# Preface

The measurement of the aerodynamic size properties of aerosols from orally inhaled products has been a long-standing topic of interest to stakeholders because of the need to provide measurements that can ultimately be related to the likely deposition in the human respiratory tract and therefore to subsequent clinical response to the active pharmaceutical ingredient(s). The challenge has been the limited choice of measurement equipment available that meets all of the requirements demanded of it. Historically, the full-resolution multistage cascade impactor has been the workhorse in the laboratory undertaking inhaler performance testing, but its successful operation requires a high degree of operator skill and know-how, and the measurement process is both laborious and time consuming.

This book has been the outcome of several years work within two cross-industry organizations: the Cascade Impaction Working Group of the International Pharmaceutical Consortium on Regulation and Science (IPAC-RS) and the Cascade Impactor Sub-Team of the European Pharmaceutical Aerosol Group (EPAG). The abbreviated impactor measurement (AIM) concept was developed in the middle of 2000 out of the realization that there is a need to offer users of the cascade impaction technique, the opportunity to make measurements of the important aerodynamic size-based metrics, without the need to determine the aerodynamic particle size distribution. From these developments came the realization that in the product quality environment, the minimum number of metrics that is needed relating to the sum and ratio of the large and small particle fractions, are all that is needed to define the APSD. If the boundary dividing them was chosen appropriately, could result in better decision-making than the currently accepted practice in the USA of accumulating the mass of active pharmaceutical ingredient collected on each stage of a full-resolution impactor into groupings that broadly reflected coarse, fine, and extra-fine particulates. This new approach was termed efficient data analysis (EDA) and is the companion concept to AIM, although EDA may be applied to data from either full or abbreviated impactor measurements.

As this volume was in the process of early development, it became evident that in order to describe the AIM and EDA concepts meaningfully, it would be necessary to place these approaches into the context of the existing apparatuses that are defined

in the pharmacopeial literature. This material is currently in disparate locations and is therefore not always easy to find quickly. A chapter has therefore been devoted to the description of the underlying theory, including key descriptive information concerning the compendia apparatuses. This chapter also addresses the potential impact that assumptions concerning the properties of the collection efficiency profiles of cascade impactor stages may have both on measurements by full and abbreviated systems, to provide assurance to the reader that such fundamental concerns have been addressed.

In addition to a chapter that reviews in detail and updates the so-called good cascade impactor practice (GCIP) concept developed in February 2002 through the US-based Product Quality Research Institute, this book also contains information on how AIM and EDA could be applied at various stages in the orally inhaled drug product life cycle. There are also several case studies that illustrate how these concepts have already been applied to the assessment of currently marketed products. The intriguing question 'When could AIM fail…?' has also been addressed through scenarios in which the underlying physical processes that influence the size distribution of inhaler aerosols are considered as well as by failure modes analyses related to the cases of pressurized metered dose inhaler and dry-powder-inhaler categories of drug products.

An extensive chapter contains a compilation of the large number of experimental validations of the AIM concept that have been undertaken since 2008. Its purpose is again to provide confidence in the robustness of the concept and, at the same time, to highlight the precautions that should be considered when beginning the process of implementing an AIM-based regimen with or without EDA.

A chapter is included that addresses the regulatory and compendia pathways that will likely need to be followed before either or both concepts become fully accepted as routine approaches by all stakeholders involved in the process of inhaler performance evaluation.

Towards the end of this book, a chapter has been included that considers how the AIM concept might be adapted in the future to explore the possibilities for greater correlation than has been possible hitherto, between impactor-generated measures of particle size and likely particle deposition in the human respiratory tract. This is a highly active topic of current research as the development of robust in vitro–in vivo relationships for the class of orally inhaled products as a whole continues to pose severe challenges.

This volume concludes with a chapter that attempts to look forward and present ideas to encourage further research into the application of both AIM and EDA concepts.

This compilation of knowledge concerning the cascade impaction technique will be of interest to all those who are involved with the day-to-day management of orally inhaled product quality testing, as well as to the researcher seeking to know how AIM and EDA might be applied in novel ways. The authors have provided new insights that will help both the novice and experienced user of the impaction method come to grips with either concept.

At the same time, the authors and editors acknowledge that this field is evolving rapidly, and no single published work could capture all of the possible angles. This book is but a stepstone on the way towards much deeper understanding of the various aspects of cascade impactor testing, and particle sizing in general, of the pharmaceutical aerosols. Future investigations and publications will undoubtedly elaborate on concepts presented here as well as introduce new data and considerations. One of the goals *Good Cascade Impactor Practices, AIM and EDA for Orally Inhaled Products* could serve, therefore, is to provide a helpful backdrop and to strengthen a foundation for further work in this important and actively debated area.

The editors pay tribute to the effort that has gone into development of each contributed chapter, making it both information rich and authoritative and therefore a valuable resource.

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