

1 **Minutes of the Teleconference**
2 **of the PQRI PSD Mass Balance Working Group**
3 **on 22 February 2006**

4 **I. OPENING**

5 Mr. Wyka opened the teleconference and welcomed the participants. Dr. Lyapustina read the
6 antitrust admonition.

7 The participants in the teleconference were:

- 8 Terry Tougas (BI) *Co-Chair*
9 Bruce Wyka (Schering-Plough) *Co-Chair*
10 David Christopher (Schering-Plough)
11 Paul Curry (Solvay)
12 Ken Furnkranz (FDA)
13 Lana Lyapustina (IPAC-RS)
14 Jolyon Mitchell (Trudell Medical)
15 Brian Rogers (FDA)

16 The objectives of the teleconference were: (i) to discuss the draft language for a Mass Balance
17 recommendation; (ii) to discuss next steps and sunseting of the Working Group.

18 **II. DISCUSSION**

19 Mr. Wyka reminded the participants that the proposed consensus language regarding Mass
20 Balance was drafted in response to the suggestion made by Dr. Poochikian at the 4 November
21 2005 DPTC meeting. Dr. Furnkranz asked whether this text is proposed as a “drop-in” for the
22 draft guidance; he noted that he had no problems with the text being added as a last paragraph
23 to the section addressing mass balance specifications in the guidance, but he was not sure how
24 that specific language would fit with the rest of the guidance. Mr. Wyka and Dr. Tougas
25 explained that this language is only a recommendation for the draft guidance.

26 Mr. Wyka invited the participants to comment on the draft circulated prior to the
27 teleconference. No one offered any comments, and the text (dated 15 February, see Appendix)
28 was approved.

29 Mr. Wyka asked for clarification of the sentence “All numerical results should be reported”. Dr.
30 Rogers explained that in the case of retesting, both the original and the retested results should
31 be reported, and that the format should be the same as that used for reporting of all other
32 results, e.g., in the annual report, or as part of the release records, or in the stability report – in
33 other words, as part of the regular GMP record.

34 The participants discussed the next steps. Dr. Tougas explained the PQRI process as follows:

- 35 • After the consensus language has been formally submitted to the DPTC, Ms. Gantt will
36 send it to the DPTC members with a request that they and their member organizations
37 provide comments and/or indicate approval.
- 38 • The DPTC is the body that provides technical oversight within PQRI, while the Steering
39 Committee provides strategic oversight.
- 40 • After the DPTC review, the Working Group will address any comments, and after the
41 DPTC approval the text will be provided to the Steering Committee and then to the
42 FDA.

43 In conclusion, Dr. Tougas noted that the DPTC is encouraging submission of proposals for new
44 projects to PQRI, and he invited the participants to consider submitting a proposal if they have
45 any concerns or suggestions for a scientific issue related to regulation.

46 **III. AGREED NEXT STEPS**

- 47 • The draft language dated 15 February 2006, without further changes, will be forwarded
48 to the DPTC for a two-week review, comment and approval.
- 49 • The Working Group will officially sunset after the final recommendation is submitted to
50 FDA and the technical paper has been published.

51 Finalized on 17 April 2006
52

52 **IV. APPENDIX**

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54 PQRI PSD Mass Balance Working Group

55 Draft Dated 15-FEB-2006

56 MASS BALANCE PROPOSAL FOR FDA GUIDANCE DOCUMENT

57 The total mass of drug collected on all stages and accessories of an impactor is an essential
58 component in accessing the validity of an APSD determination. Mass balance results should be
59 expressed on a per actuation basis as either a percent of the label claim delivery from the
60 mouthpiece or as a percent of the target mass balance. The target mass balance should fall
61 between 95% and 100% of the label claim delivery if stage wall deposition is not measured in
62 the APSD determination. The target mass balance, if different from the label claim emitted dose,
63 must be justified by and validated with data obtained using good cascade impactor practices*.
64 For each test, it is recommended that five determinations be conducted with each determination
65 coming from a separate unit. For each unit, the minimum number of actuations necessary to
66 obtain appropriate quantitation should be used in APSD determinations. The acceptance criteria
67 for each mass balance determination should typically be between 85% and 115% of the label
68 claim (or target mass balance) with one individual determination of the set allowed to be within
69 80% and 120%. Alternative limits may be considered if there is scientific rationale and data to
70 justify the limits (e.g., if the APSD determination is based on the number of actuations
71 comprising the minimum patient dose, then the above ranges may be broadened to reflect the
72 performance of the product).

73 Due to the nature and complexity of APSD determinations via cascade impactor testing, and the
74 possibility of analytical or instrument error, a detailed re-test protocol may be proposed for mass
75 balance results that fall outside the proposed limits. It is preferred that the subsequent actuations
76 from the same unit be used for re-testing where possible. The subsequent mass balance
77 determination for the test must meet the agreed upon criteria. All numerical results should be
78 reported.

79 * *Considerations for the Development and Practice of Cascade Impaction Testing Including a*
80 *Mass Balance Failure Investigation Tree. **Journal of Aerosol Medicine** 2003; 16(3):235-247.*

81

82 Post-meeting note:

83 After the teleconference, Dr. Rogers dissented with the text of the Appendix as presented above.