

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

4 **I. PARTICIPANTS**

Terry Tougas (Boehringer Ingelheim), Chair	Zoë Heaton (Aventis)
Mary Devlin Capizzi (IPAC-RS)	Lana Lyapustina (IPAC-RS)
Dave Christopher (Schering-Plough)	Guirag Poochikian (FDA)
Paul Curry (USP)	Brian Rogers (FDA)
Craig Dunbar (Alkermes)	Helen Strickland (GlaxoSmithKline)
Ken Furnkranz (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 Working Group approved the minutes of the teleconference on 19 March 2004.

13 The participants adopted the following objectives for the teleconference: (i) to review
14 results of the survey on perceived barriers to data sharing; (ii) to discuss critical elements
15 needed to meet Group's objective; and (iii) to agree on next steps.

16 **III. DISCUSSION**

17 *Results of Survey on Barriers to Data Sharing*

18 Dr. Tougas reminded the participants that following the previous teleconference, a
19 subgroup was formed and a confidential industry survey was conducted to understand what
20 prevents companies from submitting data and volunteering for experiments requested by the
21 Mass Balance Working Group. The following main issues were identified:

- 22 - concerns about proprietary information;
- 23 - uncertainty about compliance implications, especially in the case of generating new data
24 on marketed products; and
- 25 - resource requirements, especially in the case of data-mining of existing data.

26 FDA participants felt that ensuring anonymity of data would not be a problem; however
27 the industry participants explained that regardless of anonymity within PQRI, companies have
28 regulatory obligations with respect to any data gathered on a marketed product, and it is not
29 clear whether those obligations would be waived for PQRI research purposes.

30 The Working Group considered a possibility of using a 3rd party laboratory to conduct
31 the experiments, but agreed that the issues of appropriate analyst training and method transfer
32 would complicate rather than facilitate the experiments.

33 The participants discussed other data collection efforts undertaken by PQRI, and made
34 the following points:

- 35 – The Blend Uniformity Working Group conducted confidential data mining, however the
36 amount of data received in that effort was far below expectations. In addition, that data
37 mining involved only existing data, whereas generating new data on commercial
38 products is considered by industry to be associated with higher regulatory risk.
- 39 – The Leachables and Extractables Working Group conducted prospective experiments
40 and generated new data; however special test articles were manufactured for this
41 purpose, and no commercial product was directly involved.

42 *Mass Balance Working Group's Objective*

43 Dr. Tougas invited the Working Group to discuss its original overall objective, which is:
44 to clarify how mass balance observations should be treated in the QC program – namely, (i)
45 how it should be used, and (ii) what limits are appropriate. Dr. Rogers asked whether the
46 controversy over the 85-115%LC limits still needs to be addressed. He noted that since the
47 issuance of the draft guidances, the Agency's thinking has developed, the limits have been
48 allowed to widen slightly case-by-case based on data, and the 85-115% LC limits are not rigidly
49 adhered to any more. In addition, according to Dr. Rogers, the Agency has been accepting re-
50 testing scenarios so that a failing mass balance would lead to a DCU retest and/or a CI retest,
51 and these subsequent results would overrule the first failing result. Dr. Rogers mentioned that
52 the revised guidance would reflect the new thinking but could not clarify when the revised
53 guidance would be issued.

54 The Working Group felt that the issue of mass balance still needs to be addressed by this
55 PQRI Working Group. Some participants stressed that it is not simply the limits that create the
56 difficulty, but also the protocol, or the course of action with respect to mass balance
57 measurements. Industry would like to see a clear, well-thought-out guidance on mass balance,
58 for both release and stability testing situations.

59 In response to FDA participants' statements that in their experience the 85-115% limits
60 are easily met, participants commented that a transparent procedure for establishing the limits
61 is needed. Industry participants noted two scenarios that seem to recur: (i) regulators and
62 sponsors reviewing the same set of data but arriving at different conclusions regarding the
63 limits, and (ii) the two parties referring to different sets of data, especially in group discussions.
64 Both of these could be remedied if sound principles are openly defined.

65 Ms. Capizzi provided a review of the Steering Committee's discussions regarding the
66 safe harbor for PQRI research. She explained that the Agency's legal department needs to be
67 involved in crafting the safe harbor, but because of that department's high work load the timing
68 of such legal review is indeterminate at present.

69 The Working Group discussed that if the original work plan is to be followed, and in
70 light of the delays with creation of the safe harbor mechanisms for data sharing, the work of this

71 Working Group could be significantly protracted. They agreed that in the absence of data,
72 interim recommendations could be prepared based on the principles outlined in the GCIP
73 paper. When data collection becomes possible, a final report could be prepared based on the
74 data analysis.

75 Due to limited time, the discussion of practical ways to meet the Working Group's
76 objective was postponed until the next teleconference.

77 **IV. AGREED**

- 78 • On the next teleconference, the Working Group will discuss ways to meet the Working
79 Group's objectives and, in particular, the preparation of interim recommendations.

80 **V. NEXT TELECONFERENCE / MEETING**

81 The next teleconference was scheduled for 4 June.

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Finalized on 23 August 2004