

1 MINUTES OF THE TELECONFERENCE  
2 OF THE PQRI PSD MASS BALANCE WORKING GROUP ON  
3 23 July 2003

4 **I. PARTICIPANTS**

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

5 **II. OPENING**

6 Dr. Tougas welcomed the participants and explained the main objectives of the  
7 teleconference: (i) to discuss conclusions and slides from the APSD / MB Failure Causes Survey;  
8 (ii) to review the updates on data-mining, CI study and PQRI workshop; and (iii) to agree on  
9 next steps. The participants approved the proposed agenda. The Working Group approved the  
10 draft minutes of the 4 June teleconference.

11 **III. DISCUSSION**

12 *Failure Survey Results*

13 Dr. Mitchell explained that the subgroup that had been formed to review the survey  
14 results, held two teleconferences, and the outcome of those discussions is summarized in the  
15 slides provided for this teleconference. A total of 14 responses were received, 13 of which were  
16 usable. About 4300 CI runs are represented in the survey. Dr. Rogers asked whether there were  
17 any inappropriate drug products represented. Dr. Tougas replied that the survey was focused  
18 on the CI method rather than on products. Dr. Mitchell reviewed the information in the slides.  
19 He noted that the distribution of responses was bi-modal, with some laboratories having very  
20 few failures, others having many. Dr. Rogers commented that in his practice he had also seen  
21 only few failures. Other participants added that in this survey, importantly, the "failure" was  
22 defined by the companies themselves, rather than in relation to the 85-115% LC limits. Some of  
23 the survey respondents noted that they had not recorded any failures because they had no  
24 specifications for mass balance. Others may have had different limits than the 85-115% LC. The  
25 subgroup members further explained that the value of this survey was the indication of causes  
26 of failure, not of suitability of the specification limits.

27 Dr. Mitchell reported that (i) bounce and electrostatic charge were highlighted as causes,  
28 (ii) some type of check lists were used in half of the cases, and (iii) no pattern was observed for  
29 analyst-related errors (the largest common error was mis-ordering of the stages, some were due  
30 to sample handling, and one to inadequate recovery). The overall conclusion of the subgroup  
31 was that the results did not suggest any need to revise the Draft Failure Investigation Tree  
32 developed by the Working Group for the GCIP paper. The Working Group agreed with this

33 conclusion. The participants further discussed how these findings should be publicized. They  
34 agreed that a Letter to the Editor of the Journal of Aerosol Medicine should be submitted. After  
35 the Working Group's approval, the approval of the draft Letter by the PQRI senior committees  
36 will be sought.

37 **Other Updates**

38 Dr. Tougas reported that he had requested support from pharmaceutical companies in  
39 conducting the CI study. Email requests have also been issued, and all the materials have been  
40 posted on the PQRI website since early June. So far no volunteers have been identified. No  
41 submission for the data mining was received either. The participants agreed that another public  
42 request should be made at the PQRI Workshop.

43 Dr. Rogers expressed a concern that companies that have no problem with the 85-115%  
44 LC limits would not make the effort to submit their data, while companies that do have a  
45 problem would be more interested in participating, thus potentially skewing the picture. Other  
46 Working Group members replied that FDA's participation in the data-mining may help avoid  
47 the bias. Dr. Rogers indicated this question has to be discussed with the Agency's upper  
48 management. Dr. Furnkranz added that he had not received any positive response from the  
49 Office of Generic Drug management, partly because not many ANDAs for orally inhaled and  
50 nasal drug products have been received by that office so far. Dr. Tougas agreed to bring the  
51 issue of data mining, and of conducting research on marketed products, to the PQRI Steering  
52 Committee's attention. He also offered to contact individual companies. The Working Group  
53 suggested that a general letter for such contacts should be drafted.

54 In conclusion, the participants reviewed their plans for the August PQRI Workshop.

55 **IV. AGREED**

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- 57 • Dr. Mitchell will draft one or two slides summarizing the survey results. After  
58 review and comment by the Working Group, the slide(s) will be included in the  
59 electronic version of the presentation at the PQRI Workshop.
  - 60 • The Working Group agreed that the results of the survey did not suggest any need to  
61 revise the Draft Failure Investigation Tree developed by the for the GCIP paper.
  - 62 • The results and conclusions of the survey will be publicized via a Letter to the Editor  
63 in the Journal of Aerosol Medicine, as a follow-up to the GCIP publication. Dr.  
64 Mitchell will prepare and circulate the first draft of the Letter, which will be  
65 discussed at the next meeting of the Working Group.
  - 66 • The issue of data-mining and regulatory safe harbor for PQRI research will be  
brought to the attention of the PQRI Steering Committee.

67 **V. NEXT TELECONFERENCE / MEETING**

68 The next face-to-face meeting is scheduled for 3:00-4:00 PM (ET) on 5 August.

69 *Finalized on 10 October 2003*