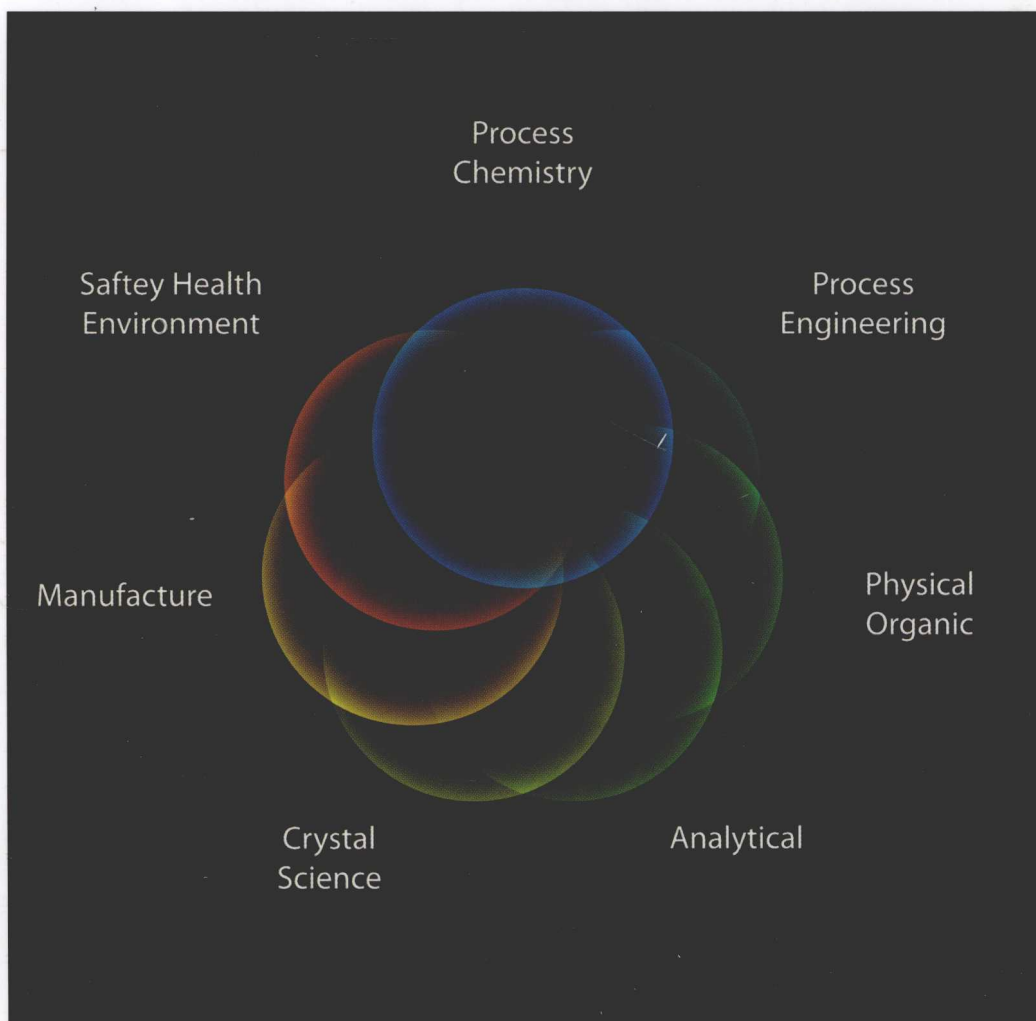


RSC Drug Discovery

Edited by A. John Blacker and Michael T. Williams

Pharmaceutical Process Development

Current Chemical and Engineering Challenges



RSC Publishing

Pharmaceutical Process Development Current Chemical and Engineering Challenges

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RSC Publishing

RSC Drug Discovery Series No. 9

ISBN: 978-1-84973-146-1

ISSN: 2041-3203

A catalogue record for this book is available from the British Library

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Published by The Royal Society of Chemistry,
Thomas Graham House, Science Park, Milton Road,
Cambridge CB4 0WF, UK

Registered Charity Number 207890

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Foreword

It is pleasing to contemplate a manufacture rising gradually from its first mean state by the successive labours of innumerable minds.

Samuel Johnson, *The Rambler*, 17 April 1750

In more than 45 years of learning and teaching chemistry I have encountered a rich array of students and colleagues whose pursuits have been animated by similar ideals. Some were driven by the intellectual stimulus and rewards of working at the frontier of knowledge. Others were driven by the urge to challenge existing tenets in the pursuit of greater understanding. Still others were inspired by the practicality of the subject and the desire to leave a beneficent legacy. The issue of practicality has loomed rather large recently as governments have sought a tangible return for very substantial investments. Evidence for the enhanced status of practicality can be gleaned from the enrichment of “standard” university programmes in chemistry with polymer chemistry, nanotechnology, material science and medicinal chemistry. Conspicuous for their absence from this short list are courses in process development; hence, there is little appreciation by university graduates of the complex and multidimensional science that transforms a reaction or sequence of reactions to a process. The absence of process development in academia can be attributed in part to the fact that most process development takes place in the industrial sphere under a veil of secrecy. However, a number of changes has taken place in the last 20 years that augur well for the future. Firstly, many companies encourage their employees to publish their work in open scientific journals, with the consequent revelation of the wealth of skill and creativity that underpins process research. Secondly, process chemists are often guests in university seminar programmes. Thirdly, the publication of high quality monographs written by experts in the field has aided dissemination. Finally, academic chemists are now aware of the many challenges in process development and they are better attuned to the benefits of exploitation.

In *Pharmaceutical Process Development: Current Chemical & Chemical Engineering Challenges*, John Blacker and Mike Williams, expert practitioners, present a brief overview of the many facets of process development and how recent advances in synthetic organic chemistry, process technology and chemical engineering have impacted on the manufacture of pharmaceuticals. It is aimed at chemistry, engineering and pharmacy undergraduates, postgraduates and early to mid-career professionals in allied disciplines. In 15 concise chapters the book covers such diverse subjects as route selection and economics, the interface with medicinal chemistry, the impact of green chemistry, safety, the crucial role of physical organic measurements in gaining a deeper understanding of chemical behaviour, the role of the analyst, new tools and innovations in reactor design, purification and separation, solid state chemistry and its role in formulation. The book ends with an assessment of future trends and challenges.

Philip Kocienski

Preface

Anyone who has helped to plan an industrial synthesis tends to pity the poverty of the criteria that academic synthesis must meet.

Sir John Cornforth, *Aust. J. Chem.*, 1993, **46**, 157.

The industrialisation of any synthetic process is a challenging endeavour, and this is particularly so for pharmaceutical agents because of their relative complexity. In addition to being efficient and atom economic, reactions used on scale to produce pharmaceuticals need to meet exacting safety and environmental standards, while the efficiency of every operation in the work-up, isolation and purification of the reaction needs to be examined. One of the key goals of process research and development (R&D) scientists is to ensure that their processes are economic. Because the price of pharmaceuticals falls sharply when their patents expire, there is a common misconception that they are overpriced by their innovator companies during their patent lifetime. The reality is usually very different: the pharmaceutical development process is both extremely costly and risky. There is no law of economics stating that the launch of a product onto the market ensures that it will be profitable, and it has been estimated that over half of all drugs that reach the market fail to recoup their discovery and development costs. Hence, process R&D scientists are charged with driving down the cost of goods of drug candidates, to help ensure their commercial viability.

Pharmaceutical process R&D is therefore an exacting, multidisciplinary effort. It has, however, been a somewhat neglected discipline in the chemical curriculum, so we were delighted to have the opportunity to contribute this volume to the RSC Drug Discovery series. The aim of this book is to communicate to those interested in the field the fascinating, and interdependent nature of activities associated with producing drug substance. The book differs from the few others in this field in its organisation, which attempts to walk the reader logically through key aspects of the chemical R&D process. In the wide

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variety of chapters, contributed mainly by current practitioners from the pharmaceutical industry, the authors have taken the opportunity to discuss the latest technological developments and their impact upon the many changes taking place in the market. It is hoped the reader will appreciate the discussions in each chapter, which are frequently animated by contemporary examples of drug syntheses and processes.

We would like to thank all of the authors for their support of this project, and for the high quality of their contributions to this book. We would also like to thank Gwen Jones at the RSC for her patience and support in bringing this volume to completion at a difficult time for the industry when sites were closing, several authors were struggling with the search for new employment, and timelines drifted. If this book contributes to the growing awareness of the complexities and challenges of process R&D, and provides a useful resource for academic and industrial scientists and engineers, then all of our efforts will have been worthwhile.

A. J. Blacker and M. T. Williams

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