

SUMMARY OF THE DISCUSSION
OF THE PQRI PROFILE COMPARISONS SUBGROUP ON
9 March 2004

PARTICIPANTS:

Dave Christopher (Schering-Plough); Craig Dunbar (Alkermes); Douglas Lee (Pfizer); Lana Lyapustina (IPAC-RS); Jolyon Mitchell (Trudell Medical)

DISCUSSED AND AGREED:

1. The subgroup discussed comments made earlier during the 9 March teleconference of the full Profile Comparisons Working Group. Dr. Dunbar and Dr. Mitchell agreed to draft an additional paper explaining the scientific reasoning for stage-width adjustments, and illustrating in particular the consequences of NOT doing the adjustment. The draft paper will be circulated to the Subgroup for review when available. It may be beneficial to publish the paper in a peer-reviewed journal.
2. A more general, impactor-independent comparison would require a continuous representation of mass and aerodynamic diameter, obtained through a stage-width adjustment. Independence of the impactor will be important, for example, when switching to the Next Generation pharmaceutical Impactor (NGI). Stage cut-off sizes will also change if the same cascade impactor is operated at different flow rates. Therefore without the adjustment, the chi-square results, and consequently the critical value, will depend on the particular impactor at a particular point in time, with particular testing conditions. The Subgroup believes that the stage-width adjustment is a necessary condition for the test (e.g., algorithm, sampling, design) and critical value to be generalizable.¹ This notion is currently under further investigation (see item 1 above).
3. The focus of the Agency participants at this point may not require the robust representation of PSD profiles provided by a continuous probability density model. The Agency participants may only be interested in stage-to-stage, component-to-component comparisons. However, profile comparisons generated on the same impactor will be affected by the stage widths. In the calculation of the chi-square statistic, the differences obtained on the wide stages are summed together with the differences obtained on the narrow stages. Without correcting for the collection characteristics of the stage, the analysis will be influenced by the width of the stage, i.e., the chi-square statistic will be more sensitive to differences on wide stages and less sensitive to differences on narrow stages.
4. In addition to the meeting at RDD, it may be beneficial to hold another face-to-face meeting of the full Working Group on the East Coast, where more of the members can be present, in order to finalize discussions on the desired properties of the test.

NEXT MEETING/TELECONFERENCE OF THE SUBGROUP: Will be scheduled as needed.

¹ Some members of the larger Working Group feel this statement has not been proven yet.