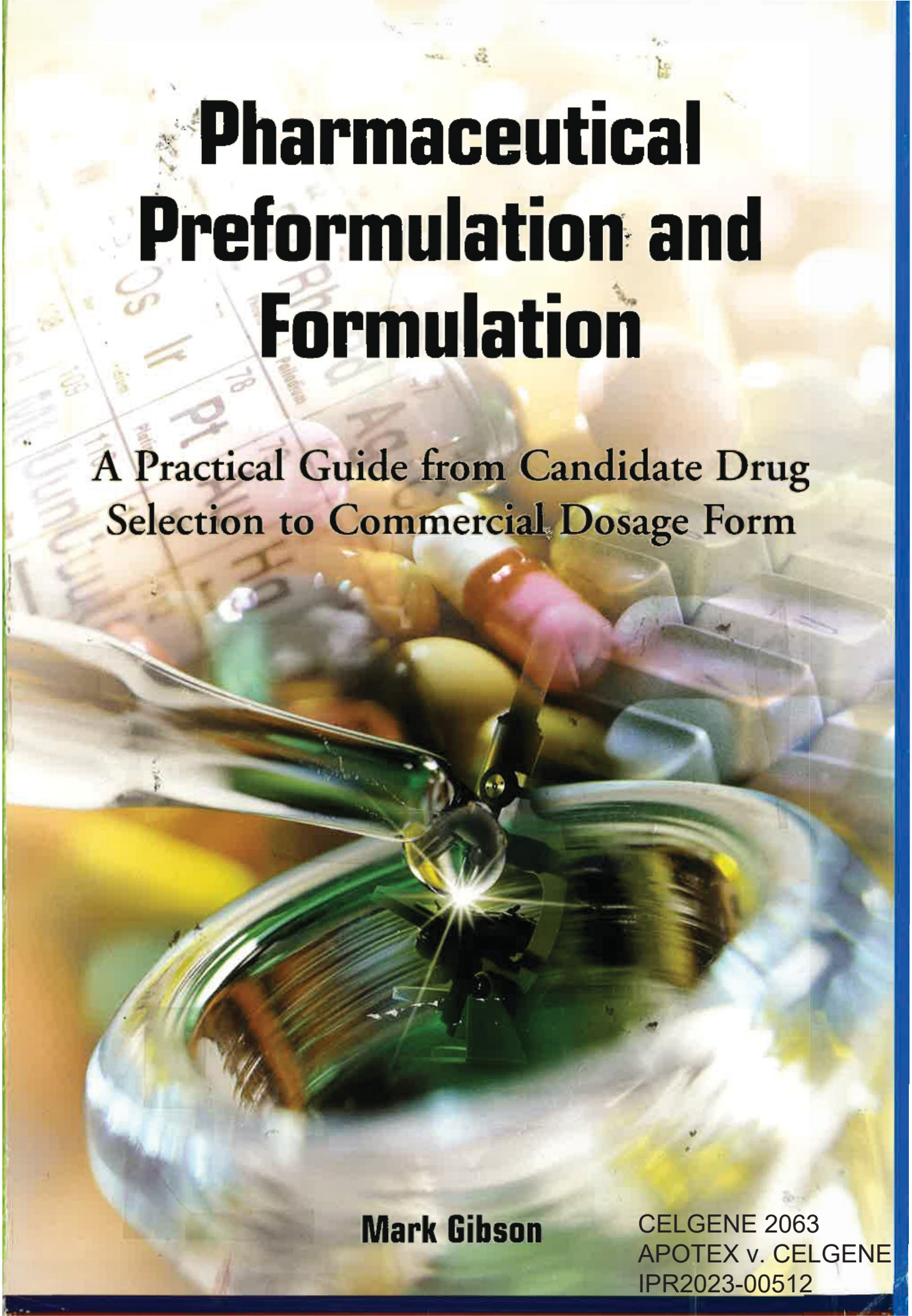
Pharmaceutical Preformulation and Formulation

A Practical Guide from Candidate Drug Selection to Commercial Dosage Form



Mark Gibson

PHARMACEUTICAL PREFORMULATION AND FORMULATION

A Practical Guide from Candidate Drug Selection to Commercial Dosage Form

Mark Gibson
Editor

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Library of Congress Cataloging-in-Publication Data

Pharmaceutical preformulation and formulation : a practical guide from candidate drug selection to commercial dosage form / Mark Gibson, editor.
p. ; cm.
Includes bibliographic references and index.
ISBN 1-57491-120-1 (hard : alk. paper)
1. Drugs—Dosage forms. I. Gibson, Mark, 1957–
[DNLM: 1. Drug Compounding. 2. Biopharmaceutics—methods. 3. Chemistry, Pharmaceutical—methods. 4. Dosage Forms. 5. Drug Evaluation. QV 778 P53535 2001]
RS200 .P425 2001
615'.14—dc21

2001016816

Commissioned in Europe by Sue Horwood of Medi-Tech. Publications, Storrington, England, on behalf of IHS® Health Group, Denver, Colorado, USA. General Scientific Advisor: Dr. Guy Wingate, UK Quality Manager, Computer Systems Compliance, Secondary Manufacturing, Glaxo Wellcome, Barnard Castle, England.

10 9 8 7 6 5 4 3 2 1

ISBN: 1-57491-120-1

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CONTENTS

1

Introduction and Perspective

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This book is intended to be a practical guide to pharmaceutical preformulation and formulation. It can be used as a reference source and a guidance tool for those working in the pharmaceutical industry or related industries, for example, medical devices and biopharmaceuticals, or anyone wanting an insight into this subject area. The information presented is essentially based on the extensive experiences of the editor and various other contributors who are all actively working in the industry and have learned "best practice" from their experiences.

There are various excellent books already available which cover the theoretical aspects of different types of pharmaceutical dosage forms and processes. A variety of books are also available that focus on the drug development process, business, regulatory and project management aspects. In my opinion, there has been a long-standing need for a pragmatic guide to pharmaceutical preformulation and formulation with an emphasis on what practical studies need to be undertaken, for what reasons and during what key stages of the drug development process. The important stages where preformulation, biopharmaceutics and formulation play a key role are candidate drug selection through the various stages of product development. This book has been written to try and address this need.

A logical approach to product development is described in the book, with the key stages identified and the preformulation, biopharmaceutics and formulation activities and typical issues at each stage discussed. Wherever possible, the book is illustrated with real or worked

examples from contributors who have considerable relevant experience of preformulation, biopharmaceutics and formulation development.

Jim Wells' book on preformulation (Wells 1988) made a strong impact on trainees and pharmaceutical scientists (including myself) working in this field of the pharmaceutical industry when it was introduced over 10 years ago. It describes the important concepts and methods used in preformulation with the underlying theory. To his credit, Wells' book is still useful today, but sadly, the book is now out of print, and existing copies are hard to obtain. It also requires updating to include modern preformulation instrumental techniques which have emerged over the last decade, such as thermo gravimetric analysis (TGA), hot stage microscopy (HSM), X-ray powder diffraction (XRPD), raman and infra-red spectroscopy and solid-state nuclear magnetic resonance (NMR), to name a few. These techniques can be used to provide valuable information to characterise the drug substance and aid formulation development using the minimal amounts of compound.

Pharmaceutical Preformulation and Formulation: A Practical Guide from Candidate Drug Selection to Commercial Formulation covers a wider subject area than just preformulation. Topics include biopharmaceutics, drug delivery, formulation and process development aspects of product development. The book also describes a logical and structured approach to the product development process, recommending at what stages appropriate preformulation, biopharmaceutics and formulation work is best undertaken.

DRUG DEVELOPMENT DRIVERS, CHALLENGES, RISKS AND REWARDS

It is important that the reader is aware of the nature of pharmaceutical research and development (R&D) in order to appreciate the importance of preformulation and formulation in the overall process.

In simple terms, the objective of *pharmaceutical R&D* can be defined as "converting ideas into candidate drugs for development", and the objective of *product development* defined as "converting candidate drugs into products for registration and sale". In reality, these goals are extremely challenging and difficult to achieve because of the many significant hurdles a pharmaceutical company has to overcome during the course of drug development. Some of the major hurdles are listed in Table 1.1.

The high risk of failure in drug discovery and development throughout the pharmaceutical industry statistically shows that, on average, only 1 in 5,000 to 1 in 10,000 compounds screened in research will reach the market (Tucker 1984). Of those that are nominated for development, the failure rate will vary from 1 in 5 to 1 in 10 compounds that will achieve registration and reach the market-place. On top of that, there is a significant commercial risk from those that are marketed; only 3 out of 10 are likely to achieve a fair return on investment. The products which give poor return on investment are often the result of poor candidate drug selection (the compound does not have the desired properties of safety, selectivity, efficacy, potency or duration) and/or poor product development (the development programme does not establish the value of the product). The latter scenario should, and can be, avoided by careful assessment at the "product design" stage of development. Product design is discussed further in Chapter 5.

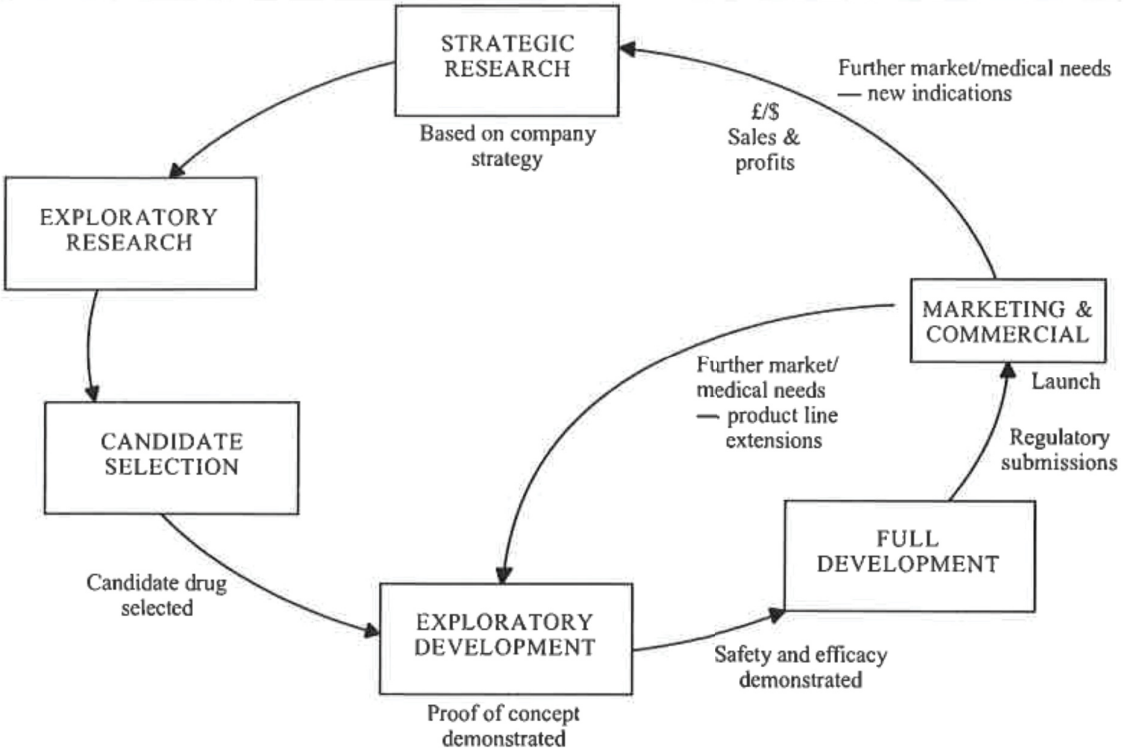
Table 1.1
Major hurdles to successful product registration and sale.

Activity	Requirements
Research	Novel compound (patentable?)
	Novel biological mechanism (patentable?)
	Unmet medical needs
	Potent and selective
Safety	High margin of safety
	Non-toxic (not carcinogenic, tetratogenic, mutagenic, etc.)
Clinical	Tolerable side-effects profile
	Efficacious
	Acceptable duration of action
Drug process	Bulk drug can be synthesised/scaled up
Pharmaceutical	Acceptable formulation/pack (meets customer needs)
	Drug delivery/product performance acceptable
	Stable/acceptable shelf-life
	Clinical trial process robust and can be scaled up
Regulatory	Quality of data/documentation
Manufacturing	Manufacturable
	Able to pass pre-approval inspection
Marketing/commercial	Competitive
	Meets customer needs
	Value for money
	Commercial return

To be successful and competitive, research-based pharmaceutical companies must ensure that new discoveries are frequently brought to the market to generate cash flow. This is required to fund the next generation of compounds to meet the therapeutic needs of patients, and of course, to benefit the shareholders. This cycle of events is sometimes referred to as the "product life cycle" and is further illustrated in Figure 1.1.

The costs of drug discovery and development to bring a New Chemical Entity (NCE) to the market are ever increasing. It is currently estimated that in excess of U.S. $500 million is required to recoup the costs of research, development, manufacturing, distribution, marketing and sales. A significant proportion of this total is for the cost of failures, or in other words, the elimination of unsuccessful compounds. R&D expenditure for an NCE tends to increase substantially as the compound progresses from drug discovery research through the various clinical trial phases of development. The pivotal Phase III patient trials are usually the largest, involving thousands of patients, and hence the most expensive. To reduce development costs,

Figure 1.1 Product life cycle.



some companies selectively screen and eliminate compounds earlier in the drug development process based on results from small-scale, less expensive studies in man and progress fewer, more certain compounds to later clinical phases.

In spite of the high risks and high costs involved, there is still a huge incentive for pharmaceutical companies to seek the financial rewards from successful marketed products, and especially from the phenomenal success of the rare "blockbuster" (reaching sales of >1 billion U.S.$ per year). This can earn the company significant profits to reinvest in research and fund the product development pipeline.

Another factor, the risk of delay to registration and launch, can also have a significant impact on the financial success of a marketed product. McKinsey & Company, a management consultancy, assessed that a product that is 6 months late to market will miss out on one-third of the potential profit over the product's lifetime. In comparison, they found that a development cost overspend of 50 percent would reduce profits by just 3.5 percent, and a 9 percent overspend in production costs reduced profits by 22 percent (McKinsey & Co. 1991). The loss of product revenue is often due to competitor companies being first to market, capturing the market share and dictating the market price, in addition to the loss of effective patent life. Hence, the importance of accelerating and optimising drug discovery and development, and getting to the market first with a new therapeutic class of medicinal product, cannot be underestimated. The second product to market in the same class will usually be compared with the market leader, often unfavourably.

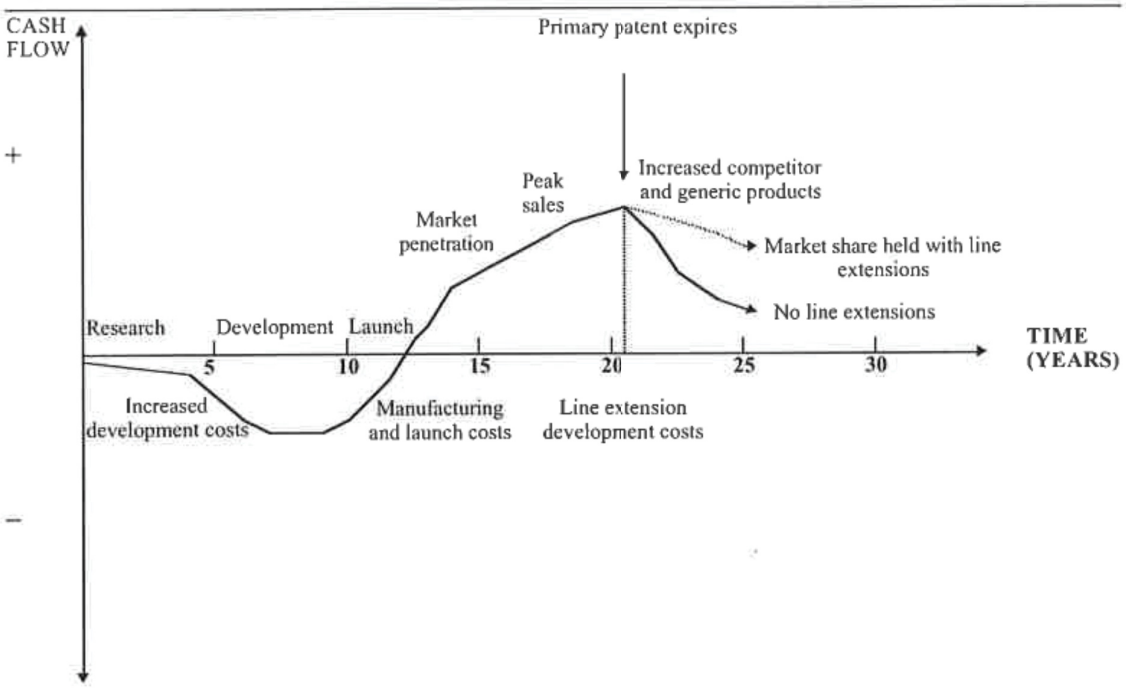
The average time from drug discovery to product launch is currently estimated to take 10 to 12 years. Several factors may have contributed to lengthening development times over the years, including an increase in the preclinical phase to select the candidate drug, and also an increase in the duration of the clinical and regulatory period required for marketing approval. Benchmarking studies show wide gaps between industry average or worst performance compared to what is achievable as best practice performance (Spence 1997). On average, the preclinical phase currently takes 4 to 6 years to complete, whereas the time from candidate drug nomination to regulatory submission takes on average 6 to 8 years, longer for treatments of chronic conditions. Most forward-looking pharmaceutical companies are aiming to reduce these times by re-evaluation and subsequently streamlining the development process, for example, by introducing more effective clinical programmes and more efficient data reporting systems, forward planning and conducting multiple activities in parallel. However, this, in turn, may put formulation development and clinical supplies on the critical path, with pressures to complete these activities in condensed time scales. Suggestions are offered throughout this book on how preformulation, biopharmaceutics and formulation can be conducted in the most efficient way to avoid delays in development times.

Any reduction in the total time-frame of drug discovery to market should improve the company's profitability. In a highly competitive market, product lifetimes are being eroded due to the pace of introduction of competitor products, the rapid introduction of generic products when patents expire and moves to "over-the-counter" (OTC) status. Successful pharmaceutical companies are focusing on strategies for optimum "product life cycle management" to maximise the early growth of the product on the market, sustain peak sales for as long as the product is in patent and delay the post-patent expiry decline for as long as possible. This should maximise the return on investment during a product life cycle to enable the company to recover development costs and make further investments in R&D. Figure 1.2 shows a classic cash flow profile for a new drug product developed and marketed. During development there is a negative cash flow, and it may be some time after launch before sales revenue crosses from loss to profit because of manufacturing, distribution and advertising costs. Profits continue to increase as the market is established to reach peak sales, after which sales decrease, especially after the primary patent expires and generic competition is introduced.

Throughout the life span of a product, it is in a company's interest to ensure the best patent protection in order to achieve the longest possible market exclusivity. Prior to the primary patent expiring (normally for the chemical drug substance), it is imperative to introduce new indications, formulations, manufacturing processes, devices and general technology, which are patent protected, to extend the life of the product and maintain revenue. A patent generally has a term of about 20 years, but as development times are getting longer, there will be a limited duration of protection remaining once the product is marketed (the effective patent life). A comparison of effective patent life for pharmaceutical new chemical entities in various countries around the world shows the same downward trend between the 1960s and the 1980s (Karia et al. 1992; Lis and Walker 1988).

Getting to the market quickly is a major business driving force, but this has to be balanced with the development of a product of the appropriate quality. There is a need to generate sufficient information to enable sound decisions on the selection of a candidate drug for development, as well as to develop dosage forms which are "fit for purpose" at the various stages of development. Anything more is wasting precious resources (people and drug substance), adding unnecessary cost to the programme and, more importantly, extending the development time. Perfect quality should not be the target if good quality is sufficient for the intended purpose. This can only be achieved if there is a clear understanding of the customer requirements.

Figure 1.2 Product life cycle management.



For example, if a simple, non-optimised formulation with a relatively short shelf life is acceptable for Phase I clinical studies, any further optimisation or stability testing might be considered wasteful, unless the data generated can be used later in the development programme.

There can be a significant risk associated with doing a minimum development programme and cutting corners to fast track to market. Post-launch, the cost of a retrospective fix due to poor product/process design and/or development can be extremely high. The additional financial cost from work in product/process redevelopment, manufacturing and validation, technical support, regulatory and sales and marketing (due to a product recall) can easily wipe out the profit from an early launch. This can have several unpleasant knock-on effects; it may affect the market share and the company's relationship with the regulatory authorities, and its credibility with customers (both externally and internally within the company) may be threatened. These factors need to be taken in to account when planning preformulation/formulation studies which can directly influence the progress of a product to market and final product quality.

CURRENT TRENDS IN THE PHARMACEUTICAL INDUSTRY

Increasing competition and threats to the pharmaceutical industry with respect to maintaining continued sales growth and income mean that successful companies going forward will be those which have a portfolio of products capable of showing volume growth. However, to show volume growth innovative new products are required. The cost of drug discovery and development is escalating because there are no easy targets left and the cost of development

and the cost of goods sold is increasing. There have been several mergers and acquisitions of research-based pharmaceutical companies, and increased collaborations and inward licensing of products and technologies, in attempts to acquire new leads, to share costs, to reduce the time to licence and to maintain growth. Unfortunately, mergers and acquisitions also result in streamlining and job losses which improve efficiency and decrease overhead costs at the same time.

There is a changing trend in the nature of the candidate drug emerging from pharmaceutical R&D, from a low molecular weight chemical to a more complex macromolecule (biologicals), which can be a peptide, protein, enzyme, antibody, nucleic acid, genetic material or a multicomponent vaccine. Some of these compounds have been derived from biotechnological processes to produce biotechnological medicinal products that fight infection and disease. The U.S. Food and Drug Administration (FDA) and European Agency for the Evaluation of Medicinal Products (EMEA) have already approved biotechnological medicinal products for anaemia, cystic fibrosis, growth deficiency, hepatitis and transplant rejection. Many more are being developed to treat cancer, human immunodeficiency virus (HIV) infections and acquired immunodeficiency syndrome (AIDS), multiple sclerosis and stroke. A major challenge to the formulator is to develop self-administered formulations to deliver macromolecules such as proteins and polypeptides into the body, for example, by the oral or inhalation route.

More sophisticated drug delivery systems are being developed to overcome the limitations of conventional forms of drug delivery systems (e.g., tablets and intravenous [IV] solutions), to overcome problems of poor drug absorption, the non-compliance of patients and inaccurate targeting of therapeutic agents. One example of an emerging drug delivery technology is the use of low-level electrical energy to assist the transport of drugs across the skin in a process known as electrophoresis. This method could be particularly useful for the delivery of peptides and proteins which are not adequately transported by passive transdermal therapy. The drug absorption rate is very rapid and more controlled compared with passive diffusion across the skin. Another example is the improvement in inhaler technology to ensure a more efficient delivery to the lungs, with minimal drug deposition in the mouth and trachea. The use of a breath-actuated aerosol is designed to co-ordinate drug delivery with the patient's inhalation to achieve this. A third example is the use of bioerodable polymers that can be implanted or injected within the body to administer drugs from a matrix which can be formulated to degrade over a long duration from one day to six months, and do not require retrieval. Some of these specific delivery systems are explained in more detail in later chapters of this book on the various dosage forms.

Futuristic drug delivery systems are being developed which hope to facilitate the transport of a drug with a carrier to its intended destination in the body and then release it there. Liposomes, monoclonal antibodies and modified viruses are being considered to deliver "repair genes" by IV injection to target the respiratory epithelium in the treatment of cystic fibrosis. These novel drug delivery systems not only offer clear medical benefits to the patient but can also be opportunities for commercial exploitation, especially useful if a drug is approaching the end of its patent life.

There are pressures on the pharmaceutical industry which affect the way products are being developed. For example, there is a trend for more comprehensive documentation to demonstrate compliance with current Good Manufacturing Practice (cGMP) and Good Laboratory Practice (GLP) and to demonstrate that systems and procedures have been validated. The trend is for more information required for a regulatory submission, with little flexibility for changes once submitted. Therefore, the pressure is for a company to submit early and develop the product "right first time".

In spite of efforts to harmonise tests, standards and pharmacopoeias, there is still diversity between the major global markets—Europe, the United States and Japan—which have to be taken in to account in the design of preformulation and formulation programmes (Anonymous 1993). This is discussed further in Chapter 5 on product design.

Other pressures facing the pharmaceutical industry are of a political/economical or environmental nature. Some governments are trying to contain healthcare costs by introducing healthcare reforms, which may lead to reduced prices and profit margins for companies, or restricted markets where only certain drugs can be prescribed. Although the beneficial effect of drugs is not questioned in general, the pressure to contain the healthcare costs is acute. Healthcare costs are increasing partly because people are living longer and more treatments are available. This may influence the commercial price that can be obtained for a new product entering the market and, in turn, the "cost of goods (CoG) target". The industry average for the CoG target is 5 to 10 percent of the commercial price with pressure to keep it as low as possible. This may impact on the choice and cost of raw materials, components and packaging for the product and the design and cost of manufacturing the drug and product.

Environmental pressures are to use environmentally friendly materials in products and processes and to accomplish the reduction of waste emissions from manufacturing processes. A good example is the replacement of chlorofluorocarbons (CFCs) propellants in pressurised metered dose inhalers (pMDIs) with hydrofluorocarbons (HFAs). The production of CFCs in developed countries was banned by the Montreal Protocol (an international treaty) apart from "essential uses", such as propellants in pMDIs, to reduce the damage to the earth's ozone layer. However, there is increasing pressure to phase out CFCs altogether. The transition from CFC to HFA products involves a massive reformulation exercise with significant technical challenges and costs for pharmaceutical companies involved in developing pMDIs, as described in Chapter 10 "Inhalation Dosage Forms". However, this can be turned into a commercial opportunity for some companies which have developed patent-protected delivery systems to extend the product life cycle of their CFC pMDI products.

LESSONS LEARNT AND THE WAY FORWARD

To achieve the best chance of a fast and efficient development programme to bring a candidate drug to market, several important messages can be gleaned from projects which have gone well and from companies with consistently good track records.

There are benefits for pharmaceutical development to get involved early with preclinical research during the candidate drug selection phase. This is to move away from an "over-the-wall" hand-over approach of the candidate drug to be developed from "research" to "development". The drug selection criteria will be primarily based on pharmacological properties such as potency, selectivity, duration of action and safety/toxicology assessments. However, if all these factors are satisfactory and similar, there may be an important difference between the pharmaceutical properties of candidate drugs. A candidate drug with preferred pharmaceutical properties, for example, good aqueous solubility, crystalline, nonhygroscopic and good stability, should be selected to minimise the challenges involved in developing a suitable formulation. This is discussed further in Chapter 2.

Another important factor is good long-term planning, ideally from candidate drug nomination to launch, with consideration for the safety, clinical, pharmaceutical development, manufacturing operations and regulatory strategies involved to develop the product. There is a need for one central, integrated, company project plan that has been agreed on by all parties

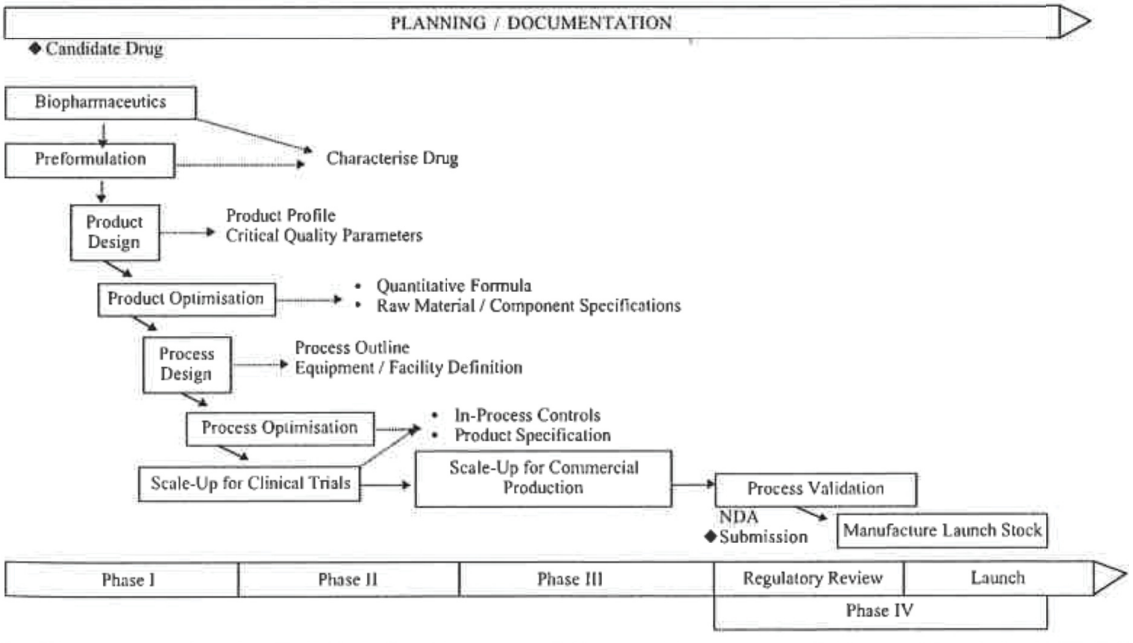
with a vested interest in the project. Needless to say, the plan should contain details of activities, timings, responsibilities, milestones, reviews and decision points. Reviews and decision points are required at the end of a distinct activity to ensure that the project is still meeting its objectives and should progress to the next stage of development. However, these reviews should not cause any delays to the programme, rather, they should ratify what is already progressing. The traditional sequential phases of product development (see Chapter 2) must be overlapped to accelerate the product to market. In reality, plans will inevitably change with time; they should be "living" documents which are reviewed and updated at regular intervals and then communicated to all parties. There may be several more detailed, lower-level plans focusing on departmental activities, e.g., for pharmaceutical development, but these plans must be linked to the top level central project plan.

Forward planning should provide the opportunity for a well thought out and efficient approach to product development, identifying requirements up front so as to avoid too much deliberation and backtracking along the way. It also should provide a visible communication tool.

Good planning is supported by adopting a systematic and structured approach to product development. The development process can be broken down into several key defined stages—product design, process design, product optimisation, process optimisation, scale-up and so on. Each stage will have inputs and outputs as shown in Figure 1.3, a simplified framework for product development. The appropriate definition and requirements at each stage are described in Chapters 5 and 8 of this text.

As product development can take several years to complete, it is important to have an effective document management system in place to record the work. The primary reference source for recording experimental work will usually be a laboratory notebook. The work should be checked, dated and counter-signed to satisfy GLP and intellectual property requirements. Experimental protocols are sometimes useful for defining programmes of work,

Figure 1.3 Framework for product development.



explaining the rationale for the studies and defining the acceptance criteria. When the studies are completed, the results can be reported with reference to the protocol and acceptance criteria. Laboratory notebooks are referenced in the protocols and reports so that the raw data can be retrieved in the event of an audit.

At the completion of key stages of the work, summary reports can be written, referencing all other protocols and reports relevant to that stage and highlighting the major recommendations and conclusions. In this way, a product development document file can be built up for transfer of information and technology, including the development history and rationale for progression. The file will also be vital for data retrieval in the event of a regulatory inspection.

Finally, successful product development is often associated with good teamwork. The process is multidisciplinary, relying on people with different specialist skills working together to make it happen. This is particularly important at the key interfaces such as preclinical research with pharmaceutical development and pharmaceutical development with manufacturing operations at the final production site. It is therefore useful to have representation on the project teams from all the key specialist functions to ensure buy-in to the plans, strategies and decisions and to have a good project management system in place.

SCOPE OF THE BOOK

This book is structured in a logical order to cover the various stages of drug development from candidate drug selection to development of the intended commercial dosage form.

In Chapter 2, the key stages of the R&D process are explained in some detail, with the outputs expected from each stage, to afford an appreciation of the entire process. The remainder of the book concentrates on candidate drug selection for development and development of the commercial dosage form where preformulation, biopharmaceutics and formulation play a vital role. Initial emphasis is on candidate drug selection and the importance of preformulation, formulation and biopharmaceutics input at this stage. Traditionally, not all pharmaceutical companies operate in this way, and the result from experience is often that pharmaceutical development has to accept whatever candidate drug comes out of research and address any unforeseen difficulties during development. The disadvantages of this approach, and the opportunities and benefits of pharmaceutical input to the candidate selection process, are clearly explained in the early chapters.

Available drug substance for preformulation and biopharmaceutics studies at the candidate drug selection stage can be a major challenge. Chapter 3 describes the preformulation studies that can be undertaken to maximise the information gained from small amounts of drug substance in order to select the preferred candidate drug for development. Various modern preformulation techniques which use minimal amounts of drug are described to evaluate the physicochemical properties of compounds, salts and polymorphs.

Chapter 4 describes the importance of drug delivery and biopharmaceutical factors in the candidate drug selection phase. Consideration is given to the intended route of administration and what predictions can be made and useful information gained from biopharmaceutical assessment of the candidate drug.

Following candidate selection, usually one candidate drug is nominated for development. The importance of establishing the product design attributes are discussed in Chapter 5. The value of this exercise is often underestimated in the rush to develop products quickly. However, the quality of the product design can often influence the success of developing a commercially viable product with a desired product profile in a timely manner to market.

Chapters 6 and 7 focus on preformulation and biopharmaceutics, respectively, as an aid to product design. The emphasis is on generating the appropriate data to characterise the candidate drug and aid product design and development. The objective at this stage is to determine the physicochemical properties of the candidate drug which are considered important in the development of a stable, effective and safe formulation. Limited availability of drug substance, speed and careful consideration of the programme of work depending on the intended dosage form and route are all considered here and illustrated with the aid of worked examples. Modern instrumental techniques and personal computer (PC)–based "expert systems" are discussed as useful tools.

To develop a product from inception to market, the product and process have to be optimised and the process scaled up and transferred to commercial production. Definitions and descriptions of the requirements for all these stages of development are discussed in Chapter 8, although the major discussion is on the preformulation/formulation input to product optimisation. The many factors which a formulator should consider in the selection of pharmaceutical excipients and packaging are discussed. Useful sources of information and techniques for selection such as expert systems and experimental design tools are included.

Drugs are generally administered via the mouth, eyes, nose, skin, or by inhalation or injection, and so these routes are covered in more detail in separate chapters of this book. Special considerations and issues for the formulation development of each route and type of dosage form are discussed, based on the considerable relevant experience of the various contributors.

REFERENCES

Anonymous. (1993). Global differences in registration requirements. *Pharmaceut. J.* 251:610–611.

Karia, R., Y. Lis, and S. R. Walker. 1992. The erosion of effective patent life—An international comparison. In *Medicines, regulation, research and risk* 2nd ed., edited by J. P. Griffin. Belfast: Queen's University Press, pp. 287–301.

Lis. Y., and S. R. Walker. 1988. Pharmaceutical patent term erosion—A comparison of the UK, USA and Federal Republic of Germany (FRG). *Pharmaceut. J.* 240:176–180.

McKinsey & Co. 1991. In *Managing product creation, a management overview*, edited by P. Burall. London: The Design Council for the UK Department of Trade and Industry.

Spence, C., ed. 1997. *The pharmaceutical R & D compendium: CMR International/SCRIP's guide to trends in R & D.* Richmond, Survey, UK: CMR International/SCRIP Publication.

Tucker, D. 1984. *The world health market, the future of the pharmaceutical industry.* Bücher, Germany: Euromonitor Publications Ltd.

Wells, J. I. 1988. *Pharmaceutical preformulation. The physicochemical properties of drug substances.* Chichester, UK: Ellis Horwood, and New York: Wiley.

About This Book

Successful pharmaceutical companies must balance [illegible]rket with development of products of high quality. Striking the corre[illegible]unt when planning preformulation/formulation studies, studies that dir[illegible]ducts to market. In addition, consideration must be given to regulatory requirements such as compliance with GLP and GMP, validation of systems and procedures, and comprehensive documentation. In *Pharmaceutical Preformulation and Formulation: A Practical Guide from Candidate Drug Selection to Commercial Dosage Form,* Mark Gibson has answered the need for a practical reference source and pragmatic guide on what studies need to be undertaken, for what reasons, and at what key stages of the drug development process. In addition to preformulation, his book covers biopharmaceutics, drug delivery, formulation, and process development aspects of product development.

Ten contributing authors have shared their experience and expertise in significant chapters divided into three useful sections: *Aiding Candidate Drug Selection, Early Drug Development,* and *From Product Design to Commercial Dosage Form.* This book should be especially useful to scientists, technicians, and managers in the pharmaceutical, medical device, and biopharmaceutical industries.

What You'll Learn

- early preformulation/formulation and biopharmaceutical information to aid in selection of the most suitable compound for development
- prediction of potential problems for further formulation development
- best use of drug substance for preformulation studies to aid candidate drug selection
- generation of appropriate preformulation/formulation data to characterize the candidate drug and aid product design and development
- instrumental techniques that use minimal amounts of drug substance to gain useful information
- PC based Expert systems to aid product design
- various dosage forms
- routes of drug administration
- pros and cons of contracting out development

About the Editor

Mark Gibson, BPharm, PhD, CChem, MRSC, MRPharmS, is responsible for parenteral and oral solid dosage form development at AstraZeneca R&D Charnwood, a division of AstraZeneca, in the UK. His experience includes formulation and preformulation development, both as a bench scientist and a manager, at Cyanamid (Lederle), Fisons Pharmaceuticals, Astra Pharmaceuticals, and AstraZeneca. He has worked on a variety of dosage forms and routes of delivery, including inhalation, oral, nasal, ophthalmic, parenteral, and transdermal, some of which have resulted in patents and marketable products. Dr. Gibson is a member of the UK Academy of Pharmaceutical Sciences, the Parenteral Society, and the Aerosol Society.

ISBN: 1-57491-120-1

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