

**MINUTES OF THE TELECONFERENCE**  
**OF THE PQRI PSD MASS BALANCE WORKING GROUP ON**  
**14 FEBRUARY 2002**

**I. PARTICIPANTS**

Terry Tougas (Boehringer Ingelheim), Chair  
Mary Devlin Capizzi (IPAC-RS)  
Ken Furnkranz (FDA)  
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. DISCUSSION**

During the teleconference, Working Group members:

- reviewed the draft work plan dated 4 February;
- discussed revisions proposed by Dr. Rogers; and
- agreed to revise the draft work plan and discuss the new version at the next teleconference of the Working Group on 25 February.

The particular points discussed during the teleconference included the following:

- the work plan should clarify that it is the industry's opinion that the use of the mass balance as a drug product specification and the acceptance criteria proposed in the draft Guidances are arbitrary and overly restrictive;
- determination of particle size distribution of aerosols requires specialized analytical skills;
- operating a cascade impactor is complicated by a number of sources of error that are difficult to control, such as correct coating of the plates, correct plate alignment, leaks, correct washing of the drug off the plates, *etc.*;
- aerosols by nature are quasi-stable, dynamic systems, which contributes to the difficulty of determining PSD precisely;
- the calibration of an impactor is a complicated, time-intensive project for a specialized laboratory, which cannot be performed routinely in a typical pharmaceutical QC laboratory;

- the difficulties cited above have inhibited the development of a consistent industry-wide standard; which in its turn has stimulated the creation of the present Working Group;
- the Working Group's hypotheses should be cast in testable terms, *e.g.*, "the variability of a PSD measurement is higher than that of a DCU measurement", and should use standard concepts, such as "random error/uncertainty", "systematic error/uncertainty";
- because the cascade impactor is not an ideal collector, the mass balance obtained via a CI measurement in general is not reflective of the delivered dose due to systemic uncertainties/bias;
- the systematic bias of a CI mass balance is drug product- and impactor-dependent;
- it would be possible and beneficial to cover different types of impactors in the *Good Cascade Impactor Practices* to be prepared by the Working Group; especially it would be important to include the Next Generation Pharmaceutical Impactor, which represents a significant improvement over existing apparatuses and is poised to replace them in the near future;
- the *Investigational Tree* should include, at each point, a list of evidence required to draw conclusions; and
- the "Potential Impact" section of the draft work plan should be revised because the Working Group is not in a position to judge whether the Agency's reviewing burden would be reduced as a result of this Group's activity.

As next steps, the Working Group agreed to the following:

- the draft work plan will be revised and circulated to the Working Group for further comment;
- the revised work plan will be discussed on the next teleconference of the Working Group on 25 February; and
- if finalized on the 25 February teleconference, the work plan will be submitted to the PQRI Drug Product Technical Committee (DPTC) and presented at the 28 February DPTC meeting by Dr. Tougas.

### III. NEXT TELECONFERENCE/MEETING

The next teleconference of the PSD Mass Balance Working Group is scheduled for **Monday, 25 February at 10:00 AM (US ET)/15:00 (UK)**.

**IV. ADDRESSEES**

PQRI PSD Mass Balance Working Group:

Ken Furnkranz (CDER/FDA)  
Martin Lavery (Aventis)  
Margareth Marques (USP)  
Deborah Miran (GPhA)  
Jolyon Mitchell (Trudell Medical)

Brian Rogers (CDER/FDA)  
Terry Tougas (BI), Chair  
Bruce Wyka (Schering-Plough)  
Kahkashan Zaidi (USP)

Copy:

Jeffrey Blumenstein (Pfizer, DPTC)  
Sylvia Gantt (PQRI)  
Sid Goldstein (Prasco, DPTC)  
Chris Moreton (DPTC)  
Guirag Poochikian (FDA, DPTC)  
PQRI PSD Profile Comparisons Working Group

*Finalized on 13 May 2002*