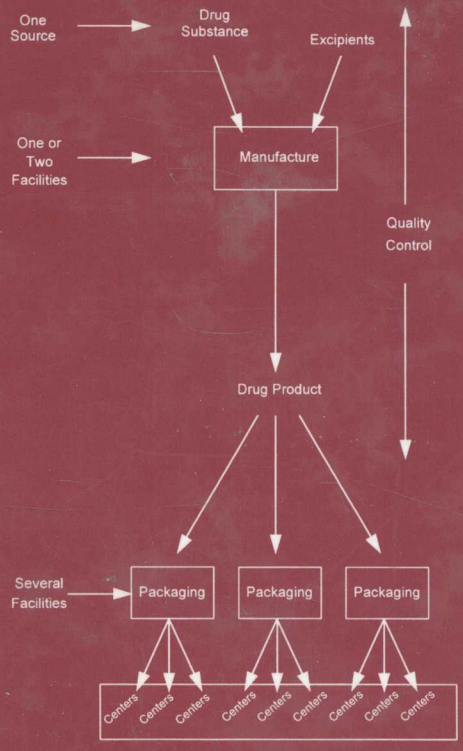
DRUGS AND THE PHARMACEUTICAL SCIENCES VOLUME 87

Drug Products for Clinical Trials

An International Guide to Formulation • Production • Quality Control



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An International Guide to Formulation • Production • Quality Control

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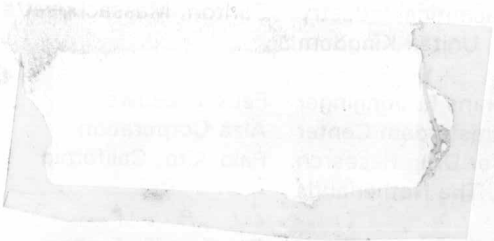

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Preface

Our objective in assembling this book was to call attention to a core competency in the arena of pharmaceutical development. We wanted to highlight the fact that the area of clinical trials materials was fundamental to any company's operations and that quite frequently the ability to produce and control such materials quickly and efficiently could lead to a competitive advantage. We were particularly attuned to this because of the checkered history of the discipline, and, since the whole industry has been undergoing massive restructuring, we felt it important to raise consciousness as to some of the issues and procedures that would allow the practitioner to flourish in an ever-changing environment. Accordingly, this book should not be regarded as a "how-to" book, nor is it to be regarded as overly comprehensive. Rather, we selected topics that addressed contemporary issues which would inform the reader about the concerns that the clinical trials manager faced in performing his/her tasks, and which would highlight some of the newer technologies that affected the way in which clinical trial materials are produced.

In the first half of the 1990s, pharmaceutical companies consolidated and reduced headcount in reaction to the converging pressures of thinning product pipelines, the increasing presence of generics, and budding managed care market power. Although these pressures have not yet dissipated, the consolidation of the industry will continue; companies are beginning to shift their focus to long-term growth opportunities and strategic positioning. Accordingly, as

editors, we identified topics that we thought were most significant for growth in the clinical supplies area, and that would help identify the best strategies and tactics that the practitioner could employ to achieve continued success and growth. Therefore, topics such as how to write SOPs and CANDAs, how best to deal with the FDA, the role of an IRB, labeling and legal aspects, patient/subject/investigator compliance, and safety monitoring have not been included, because this information is available in other medical publications, and we wanted to ensure that our contribution was a valuable addition to the armamentarium of those practicing in the field.

Several major themes related to current and future growth opportunities, and the challenges that pharmaceutical organizations face in achieving growth in the tumultuous healthcare market, are addressed in this book. These include:

- *Pharmaceutical firms' strategies must include product innovation, in both pharmaceuticals and biotechnology, rather than merely focus on winning price wars.*

  The chapter by Andrew J. Gorman and David Bergstrom addresses how innovation is encouraged in the discovery process, and the chapter by Vasken Paragamian discusses how innovation is so important in discovering cost-effective synthetic processes in scaling-up methods for producing large quantities of a new drug entity. John M. Baldoni and Choon K. Oh provide special insight into how innovation in the preclinical arena can enhance decision making as to the best chemical candidate with which to conduct clinical trials. New ways of treating stability data are introduced by Jens T. Carstensen in his usual inimitable fashion. As emphasized in Chapter 1, the clinical trials materials manager must stay abreast of new technologies to maintain effectiveness and grow professionally.

- *Companies can expect to form domestic and international alliances with other pharmaceutical and biotechnology firms in the next five years.*

  The chapter by Christopher J. Potter and the one authored by Peter J. Baines, Susan A. Charman, Gillian M. Clarke, Robin S. Roman, and Susan M. Walters both concern cross-functional areas affecting how clinical trials materials are handled in a transnational environment. Both address the different rules and regulations in Europe, and the latter addresses circumstances unique to Australia and Japan.

- *Companies anticipate outsourcing many functions that had once been considered necessary core competencies of classic fully integrated pharmaceutical firms. Such decisions are influenced by strategic focus, resource allocations, competitive market factors, and costs. Some of the larger*

fully integrated drug firms will spend millions of dollars in upgrading their own facilities, whereas the small biotech firms will elect to preserve their precious capital and outsource the production and control of clinical supplies materials.

To consider outsourcing, we commissioned an excellent chapter from Maureen E. Spataro and Michael G. Dragoon, who are intimately involved with this area from a provider and receiver's perspective on a day-to-day basis. In addition, this chapter raises the importance of accurate cost accounting. On the other hand, John E. Vogan and Jean Corriveau address the difficult area of handling toxic substances, which in reality is impractical to outsource.

- *Some companies rank information systems and corporate culture as the most significant challenges to internally developing and maintaining a competitive edge in their core competencies. Human resources are also regarded as very challenging. We believe that this concern reflects the difficulty in attracting and retaining people who are able to provide the knowledge and leadership required in the increasingly sophisticated areas throughout the organization that rely on the timely provision of clinical trials materials of high quality.*

In Chapter 1, we introduce the concept of emotional intelligence and its utility in selecting staff to fulfill the critical role of a clinical trials materials manager. Nicholas P. Barker in his chapter on Total Quality Management speaks to the intricacies of how quality is measured in a clinical supplies department and provides food for thought regarding continuous improvement in people skills.

- *There will be an increasing awareness in the importance of information systems and data management in the next few years. This will lead to a burgeoning demand for just-in-time manufacturing, better communication systems, accurate cost reporting, and contract data in the industry.*

In its totality, the book is really about how different groups best communicate with one another. The seminal work by Cary Blume stresses the importance of frequent and honest communication between the medical department and the clinical supply department. This concept is reinforced in the chapters by Graham J. Frank and by Thomas L. Jeatran and James Clark. The excellent chapter by Dorothy M. Dolfini and Frank J. Tiano highlights how crucial communication is in designing packaging systems for clinical trials supplies. Jeffrey D. Kosterich touches on how computers can make the difficult task of data tracking so much

easier. Chapter 1 introduces the future utility of artificial intelligence and rapid prototyping to the clinical trial formulations arena, and Gary W. Goodson and William C. Stagner expertly consider the critical aspects affecting clinical supply manufacturing.

- *The constantly evolving and easing of regulatory approval processes and harmonization of practices will impact the clinical trials arena in a significant and positive way. They have the opportunity to boost R & D efforts by adding time at the front end of the product life cycle.*

  Here we have chosen to address these issues in a multitude of works, viz., the previously cited multinational chapter by Peter Baines and colleagues; the concept of a time-based company is introduced in Chapter 1; Christopher J. Potter puts the concept of analytical validation in a unique perspective; and Gary W. Goodson and William C. Stagner address various GMP considerations affecting manufacturing. Bioequivalency considerations from a regulatory perspective are also discussed by C. T. Rhodes in Chapter 4.

In conclusion, we believe that the topics we have selected to form the basis of this book provide resonance to the stated purpose of discussing issues germane to the executive and practitioner alike regarding the important discipline of producing and controlling clinical trials materials.

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