

MINUTES OF THE TELECONFERENCE
OF THE PQRI PSD MASS BALANCE WORKING GROUP ON
MONDAY, 19 NOVEMBER 2001

I. PARTICIPANTS

Terry Tougas (BI), Chair
Jeff Blumenstein (Pfizer)
Mary Devlin Capizzi (IPAC-RS)
Sylvia Gantt (PQRI)
Martin Lavery (Aventis)
Lana Lyapustina (IPAC-RS)
Jolyon Mitchell (Trudell Medical)
Brian Rogers (CDER/FDA)
Bruce Wyka (Schering-Plough)
Kahkashan Zaidi (USP)

II. OPENING

Dr. Tougas welcomed the participants. He explained the objectives of the teleconference as follows: (i) to introduce Working Group members; (ii) to establish ground rules; (iii) to review objectives of the Working Group; (iv) to agree on a process to achieve the Working Group's objectives; and (v) to agree on next steps.

The participants introduced themselves, described their background, relevant experience and their interest in the PQRI PSD Mass Balance Working Group. Dr. Rogers explained that he will participate in the Working Group teleconferences until a permanent FDA representative has been identified. Dr. Zaidi, USP's scientific liaison to the USP Aerosols Expert Committee, noted that USP is seeking to improve their Chapter <601> on aerosols and that the work of the PSD Mass Balance and other PQRI pulmonary working groups could be relevant in that process.

III. DISCUSSION

Structure of PQRI and Role of PSD Mass Balance Working Group

Ms. Capizzi reviewed the general organization of PQRI and the role of the PQRI PSD Mass Balance Working Group within it. She explained that PQRI was designed as a unique collaboration involving industry trade associations, academia, government and pharmacopeia to conduct research in support of regulatory policy. Currently, PQRI has the following ten members:

[AAPS](#) American Association of Pharmaceutical Scientists
[CHPA](#) Consumer Healthcare Products Association
[FDA/CDER](#) U.S. Food and Drug Administration, Center for Drug Evaluation and Research
[GPhA](#) Generic Pharmaceutical Association (formerly GPIA, NPA, and NAPM)

[IPAC-RS](#) International Pharmaceutical Aerosol Consortium on Regulation & Science
[IPEC-Americas](#) International Pharmaceutical Excipients Council of the Americas
[ISPE](#) International Society for Pharmaceutical Engineering
[PDA](#) Parenteral Drug Association
[PhRMA](#) Pharmaceutical Research and Manufacturers of America
[USP](#) United States Pharmacopeia

The organizational chart, which was circulated to all participants prior to the teleconference, shows that PQRI is governed by a Board of Directors. The PQRI Steering Committee (SC) provides scientific and technical oversight to the Technical Committees. Technical Committees oversee the research conducted by the Working Groups.

The findings of the PSD Mass Balance Working Group will have to be reviewed and approved by the Drug Product Technical Committee (DPTC) and the Steering Committee. Drs. Blumenstein and Poochikian, DPTC members, will serve as liaisons between DPTC and the pulmonary Working Groups. Dr. Blumenstein described his role as that of an advocate and a facilitator of interactions among the three pulmonary Working Groups, DPTC and SC.

Role of Working Group Chair, Members and Secretariat

Dr. Tougas explained that as a Working Group Chair, he will facilitate the Working Group's discussions and chair teleconferences and meetings. Dr. Tougas stated that he will also participate as a technical member, contributing his scientific expertise to the Working Group's research and deliberations.

Dr. Tougas reviewed the role of Working Group members. He noted that each participant was nominated to the Working Group because of an interest expressed by each individual. Dr. Tougas expressed confidence that all Working Group members will be fully active and constructive, and that the Working Group as a whole will move quickly to achieve progress within reasonable timeframe.

Ms. Capizzi described the role of the IPAC-RS Secretariat. She explained that the Secretariat will arrange meetings and teleconferences, draft agendas and minutes, assist in drafting of the Working Group's technical documents, coordinate the implementation of agreed actions, compile and circulate comments and background information, and offer other administrative support as requested by the Working Group. Dr. Lyapustina added that the Secretariat will also facilitate gathering of the confidential industry database, should the Working Group agree to collect one. She briefly reviewed the general principles followed by IPAC-RS in its data collection:

- prior to soliciting the data, the Working Group has to discuss and agree on the exact purpose of the data gathering, specific qualifications of the data (amount, type, quality, etc.), plans for analyzing the data, and type of information that should be included in the industry files submitted to the Secretariat;
- once the Data Template and the Protocol governing the use of and access to the database have been drafted and finalized by the Working Group, the Secretariat will circulate the Template and the Protocol to the relevant companies, and subsequently receive and blind industry data;

- the blinded database is not available to all Working Group members, but only to a small number of designated statisticians, each of whom is required to sign a non-disclosure agreement; the results of the statistical analyses, however, are open to the discussion by the full Working Group; and
- the data remains the property of the company supplying it, and thus the company approval is required for every particular use of the data.

Data and Objectives of PSD Mass Balance Working Group

Dr. Rogers stated that the data used by the Working Group should have sufficient level of detail for drawing conclusions and basing recommendations. Dr. Lyapustina reiterated that the Working Group will have the opportunity to discuss and agree on specific details of the requested data before the data is collected.

Dr. Rogers inquired whether only one or all members of the Working Group could supply the data. Dr. Tougas replied that the Working Group is open to proposals regarding the source of data, and that all possible sources should be carefully considered. He mentioned that ITFG/IPAC-RS had a database for investigating the mass balance issue, and that it might be possible to use that database by the present Working Group if appropriate.

Dr. Rogers further inquired about the composition and size of the ITFG/IPAC-RS database. Dr. Tougas answered that the summary of the database is contained in the paper entitled [*Initial Assessment of the ITFG/IPAC Aerodynamic Particle Size Distribution Database*](#). This paper was submitted to the FDA in August 2000 and is available through the FDA docket for the draft CMC Guidances for OINDP and at the following websites:
http://www.fda.gov/ohrms/dockets/ac/00/techrepro/3609_reports.htm and
http://www.ipacrs.com/particle_size.html.

Dr. Rogers asked whether standardized test conditions (such as USP throat, flow rates, etc.) and equipment (e.g., CI) were used for obtaining the data. Dr. Tougas replied that the ITFG/IPAC-RS database comprises data for a variety of products tested with a variety of methods. The database does include information about specific test conditions such as the flow rate and the apparatus type. Dr. Rogers asked whether the present PQRI Working Group intended to consider different standards for PSD control. Dr. Tougas explained that the focus of this Working Group is to develop scientific recommendations specifically regarding the use of PSD mass balance, i.e., what requirements are appropriate for PSD mass balance, what is the appropriate role of PSD mass balance in the overall product quality control, and how PSD mass balance should appropriately be used.

Dr. Rogers expressed his view that the draft CMC Guidances spell out clearly that the mass balance requirement applies to Andersen cascade impactors. He asked whether the Working Group was seeking a more lenient language in the draft Guidances with respect to mass balance or the inclusion of a different (not CI) impactor. He stated that PSD mass balance quantifies fine particle dose and that no product has been approved yet using a different (not CI) impactor. Dr. Tougas pointed out that the Working Group will discuss the technical details of the PSD mass balance issue at a later time, and that the objective of this first teleconference is to discuss in general terms the purpose and ground rules for the present PQRI Working Group.

Dr. Rogers inquired whether within PQRI, FDA was expected to provide blinded data from past drug product applications. He noted that the Agency has a sizable database, which comprises data from validated, approved methods, from approved products in their final form. Ms. Capizzi and Ms. Gantt replied that in the past, the Agency had contributed its data to some PQRI projects but not to others. Dr. Tougas thanked Dr. Rogers for his suggestions and stated that the use of the Agency's database should be considered by the Working Group in detail in due course.

Communication within Working Group

Dr. Tougas listed the following ways in which the Working Group members will communicate with each other: teleconferences (this will be the main means for discussion and exchange of information), email and face-to-face meetings. Participants agreed to hold their first face-to-face meeting in conjunction with the upcoming PQRI Training Workshop scheduled for 29-30 January 2002. The PSD Mass Balance Working Group will meet from 1 PM to 4 PM on 30 January and from 9:00 AM to 1 PM on 31 January. Dr. Lavery will participate in the meeting via phone and possibly live internet connection.

Confidentiality

Dr. Zaidi inquired what confidentiality rules are to be followed within PQRI. Dr. Tougas explained that with respect to commercially sensitive information, each participant is expected to observe confidentiality procedures established by the participant's company. However, PQRI itself is a public process, so this Working Group's discussions, research findings and recommendations are open to public review and scrutiny. Ms. Capizzi added that minutes of PQRI meetings and teleconferences are available publicly online at the organization's website www.pqri.org. Ms. Capizzi noted that PQRI process is transparent by design, since it is meant to provide a forum where representatives of industry and government could exchange information and conduct collaborative research in support of regulatory policy. Ms. Gantt corroborated this understanding and confirmed that PQRI process is public.

Dr. Zaidi asked whether research proposals could be circulated broadly without confidentiality restrictions. Ms. Capizzi noted that the Working Groups may wish to keep incomplete or preliminary drafts within the Working Group, but that in general, PQRI research proposals are also public documents.

Dr. Lyapustina further explained that within PQRI, each Working Group member represents not just himself/herself, but the entire organization that nominated that individual. In light of that, each participant has the responsibility to update his/her organization on the PQRI activities and to bring the feedback and input from the nominating organization to the PQRI Working Group. Dr. Tougas summarized the discussion on confidentiality by saying that PQRI is an open public process and that each that participant is expected to consult with other colleagues within his or her organization.

Decision Making Process

Dr. Tougas explained that within the Working Group, decisions will be made based on consensus among all participants. If immediate consensus cannot be reached, additional data

gathering and research may be undertaken to resolve any open issues. In addition, the PQRI Steering Committee and DPTC may be asked to intervene if necessary. Dr. Mitchell commented that the consensus-building process, as practiced by the ITFG/IPAC-RS technical teams, proved to be the most effective way to arrive at decisions.

Adding and Deleting Members

The participants briefly reviewed procedures for adding new members and deleting inactive members. In general, suggestions for changes in the membership should be forwarded to DPTC. Participants agreed to review the CVs of all current Working Group members in order to determine whether additional expertise is necessary to carry out proposed research.

IV. AGREED ACTIONS

The participants agreed that:

- The next teleconference should be scheduled for Friday, 30 November, at 11:00 AM EST;
- The primary objectives of the next teleconference will be: (i) to discuss main elements of the research proposal and workplan, and (ii) to discuss need for additional expertise; and
- Ms. Gantt will circulate to the Working Group the CVs of all WG members.

V. NEXT TELECONFERENCE/MEETINGS

The next teleconference of the PSD Mass Balance Working Group is scheduled for **Friday, 30 November at 11:00 AM (US EST)/16:00 GMT.**

The all-PQRI Executive Training Workshop is scheduled for **Tuesday-Wednesday, 29-30 January in Rockville, MD.**

The first face-to-face meeting of the Working Group is scheduled for **Wednesday, 30 January 2002, 1:00 PM- 4:00 PM (US EST)** and **Thursday, 31 January, 9:00 AM – 1:00 PM (US EST) in Washington, DC.**

VI. ADDRESSEES

PQRI PSD Mass Balance Working Group:

Martin Lavery (Aventis)
Jolyon Mitchell (Trudell Medical)
Brian Rogers (CDER/FDA)
Terry Tougas (BI),
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Copy: PQRI DPTC, PQRI Exec. Secretary