

1 MINUTES OF THE TELECONFERENCE  
2 OF THE PQRI PSD MASS BALANCE WORKING GROUP ON  
3 4 JUNE 2004

4 **I. PARTICIPANTS**

Terry Tougas (Boehringer Ingelheim), Chair	Lana Lyapustina (IPAC-RS)
Mary Devlin Capizzi (IPAC-RS)	Jolyon Mitchell (Trudell Medical)
Dave Christopher (Schering-Plough)	Guirag Poochikian (FDA)
Paul Curry (USP)	Brian Rogers (FDA)
Bill Doub (FDA)	Helen Strickland (GlaxoSmithKline)
Rik Lostritto (FDA)	Bruce Wyka (Schering-Plough)

5 **II. OPENING**

6 Dr. Tougas welcomed the participants and opened the meeting. Dr. Lyapustina  
7 reminded the participants that their discussion is subject to the anti-trust guidelines applicable  
8 in the United States and European Union, and that nothing discussed at this meeting may be  
9 intended to restrict trade or individual decision-making of any company; she further instructed  
10 the participants to avoid discussion of competitively sensitive subjects, such as confidential  
11 marketing, sales, and pricing information.

12 The main objective of the teleconference was to continue the discussion started on 1 June  
13 and, specifically, to agree on the ways to meet the Working Group's objective in the absence of a  
14 safe harbor mechanism for data sharing.

15 **III. DISCUSSION**

16 Recognizing that obtaining a safe harbor and data may take a while, the Working Group  
17 agreed to prepare and submit to FDA, as a current work product of this Working Group, the  
18 consensus Interim Recommendations on how the mass balance measurement should be treated  
19 in the quality control program. After the safe harbor mechanism has been established, and data  
20 collections planned by the Working Group originally, have been carried out and results have  
21 been analyzed, the Final Recommendations would be prepared and submitted to the Agency.

22 With regard to the content of the Recommendations, participants of today's  
23 teleconference agreed that the Addendum to the 19 March minutes could be used as a starting  
24 point. In addition, the following points were suggested for consideration and potential  
25 inclusion in the Interim Recommendations:

- 26 – mass balance should not be used as a de-facto dose content uniformity test.
- 27 – mass balance measurement is neither a purely product specification nor a purely system  
28 suitability requirement.
- 29 – the limits for mass balance need to be based on product's data but be close to 85-115%  
30 LC because the Agency has not seen problems with these limits.
- 31 – the procedure for evaluating a batch and applying mass balance limits should include a  
32 possibility for re-testing if mass balance is outside of the established limits, but it also

33 needs to prevent "retesting into compliance". A tiered approach may be considered,  
34 that takes into account the degree and frequency of mass balance measurements outside  
35 the limits. For example, it might need to distinguish between cases where (A) mass  
36 balance is at 84% LC and all stage specifications are within limits, and (B) where mass  
37 balance is at 27% LC and none of the stages are within specifications.

38 – the scope of the future planned experiment and data collection could be outlined in the  
39 Interim Recommendations.

40 The Working Group agreed that rather than having a separate drafting group, all  
41 members of the Working Group should participate in drafting and revising the  
42 Recommendations. The participants noted that after finalization by the Working Group, and  
43 approval by the senior PQRI committees and PQRI member organizations, the Interim  
44 Recommendations will be submitted by PQRI to FDA, for inclusion in FDA's guidance currently  
45 under preparation, or for otherwise publicizing it as an element of current review practice by  
46 the Agency.

#### 47 **IV. AGREED**

- 48 • The Working Group will draft the Interim Recommendations in the coming weeks by  
49 email, will discuss them during the teleconference and aim to finalize them at the next  
50 face-to-face meeting.

#### 51 **V. NEXT TELECONFERENCE / MEETING**

52 The next teleconference was scheduled for 28 June, and the next face-to-face meeting, for  
53 20 July in Rockville, MD.

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*Finalized on 23 August 2004*