunities to proactively engage in non-IPAC-RS led initiatives with an impact on OINDP regulatory and scientific matters (e.g., ISO, ICH, Asian Harmonization WP).

K. IPAC-RS 2008 CONFERENCE ORGANIZING COMMITTEE

Objectives

- To organize a follow-up OINDP industry conference to the 2006 inaugural event.

Activities

- Develop a premier OINDP regulatory conference program.
- Invite leading experts from industry, international regulatory agencies, and academia to participate in the Conference as presenters, moderators, and panelists.

L. ISO ACTIVITIES

Objectives

- To ensure that the ISO standards for inhalers and nebulizers are not redundant to or contradict existing regulations or products' capabilities and do not create new, unnecessary burdens for OINDP.

Activities for 2007

- Actively participate in the discussion of comments and revision of the draft ISO standards.

LEGACY IPAC-RS INITIATIVES

M. PTIT PUBLICATIONS TEAM AND DDU WORKING GROUP

Objectives

- To monitor and report on ongoing developments (e.g., regulatory guidances, pharmacopeial revisions, ISO standard, conference presentations and published articles) affecting DDU specifications or use of PTIT in OINDP.
- As appropriate, address proposed standards and regulations affecting DDU specifications or use of PTIT in OINDP.

Activities

- The PTIT Publications Team will prepare several articles for publication in peer-reviewed journals. For 2007, the Team is focusing on characterization of the parametric tolerance interval test proposed by regulators for control of DDU in OINDP.

N. LEACHABLES AND EXTRACTABLES (through PQRI)

Objectives

- To communicate and promote the PQRI L&E Recommendations through publications, presentations, and training courses.

Activities

- Publish the L&E best practices and safety thresholds work in peer-reviewed journals and books.
- Hold Training Courses on the Recommendations.

O. MASS BALANCE WORKING GROUP (through PQRI)

Objectives

- To submit recommendations on approaches to setting cascade impactor (CI) mass balance limits and to publicize a scientific evaluation of the same.

Activities

- Respond to comments on the Working Group's recommendations.

P. PROFILE COMPARISONS WORKING GROUP (through PQRI)

Objectives

- To complete assessment and document capabilities of the FDA-proposed statistical method for determination of equivalence of CI profiles and publicize the results.

Activities

- Complete the Final Report characterizing FDA-proposed tests for profile comparisons of aerodynamic particle size distribution.
- Publish paper based on Report.
- Consider presenting the work, method and findings at public symposia or seminars.

VI. APPENDIX A – IPAC-RS BOARD MEMBERS

Board of Directors

1. Kathy Ledoux, 3M Drug Delivery Systems, Technical Manager US Inhalation Drug Delivery
2. Richard Moody, 3M Health Care Limited, Laboratory Manager Global Inhalation Drug Delivery
3. Barbara Falco, Abbott, Executive Director of Quality
4. David Cipolla, Aradigm, Director Pharmaceutical Sciences (CHAIR)
5. Jim Blanchard, Aradigm, Staff Scientist, Preclinical Development
6. Thomas Lööf, AstraZeneca, Associate Director Pharmaceutical & Analytical R&D
7. Andy Rignall, AstraZeneca, Associate Director Analytical Development
8. Liuda Shtohryn, AstraZeneca, CMC Regulatory Affairs Director *
9. Terry Tougas, Boehringer Ingelheim, Highly Distinguished Scientist (CO-CHAIR)
10. Helmut Bender, Boehringer Ingelheim Pharma GmbH & Co. KG, Vice President Drug Delivery Department
11. Stefan Leiner, Boehringer Ingelheim Pharma GmbH & Co. KG, CMC Expert
12. Susan Holmes, GlaxoSmithKline, Associate Director, CMC Regulatory Affairs
13. Dave Parkins, GlaxoSmithKline, Director DPI Product Development
14. Mitch Rosner, Nektar Therapeutics, Director, Pharmaceutical Development
15. Mary Ann Smith, Nektar Therapeutics, Associate Director Regulatory Affairs
16. Paul Colthorpe, Novartis Pharma AG, Global Head of Inhalation & Device Development Department
17. Orin Tempkin, Novartis Pharmaceuticals Corporation, Associate Director Global Regulatory CMC
18. Johan Waldeck, Novo Nordisk, A/S, Principal Scientist Concept Research
19. Lou Fries, Novo-Nordisk Pharmaceuticals Inc., Director CMC Regulatory
20. Jackie Schumacher, Pfizer Global Research & Development Associate Research Fellow - Regulatory CMC
21. John Hart, Pfizer Limited, Senior Director
22. Mark Broughton, sanofi-aventis Ltd., Head of Quality Operations
23. Janice Kitson, sanofi-aventis Pharmaceuticals Assistant Director
24. Robert Berger, Schering-Plough Corporation, Associate Director Respiratory Product Development
25. Donald Chambers, Schering-Plough Corporation, Senior Director Respiratory Product Development
26. Axel Perlwitz, Teva, Associate Director, Regulatory Affairs
27. Steve Viti, Teva, Senior Director Global Regulatory Affairs

* Ex officio position, IPAC-RS Immediate Past Chair

ABBREVIATIONS

| | |
|-------|--|
| APSD | Aerodynamic Particle Size Distribution |
| CI | Cascade Impaction |
| DDU | Delivered Dose Uniformity |
| L&E | Leachables and Extractables |
| OINDP | Orally Inhaled and Nasal Drug Products |
| PQRI | Product Quality Research Institute |
| QbD | Quality by Design |

If you have any questions on this Strategic Plan, please contact the IPAC-RS Secretariat:

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