

1 **Minutes of the DPTC Teleconference**  
2 **on 8 September 2004**

3 **ATTENDEES**

Terry Tougas, *Chair* (Boehringer-Ingelheim, IPAC-RS)  
David Christopher (Schering-Plough, IPAC-RS)  
Frank Holcombe (OGD/FDA)  
Sylvia Gantt (PQRI Executive Secretary)  
Lana Lyapustina (IPAC-RS Secretariat)

Russ Somma (IPS, ISPE)  
Rajendra Uppoor (FDA)  
Bob Wiens (Eli Lilly, IPEC)  
Lee Nagao (IPAC-RS)

4 **DECISIONS MADE**

- 5 1. Dr. Tougas will propose to the Steering Committee that DPTC, in collaboration with MTC as  
6 appropriate, establish a working group (or groups) to address a specific issue illustrating how  
7 in-process testing could be correlated to end-process results in order to eliminate or reduce a  
8 particular end-product test.
- 9 2. Specific issues will be considered after the SC approves the general idea and clarifies the  
10 respective roles of MTC and DPTC.
- 11 3. Some of the work and data analyses conducted by the Test and Methods (T&M) Technical  
12 Team of the ITFG/IPAC Collaboration may be used for such a project. Dr. Nagao will  
13 provide for Dr. Tougas' review additional documents prepared by the T&M Team. Although  
14 those examples are specific to inhalation and nasal products, the approaches might be useful  
15 in further discussions.
- 16 4. The DPTC would like to address a broad scope of dosage forms, such as conventional solid  
17 oral and combination products (device + formulation).

18 **DISCUSSION SUMMARY**

19 *Opening*

20 Dr. Tougas opened the meeting. The following antitrust admonition was read: "Our  
21 discussions today are subject to the anti-trust guidance applicable in the U.S. Nothing  
22 discussed at this meeting is intended to restrict the individual decision-making of any  
23 member company or to represent an agreement to coordinate marketing or sales conduct.  
24 Those participating in this meeting are instructed to avoid discussion of competitively  
25 sensitive subjects, including, confidential marketing, sales, and pricing information."

26 Dr. Tougas explained that purpose of the teleconference is to brainstorm for strategic ideas  
27 about future direction and projects for the DPTC.

28 **Potential Future DPTC Topics**

29 Before the teleconference, the DPTC members were encouraged to review the following  
30 reports for stimulating a discussion on future DPTC projects:

- 31 • Report of the ITFG/IPAC Technical Team “Recommendations for Tests and Methods  
32 in Orally Inhaled and Nasal Drug Products.” (<http://ipacrs.com/tests.html>, 2001)
- 33 • The Gold Sheet article “FDA Moving Toward PAT Standardized Nomenclature And  
34 Definitions” (Vol. 38, No. 7 July 2004)

35 Dr. Tougas explained that much of attention has been focused recently on the PAT initiative  
36 and in-process testing. What has not been discussed much yet, is how in-process testing  
37 could be applied to eliminate some of the end-product testing.

38 Dr. Tougas also mentioned his conversation with Dr. Poska, who had suggested assessing the  
39 existing FDA CMC guidances for drug products in order to identify potential areas for future  
40 DPTC projects. It is not clear, however, how much value this activity would bring since the  
41 Agency is re-thinking its approach to guidances.

42 Dr. Uppoor provided an overview of the PAT ideology. All participants strongly supported  
43 the idea of specific projects about the correlation between in-process controls and end-  
44 product testing with an aim of eliminating or reducing the end-product testing. Such a DPTC  
45 project could generate a good example of successful and beneficial use of the PAT concepts.  
46 Dr. Holcombe commented that this approach puts the PAT concepts in a broader context.

47 The DPTC members were not sure, however, whether the Manufacturing Technical  
48 Committee (MTC) of PQRI might also have an interest in pursuing similar topics. Dr.  
49 Tougas agreed to clarify with the Steering Committee (SC) the division of responsibilities  
50 between the two Committees.

51 Dr. Tougas provided illustrations from the test requirements for metered dose inhalers  
52 (MDIs) world. For example, the first report quoted above presents a case of spray pattern  
53 testing, which could be appropriately controlled through dimensions on the device  
54 components and details of the formulation rather than through end product testing. Mr.  
55 Christopher suggested that a project could consist in producing clear recommendations about  
56 how the correlations could be established in order to justify the elimination of end product  
57 testing.

58 Dr. Norwood provided another example of the requirements to test for PNAs and  
59 nitrosamines even though modern rubbers for MDIs do not have those contaminants. Dr.  
60 Norwood also mentioned that the IPAC-RS Supplier Quality Control Group has prepared  
61 GMP guidelines for suppliers of device components (including rubber materials), and he  
62 would need to discuss with the Leachables and Extractable (L&E) Working Group of PQRI  
63 how those supplier GMPs would interact with the recommendations developed by the L&E  
64 WG.

65 Mr. Wiens proposed that the DPTC's contribution be to determine, in a general way, the  
66 quality attributes that should be tested on the finished product, and then identify appropriate in-  
67 process test that would control those attributes. Currently, there is little understanding of the  
68 quality parameters that are important to the product's performance. Dr. Tougas agreed, and  
69 gave an example of particle size distribution (PSD) testing in inhalation products, where  
70 beyond a general understanding that fine particles have a better chance of reaching the lungs,  
71 very little consensus exists about the subtle changes in PSD and their importance.

72 The participants also discussed the fact that 3-6 lots normally available at the time of  
73 approval is not enough, from the statistical perspective, to assess variability of the  
74 manufacturing process. Mr. Christopher explained that process capability calculated from  
75 such limited data would have a high degree of uncertainty (error) associated with it. Dr.  
76 Uppoor believed that conducting clinical trials at the extremes of quality acceptance criteria  
77 would be one way to set specifications.

78 Returning to the issue of potential topics for DPTC, Mr. Wiens proposed to look at how  
79 variability of raw materials affects the final product.

80 In conclusion, Dr. Somma applauded the work of IPAC-RS, but stressed it would be  
81 important for DPTC to address combination products (formulation+device) and conventional  
82 tablets. The other participants agreed.

### 83 **NEXT MEETING/TELECONFERENCE**

84 To be determined.

85

Finalized on 1 October 2004