

1 MINUTES OF THE TELECONFERENCE
2 OF THE PQRI PSD MASS BALANCE WORKING GROUP ON
3 14 May 2003

4 **I. PARTICIPANTS**

Terry Tougas (Boehringer Ingelheim), Chair	Jolyon Mitchell (Trudell Medical)
Paul Curry (USP Aerosols Expert Committee)	Brian Rogers (FDA)
Bill Doub (FDA)	Helen Strickland (GlaxoSmithKline)
Ken Furnkranz (FDA)	Yi Tsong (FDA)
Lana Lyapustina (IPAC-RS)	Bruce Wyka (Schering-Plough)

5 **II. OPENING**

6 Dr. Tougas opened the teleconference and welcomed the participants. He introduced
7 the objectives of the teleconference as follows: (i) to discuss the design and next steps for the CI
8 variability study; (ii) to review templates for the data-mining; (iii) to briefly update on the MB /
9 APSD failure survey; (iv) to discuss other updates; and (v) to agree on next steps.

10 The Working Group noted that the draft minutes of the 3 April teleconference had been
11 circulated for review recently, and will be finalized on the next teleconference.

12 The Working Group briefly discussed feedback from the Drug Product Technical
13 Committee (DPTC), which held a meeting in the morning on 14 May. At that meeting, the
14 DPTC Chair inquired about the progress of the surveys being conducted and planned by the
15 Working Group.

16 **III. DISCUSSION**

17 *CI Variability Study*

18 Ms. Strickland reviewed the following two types of statistical designs for the CI
19 variability study: (i) the Incomplete Block Design with Latin Square, and (ii) the Split Plot
20 Design with Graeco Latin Square; and advantages and disadvantages of each. Based on her
21 simulation results, she explained what information each design would be able to yield, and with
22 what accuracy.

23 Ms. Strickland in particular noted that the Split Block design has better ability to make
24 correct decisions if there is some impactor-by-analyst interaction. However, with this design
25 the analysts will have to exchange impactors and test containers during the day in a
26 synchronized fashion. The Incomplete Block design might be easier to implement logistically,
27 but the percentage of correct decisions is lower if impactor-by-analyst interaction is present.

28 In response to questions, Ms. Strickland explained that in both designs, within-day
29 variation is included with the product variation. She offered to provide details of her
30 simulations to the other statisticians if desired.

31 The Working Group considered the presented information and agreed that the Split
32 Block design should be pursued, because the impactor-by-analyst interaction is not unlikely,
33 and the exchange of three impactors and three test containers during the day is feasible.

34 With the study design complete, the participants discussed how the study could be
35 conducted practically, *i.e.*, what product(s) and at what laboratory(ies) would be studied. They
36 noted that the design calls for three cascade impactors (of the same model, and as identical as
37 possible), twenty-seven test units (randomly selected from a batch), three analysts (adequately
38 trained in the method for the test product) and nine days of laboratory time. Because the
39 purpose of the study is to evaluate variability of the method, all other variabilities (*e.g.*, batch-to-
40 batch, or lab-to-lab) should be avoided, and thus only one batch and one laboratory per product
41 would be involved. On the other hand, the study could proceed on several different products
42 in several laboratories in parallel.

43 The GCIP guidelines would be recommended to follow. Other experimental details
44 such as temperature, impactor flowrate, sample preparation, *etc.* would have to be product-
45 specific, and conform to the method in the NDA or IND. A schematic of the testing sequence
46 would be provided by Ms. Strickland and Mr. Christopher. In order to get a true measure of
47 variability, all observation results must be retained and presented for data analysis.

48 The Working Group suggested that pharmaceutical companies should be asked to
49 volunteer for this study. The identities of companies and products need not be disclosed.
50 However, there are questions about legal and regulatory implications of testing real products
51 during this PQRI experiment. Dr. Rogers agreed to clarify these questions with the appropriate
52 experts at the Agency.

53 MB/APSD Failure Cause Survey

54 Dr. Lyapustina reported that several additional responses on the MB/APSD Failure
55 Cause Survey had been received since the last teleconference, and several more are anticipated
56 in the coming weeks. The Working Group agreed that a preliminary compilation of responses
57 should be prepared and presented for discussion at the next teleconference. Late responses may
58 be added to the initial compilation when available.

59 Data-Mining

60 The Working Group reviewed the draft data template, request for data and
61 confidentiality protocol for the retrospective data-mining, and suggested several minor editorial
62 changes.

63 Participants discussed whether the impactor type and test conditions should be
64 restricted, but agreed that this is not necessary, since such information would be submitted with
65 the data, and if necessary the results could be removed from the final compilation.

66 The Working Group agreed that the data mining should be initiated, and that the
67 finalized survey request, data template and confidentiality protocol will be forwarded to Ms.
68 Gantt for posting on the PQRI website.

69 Dr. Furnkranz reported that he had inquired about the possibility of submitting the
70 Agency's data in this survey. The responsible division at the Agency indicated they do not
71 have resources to assemble the data.

72 *Respiratory Drug Delivery Conference*

73 The Working Group discussed the call for papers and posters for the 2004 conference
74 *Respiratory Drug Delivery IX*. The participants agreed not to apply for a podium presentation,
75 but to prepare a poster or posters based on the findings of the Working Group by the end of
76 2003, and subject to the PQRI review and approval in accordance with the PQRI policy for
77 publications and presentations.

78 **IV. AGREED ACTIONS**

- 79 • The results of the survey of mass balance / particle size distribution failure causes
80 will be compiled and presented to the Working Group for discussion on the next
81 teleconference.
- 82 • The documents for data-mining will be finalized as discussed on the teleconference
83 and forwarded to Ms. Gantt for posting on the PQRI website.
- 84 • Ms. Strickland will finalize the statistical design of the CI variability study and
85 prepare a brief description of resource requirements, as an aid in the search for
86 laboratories willing to participate in the study.
- 87 • Dr. Rogers will inquire about regulatory and legal implications of drug product
88 testing during the Working Group's planned study of cascade impactor variability.

89 **V. NEXT TELECONFERENCE / MEETING**

90 The next teleconference of the PQRI PSD Mass Balance Working Group is scheduled for
91 Wednesday, 4 June, at 11:00 AM Eastern Time / 10:00 AM Central Time / 16:00 UK Time.
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Finalized on 4 June 2003