International Journal of Pharmaceutics 418 (2011) 149–150

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Editorial

A priori Performance Predictions in the Pharmaceutical Sciences

A famous quote from George Box (Box and Draper, 1987) states that, "All models are wrong, but some are useful." Any scientist who has engaged in research involving the use of models has grappled with the insight provided by these words, whether or not they encountered Box's quote at some point during their experience. In the quest to model complex phenomena we all must concede that even the most carefully constructed model will be challenged in some respect by something we had not considered. Nonetheless, pharmaceutical research moves forward because, despite their limitations, many of the models that continue to emerge from our laboratories have proven useful in helping to refine our understanding of the drug delivery landscape.

Early models in the pharmaceutical sciences, such as Higuchi's root-time dependent delivery from polymer matrices (Higuchi, 1961), drew upon basic models from engineering and physical chemistry. Though limited to the constraints of its assumptions, very few pharmaceutical scientists would suggest that the Higuchi Equation is not useful. The use of computational tools in the pharmaceutical sciences harkens back to the early days of pharmaceutics, and the pioneering efforts of Higuchi and others. Interestingly, formal departments of pharmaceutics began to be established at the dawn of the computing era, meaning that predictive models developed at that time required expertise not only in the physical sciences, but in the emerging skills required to program computers. Every school of pharmaceutical sciences has, tucked away in some corner, boxes of computer cards that were used to parameterize a single equation. That empirical and semi-empirical modeling has grown to where it is today is a testament to the rapid pace with which computing has advanced, creating sophisticated tools that can be readily used to simulate and describe very complex systems.

As *a priori* models have "grown up" with the pharmaceutical sciences, they have often been criticized as not being practically useful, but rather "academic toys" with so many constraints and limitations that they have no hope of application to real pharmaceutical problems. Such criticism certainly embraces Box's "all models are wrong" concession, but it also implies that *none* are useful. Despite continued development in the last two decades, *in silico* polymorph predictions are often viewed in this light and their adoption by industrial groups as part of the toolbox for early candidate development still remains limited. It could be argued, however, that although this predictive tool is still in its adolescence, even rudimentary applications could potentially help prevent the next Ritonavir™ (Chemburkar et al., 2000) from happening. In fact, one could argue that industrial scientists are frequently required to use incomplete datasets to make decisions, and it is the existence of models that provides confidence to extrapolate beyond the immediately accessible data. Such modeling helps direct the efforts of industry and academia to partner with worldwide regulatory agencies to embrace initiatives such as Quality by Design, which seeks to minimize risk in the pharmaceutical decision-making process by better understanding the interplay of materials, process equipment, humans, etc.

In this special theme issue of the *International Journal of Pharmaceutics*, we are delighted to bring together a wide array of disciplines contributing to *A priori Performance Predictions in the Pharmaceutical Sciences*. It is our goal in this issue to provide examples to help demystify the use of predictive approaches in 21st century pharmaceutics. Contrary to the perception that modeling is reserved for academics, this issue presents nineteen research articles from academia, industry, *and* collaborations between the two, with specific examples of the practical usage of predictive tools in the worldwide pharmaceutical industry.

In assembling the topics for this theme issue, we, as an editorial team, attempted to span the breadth of the diverse sub-disciplines in which *a priori* modeling is being used. Here we present manuscripts reporting developments in physical pharmacy, solid state mechanics, manufacturing and process analytical technologies, biopharmaceutics, and chemical reactivity. Reinforcing the widespread use of modeling to make performance predictions, throughout the many months that we have been editing this theme issue, we were very encouraged to find just how many subdisciplines of pharmaceutics are using these techniques to advance the field. With the opportunity to save development time, money and resources, it is clear that these approaches represent the future of pharmaceutical development. Thank you to all of our contributors who have helped translate this issue from an idea to a reality. We hope that the reader will enjoy this issue as much as we have enjoyed putting it together.

References

Box, G.E.P., Draper, N.R., 1987. Empirical Model-Building and Response Surfaces. Wiley, New York.

Higuchi, T., 1961. Rate of release of medicaments from ointment bases containing drugs in suspension. J. Pharm. Sci. 50, 874–875.

Chemburkar, S.R., Bauer, J., Deming, K., Spiwek, H., Patel, K., Morris, J., Henry, R., Spanton, S., Dziki, W., Porter, W., Quick, J., Bauer, P., Donaubauer, J., Narayanan, B.A., Soldani, M., Riley, D., McFarland, K., 2000. Dealing with the impact of ritonavir polymorphs on the late stages of bulk drug process development. Org. Proc. Res. Dev. 4, 413–417.

0378-5173/$ – see front matter
doi:10.1016/j.ijpharm.2011.06.023

Bruno C. Hancock is a Research Fellow at Pfizer Inc. in Groton, CT where he leads a group that is responsible for the creation and implementation of 21st century approaches to drug product manufacturing. His research is focused on developing state-of-the-art predictive approaches to drug product design and manufacturing and on using them to improve the way in which new medicines are developed.

Prof. Kenneth R. Morris studies pharmaceutical materials, dosage form design and processing. His research is widely recognized for its contributions to modernizing dosage form development in the pharmaceutical industry. Integration of advanced solids analytical techniques, with physical chemical and engineering principles to predict the response of pharmaceutical crystalline material to processing stress is used to systematically design dosage forms that perform as needed and are capable of being produced at scale.

Peter L.D. Wildfong has been a faculty member at Duquesne University since 2004 and is currently an Associate Professor of Pharmaceutics. His research focuses on modeling complex physical phenomena associated with pharmaceutical materials, emphasizing the link between fundamental structural properties of active pharmaceutical ingredients and other formulation components, and how these dictate the physical and chemical behavior of organic materials.

Bruno C. Hancock*
Pfizer Inc., Groton, CT, USA

Kenneth R. Morris
University of Hawaii-Hilo, Hilo, HI, USA

Peter L.D. Wildfong
Duquesne University, Pittsburgh, PA, USA

* Corresponding author. Tel.: +1 860 715 2484;
fax: +1 860 715 7972.
E-mail address: bruno.c.hancock@pfizer.com
(B.C. Hancock)

Available online 25 June 2011