

1 **Minutes of the DPTC Teleconference**
2 **on 29 June 2006**

3 **ATTENDEES**

4 Terry Tougas, *Chair* (Boehringer Ingelheim, IPAC-RS)
5 David Christopher (Schering-Plough, IPAC-RS)
6 Bob Dana (PDA)
7 Sylvia Gantt (PQRI Exec. Secretary)
8 Michael Golden (GlaxoSmithKline, IPAC-RS)
9 Lana Lyapustina (IPAC-RS Secretariat)
10 Dan Malinowski (Pfizer, PhRMA)
11 Chris Moreton (Idenix Pharmaceuticals, IPEC)
12 Dan Norwood (Boehringer Ingelheim, IPAC-RS)
13 Lee Nagao (IPAC-RS Secretariat)
14 Rich Poska (Abbot, PhRMA)
15 Russel Somma (IPS, ISPE)
16 Raj Uppoor (FDA)
17 Bob Wiens (Lilly, IPEC)
18 Bruce Wyka (Schering-Plough, IPAC-RS)

19 ***Absentees***

20 Tony Amann (GPhA)
21 Clyde Anthony (USP)
22 Frank Holcombe (FDA)
23 Nakissa Sadrieh (FDA)
24 Vilayat Sayeed (FDA)
25 Robert Seevers (Lilly, PhRMA)
26 Bill Williams (University of Texas, AAPS)

27 **EXECUTIVE SUMMARY**

- 28 • Questions about copyright agreement for the Excipients Working Group's publication should
29 be forwarded to ECAS.
- 30 • The Container Closure WG's protocol will be finalized during the next DPTC call.
- 31 • The process for posting the L&E Recommendations on the PQRI website will be discussed
32 by the DPTC and SC Chairs.
- 33 • The revised L&E Recommendations will be reviewed for final approval within 4 weeks.
- 34 • Appropriate next steps for a book on toxicological aspects of the Leachables and Extractables
35 Recommendations will be considered by the Chairs of the L&E WG, DPTC and SC.
- 36 • Issues concerning the FDA's algorithm for PBE have been resolved and the Profile
37 Comparisons Working Group's Final Report has been rescheduled for 3Q06.

- 38 • The recommended language for use of Cascade Impactor Mass Balance will be forwarded to
39 the DPTC Chair for submission to the SC and FDA.
- 40 • The next DPTC teleconference will focus on the discussion of new projects.

41 **DISCUSSION**

42 *Opening*

43 Dr. Tougas opened the meeting and read the antitrust admonition: “Our discussions today are
44 subject to the anti-trust guidance applicable in the U.S. and E.U. Nothing discussed at this
45 meeting is intended to restrict the individual decision-making of any member company or to
46 represent an agreement to coordinate marketing or sales conduct. Those participating in this
47 meeting are instructed to avoid discussion of competitively sensitive subjects, including, but
48 not limited to, confidential marketing, sales, and pricing information.”

49 The proposed objectives of the meeting were to discuss updates on all Working Groups and
50 review proposals for new projects.

51 *Excipients*

52 Mr. Wiens noted that the publication prepared by the Working Group had been submitted to
53 Pharmaceutical Technology, and the only issue awaiting resolution is the copyright
54 agreement. It was agreed that this issue will be addressed to ECAS.

55 The Working Group is recruiting moderators and scribes for the upcoming Workshop
56 (<http://pqri.org/workshops/Excipient/Excipient06.asp>), especially the scribe for the skip-lot
57 testing topic. Dr. Uppoor, who had spoken with Ms. Helen Winkle about the Workshop, said
58 that the Agency is interested in hearing about the current state of affairs in the industry and
59 about areas where further guidance or other regulatory action is needed, but the Workshop
60 attendees should not expect to hear an interpretation of current regulations from FDA
61 speakers.

62 Dr. Tougas asked what would be the most helpful outcome for the Agency from the
63 Workshop, to which Dr. Uppoor replied – identification of problems that may cause drug
64 product failures. Dr. Uppoor further noted that even within current regulations, opportunities
65 for less burdensome approaches exist, e.g., skip lot testing can be used for drug product, and
66 is already used both by pharmaceutical and excipient manufacturers. Dr. Uppoor
67 emphasized, however, that USP monograph criteria should be met for every single batch, and
68 that the law requires that someone be testing every batch of excipients for all monograph
69 aspects before releasing the batch to the market. Dr. Uppoor stated that the Agency believes
70 its current approaches to excipients control are reasonable but the Agency would like to
71 understand who is doing the testing and what risks exist for the drug product manufacturing.

72 ***Leachables and Extractables***

73 Dr. Norwood noted that the L&E Training Course will be held on 20-21 September 2006 in
74 Washington, DC. The curriculum and speakers have been set and the current work focuses on
75 the presentations themselves (http://pqri.org/workshops/leach_ext/pqrilandeworkshop.asp).

76 The L&E Working Group's Recommendations are being finalized. The comments collected
77 during the 2005 Workshop and from FDA are being addressed. Responses are reflected in
78 the revised Recommendations and are also being sent to the original commentators. The
79 revised Recommendations should be provided to the DPTC in the near future. The DPTC
80 agreed that the review and final approval of the document could be accomplished within 4
81 weeks. The DPTC emphasized that this round of review should focus only on the recent
82 changes and not open the entire document, which had been thoroughly reviewed and
83 approved previously. (The Recommendations document numbers about 150 pages, with a
84 120-page appendix. The recent changes, however, take up only 20 pages).

85 The DPTC briefly discussed when the final Recommendations could be made available on
86 the PQRI website. Dr. Tougas noted that the current PQRI process has been streamlined and
87 may not necessarily follow the BU process. He will discuss this issue with the SC Chair.

88 Dr. Norwood further reported that at the Society of Toxicology meeting earlier this year, the
89 Working Group was approached by representatives of John Wiley publishers with an
90 invitation to write a book based on that Symposium's discussions. Since then, the
91 toxicologists of the L&E Working Group have prepared an outline of the book (which has
92 also been circulated to the DPTC). John Wiley publishers had the outline peer-reviewed and
93 approved, met with the authors several times to discuss plans and content of this publication,
94 and have now presented the authors with a contract, which needs to be reviewed by legal,
95 financial and other appropriate experts within PQRI.

96 Dr. Norwood noted that besides publishing the toxicological considerations through this
97 book, another publication is being considered by the Working Group, which will focus on
98 best practices for control of leachables and extractables. That publication will be offered to
99 AAPS or PDA. Mr. Dana encouraged the group to consider publication of the tox.book
100 through PDA, although he recognized and acknowledged that since the interactions with
101 Wiley had progressed as they did, this might not be possible or appropriate. The DPTC
102 agreed that discussion of the contract and publishing arrangements is outside the
103 Committee's scope and directed Dr. Tougas and Dr. Norwood to consult with the SC Chair
104 as a first step. Dr. Tougas further encouraged the Working Group to consider sun-setting its
105 current activities and starting the book project as a new PQRI project. It was also agreed that
106 future publication opportunities would focus on PQRI members with publishing capabilities;
107 e.g., AAPS and PDA.

108 ***Container Closure System***

109 Mr. Malinowski noted that the Working Group is close to finalizing the next protocol for
110 multiunit containers. He suggested that any questions DPTC has on the protocol be
111 answered during the next DPTC teleconference rather than through a separate circulation and

112 approval of the document. The participants agreed. The experiments are ready to commence
113 immediately upon the protocol's approval.

114 *Profile Comparisons*

115 Mr. Christopher reminded the participants that the Working Group earlier this year had
116 integrated a PBE test for impactor-sized mass into the overall APSD profile assessment. The
117 challenge since then has been to ensure that the PBE applied by the Working Group is
118 consistent with the current Agency's thinking, and specifically, the program code being
119 developed for FDA but not available to the public yet. After 3-4 months of working 'blind',
120 the statisticians of the Working Group were given permission to see the code and in the last
121 few days were able to obtain the results that are matching those produced by the FDA code.
122 The Working Group now needs to evaluate the combined PBE + chi-square test using the
123 correct PBE algorithm, and after that the Final Report could be prepared. The original target
124 for completing the Final Report was 30 June, but due to the unforeseen circumstances
125 explained above, the Working Group's timeline has to be extended, e.g., until August.

126 *Mass Balance*

127 No activities have been reported since the last DPTC meeting. Mr. Wyka will forward the
128 proposed language for the guidance to Dr. Tougas, for submission to the SC and FDA.

129 *New Projects*

130 Dr. Tougas reported that the SC discussed the proposed new projects at its recent meeting.
131 The Arrhenius equation proposal was declined on the balance of expected length of the
132 project vs. perceived benefit.

133 The proposal on specifications and stability/shelf life determinations was returned to the
134 authors for revision, to stress the statistical nature of the proposal and to distinguish it from
135 the other QbD projects.

136 The QbD project proposed by Mary Oates has been approved. A Steering Team comprising
137 Mary Oates and the chairs of all four Technical Committees has been formed. The Working
138 Group is being actively populated.

139 **NEXT MEETING/TELECONFERENCE**

140 The next DPTC teleconference is scheduled for 2 August.

141 Finalized on 1 August 2006