

1 **Minutes of the DPTC Teleconference**
2 **on 12 December 2006**

3 **ATTENDEES**

4 Terry Tougas, *Chair* (Boehringer Ingelheim)
5 David Christopher (Schering-Plough)
6 Pat Forenzo (Novartis)
7 Sylvia Gantt (PQRI)
8 Frank Holcombe (FDA)
9 Lana Lyapustina (IPAC-RS)
10 Dan Malinowski (Pfizer)
11 Chris Moreton (Idenix Pharmaceuticals)
12 Jim Schwenke (BI)
13 Russel Somma (IPS)
14 Raj Uppoor (FDA)
15 Bob Wiens (Lilly)
16 Bruce Wyka (Schering-Plough)

17 ***Absentees***

18 Tony Amann (GPhA)
19 Clyde Anthony (USP)
20 Bob Dana (PDA)
21 Michael Golden (GlaxoSmithKline)
22 Lee Nagao (IPAC-RS)
23 Dan Norwood (Boehringer Ingelheim)
24 Rich Poska (Abbot)
25 Nakissa Sadrieh (FDA)
26 Vilayat Sayeed (FDA)
27 Bill Williams (University of Texas)

28 **AGREED ACTIONS**

- 29 • Dr. Tougas will discuss with the SC process for submitting PQRI final documents to the
30 FDA docket.
- 31 • Further clarifications will be requested regarding nominations for the Specifications Design
32 and Lifecycle Management Working Group.
- 33 • A justification for the recent additional nomination to the Stability Shelf Life Working Group
34 will be provided to the DPTC.

35 **DISCUSSION**

36 *Opening*

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

43 The main objective of the teleconference was to review updates on the Working Groups.

44 *Container Closure Working Group*

45 Mr. Malinowski reported that the screening experiments being conducted in four laboratories
46 by member companies and are into their 2nd month; one set has been completed and is ready
47 for analysis while the 90-day arm will be completed in January. The conclusions of the
48 screening experiments will be drafted and distributed for discussion; these conclusions are
49 needed to design a larger study. In addition the Working Group needs to select unit dose
50 packaging and formalize screening studies (time to reach equilibrium, effects of temperature
51 on permeation rates of the barrier foil). This work is expected to start in early 2007.

52 In response to questions, Mr. Malinowski explained that HDPE bottles are being tested, in
53 one bottle size commonly used in the industry but with two barrier types – foiled and capped
54 (high barrier) and capped but with broached foil (low barrier).

55 *Profile Comparisons*

56 Mr. Christopher reminded the participants that the Working Group is now preparing a Final
57 Report, which demonstrates that the chi-square ratio method for APSD profile comparisons
58 is not always consistent with the Working Group’s judgment. He reported that in the last
59 review cycle, it was suggested that one additional critical value be studied for the chi-square
60 ratio test, to demonstrate the effect of changing the critical value. These calculations have
61 now been completed and the Final Report is expected to be finalized by the Working Group
62 in early January, and provided for review and approval to the DPTC around mid-January.
63 The Working Group may eventually consider educational presentations.

64 *Excipients*

65 Mr. Wiens thanked Ms. Gantt and Ms. Walsh for their help in organizing the Excipients
66 workshop; he also thanked USP and IPEC who served as sponsors. The Working Group is
67 now preparing a paper summarizing the Workshop’s proceedings in an article targeted for
68 submission to the *Pharmaceutical Technology* in Q1 2007. Dr. Uppoor added that the
69 Workshop had aimed to identify difficulties with excipients, and the Working Group’s

70 ultimate submission to FDA may include a description of such difficulties, an explanation of
71 current regulations in this area, and a request to change regulations. Dr. Uppoor further
72 explained that appropriate understanding, availability and use of excipients is necessary for
73 implementing QbD initiatives. Mr. Wiens and Dr. Uppoor indicated that after completion of
74 the remaining tasks, which could take up to 6 months, the Working Group could be sunset.

75 ***Mass Balance***

76 Mr. Wyka reminded the Committee that the Working Group's MB WG's recommendation
77 for an FDA guidance had been submitted to FDA. He reported that the technical paper
78 regarding Mass Balance tests has been accepted for publication in the *Journal of Aerosol*
79 *Medicine*, with only minor revisions. Dr. Uppoor indicated that the PQRI submission had
80 been distributed among Agency's reviewers, who now recognize the limitations of that test
81 method. Dr. Uppoor recommended that the Working Group's recommendation
82 (<http://www.pqri.org/publications/pubreg.asp>) be submitted to the FDA docket for easy
83 public access.

84 ***Leachables and Extractables***

85 Dr. Lyapustina and Dr. Tougas reported that following the submission of the L&E
86 Recommendations to the FDA and the successful L&E training course in September 2006,
87 the Working Group has been planning two additional training courses in 2007 (one in Europe
88 and one in Chicago. Dr. Moreton mentioned the PIRA workshop in early 2007 on a similar
89 topic and suggested that the overlap in dates be avoided. Dr. Tougas also mentioned that
90 PQRI was invited but declined to co-sponsor PIRA's workshop.

91 The Working Group's article on the derivation and use of the safety thresholds has been
92 recently accepted for publication in *Toxicological Sciences*. The Working Group is also
93 preparing a journal article on chemistry work and recommendations, for *Pharmaceutical*
94 *Research*. In addition, the toxicology work and overview of chemistry may eventually be
95 published in book form; proposed contract amendments are currently under review by Wiley.
96 Dr. Uppoor recommended that the L&E Recommendations be submitted to the FDA docket
97 for relevant guidances; he suggested that the cover letter include a reference to the PQRI
98 website where the recommendation is posted (<http://www.pqri.org/publications/pubreg.asp>).

99 ***Specifications Design and Life Cycle Management***

100 The participants reviewed progress of voting on the candidates proposed for the DPTC
101 endorsement. The DPTC requested Dr. Lyapustina to clarify with Dr. Anthony the total size
102 of the applicant pool, the criteria used in selection of the recommended candidates, and the
103 list of Working Group members participating from the MTC side.

104 ***Stability & Shelf Life***

105 Mr. Forenzo reported that the SSL WG has held an introductory teleconference and a face-to-
106 face meeting, and is now focusing on preparing a detailed Work Plan, which will include

107 CMC, statistical and data-collection aspects. The Working Group is also actively liaising
108 with the PhRMA Stability Group and the PhRMA CMC Statistics Group. Dr. Upoor
109 commented on the importance of having real data and not only theoretical work; he indicated
110 that the Agency is still considering nominating a representative to this Working Group. The
111 DPTC members discussed the additional late nomination; Mr. Forenzo agreed to speak with
112 the applicant and provide further justification to the DPTC. Dr. Schwenke added that the
113 Working Group has had a good start and is enthusiastic about its work.

114 ***Conclusion***

115 In conclusion, the DPTC members thanked Ms. Gantt for her support of the PQRI.

116 **NEXT MEETING/TELECONFERENCE**

117 The next meeting or teleconference will be scheduled by email.
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Finalized on 15 January 2007