

27 **B. Discussion of the Final Report**

28 Mr. Christopher reminded the Working Group that in parallel with the statistical
29 confirmation, the preparation of the Final Report had been started to enable discussions
30 of its structure, content and messages.

31 Dr. Byron said he had expected the Final Report to include an explicit statement that
32 'these are the best practices for comparing APSD profiles'.

33 Mr. Christopher agreed that this Working Group had started with such an objective – to
34 develop a robust method for comparing APSD profiles. However, this objective had
35 been modified after preliminary results on the chi-square method had been obtained.
36 The modified objective has been to evaluate the chi-square ratio test's capability for
37 being able to make equivalence determinations, and in particular when the chi-square
38 ratio test is combined with the ISM test. Since this may not be the best possible test or
39 combination of tests, it would be inappropriate to entitle the Final Report 'best
40 practices'. In fact, through a conscious choice and in the interest of time, the Working
41 Group had decided not to explore any alternatives to the chi-square ratio test, other than
42 supplementing it with the ISM test. For this reason, the Working Group had also
43 decided against the term "Recommendations" in the title of this document.

44 Dr. Adams supported this description of the Working Group's goals. He said that it
45 would be helpful to understand the characteristics of the chi-square ratio method, its
46 limitations and its value. For example, if the ISM test is the main factor in the
47 equivalence determination, what value does the chi-square ratio method add? Mr.
48 Christopher explained that the PBE method incorporates both the distance in the mean
49 deposition (between Test and Reference products) and the reference scaling to account
50 for differences in the variabilities. However, the ISM test does not address the full
51 profile. The differences in the outside-impactor depositions may be better detected by
52 the chi-square ratio test, and in fact the lower sensitivity of the chi-square ratio test could
53 be appropriate for that portion of the profile. Dr. Adams added that the Single
54 Actuation Test (SAC) in the draft BA/BE guidance is a different test, and does not
55 address the profile either. He speculated that the chi-square ratio test might serve as a
56 complimentary and not a definitive test.

57 Dr. Morgan asked whether the Final Report would have recommendations for specific
58 parameters used in the two statistical methods explored, such as critical values, scaling
59 variable, acceptable difference in the means, and others. Mr. Christopher confirmed that
60 the Final Report will definitely include all the specific parameters used to generate the
61 assessment results. Moreover, the Report would provide all the details necessary to
62 repeat the results or to modify the methods. And strictly speaking, the conclusions of
63 the Final Report are only valid for the particular implementation of the tests. Different
64 parameters might lead to different conclusions.

65 The participants further discussed that the Final Report should outline the situations
66 where the studied tests would be inappropriate, and areas of the tests' limitations. Dr.
67 Adams said that if there are too many situations where the studied combination of tests

68 or the chi-square ratio test are inapplicable, perhaps they should not be used as a
69 standard tool. This information, though 'negative', could be helpful to the regulators
70 and decision makers.

71 The Working Group, including Dr. Byron, agreed that the Final Report should not claim
72 to be 'Best Practices'; and also agreed that it would be important nevertheless to
73 document the particular implementation of the combination of tests, as well as
74 capabilities and limitations of that combination. It would also be important to document
75 the thought process that the Working Group had gone through, as well the various
76 disciplines that were involved in this discussion. This would allow others to continue
77 the work and build on it.

78 **C. Cohort Design**

79 Mr. Christopher invited the participants to discuss briefly the cohort design that should
80 be recommended for APSD testing regardless of the particular statistical method. Such
81 design is necessary because the cascade impaction results tend to be influenced by the
82 particular equipment, analyst, day/time conditions, and in order to balance out these
83 factors, which are not related to the studied products, both Test and Reference products
84 should be tested in a certain pattern. Dr. Mitchell reminded the group that the Mass
85 Balance Working Group had already developed the details of a designed experiment to
86 address this issue and he suggested that it be used here. All agreed that a detailed
87 description of that design in open public literature would be immediately useful. The
88 Working Group recommended that the design be supplemented with a justification
89 explaining why such cohorts-testing approach is necessary.

90 **IV. AGREEMENTS**

- 91 • The draft outline will be revised and sent to the Working Group members for a 2 week
92 review. All comments will be compiled and a new version of the draft could be issued
93 for discussion before the next teleconference.
- 94 • The Final Report will include all statistical details, as well as a description of the
95 methods used by the Working Group members in their evaluation of the profiles.

96 **V. NEXT TELECONFERENCE/MEETING.**

- 97 • The next teleconferences will be held on 12 April and on 17 May, both days at 9:00 AM
98 ET.

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Finalized on 3 April 2006

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