

Commercializing Successful Biomedical Technologies

Successful product design and development requires the ability to take a concept and translate the technology into useful, patentable, commercial products.

For scientists and engineers, this book demystifies the commercialization process, guiding the reader through each practical stage, describing key issues including market analysis, product development, intellectual property and regulatory constraints.

- A robust product development plan is provided through a step-by-step model, from concept to regulated, commercially viable product.
- Highlights key business issues taking into account critical business aspects, such as budgetary impact, time constraints and quality control in the development cycle.
- Case studies and contributions from industry are included for a practical perspective.
- Learning points and exercises re-enforce the most important concepts and strengthens understanding.

Written in a concise manner, this book will be the indispensable guide for professionals and entrepreneurs in biomedical technology development. With the increasing need for students to be fluent in such business skills, this book is an ideal accompaniment to a capstone design course in engineering and biotechnology.

Foreword written by **Frank L. Douglas Ph.D., M.D.** *Former Executive Vice President, member of Board of Management and Chief Scientific Officer of Aventis Pharmaceutical, Former Professor of the Practice and Executive Director of the MIT Center for Biomedical Innovation and Partner at Pure Tech Ventures.*

Shreefal S Mehta is Clinical Associate Professor of Biotechnology Management and Biomedical Engineering, Rensselaer Polytechnic Institute and Vice President, Business and Corporate Development, Cytopia Inc. He was CEO and co-founder of Myomatrix Therapeutics, a cardiovascular pharmaceutical startup and recipient of the “40 under 40” award for rising business leaders in New York. He has been a reviewer for the NSF Biotechnology Commercialization SBIR Review panel.

Commercializing Successful Biomedical Technologies

Basic Principles for the Development of Drugs,
Diagnostics, and Devices

SHREEFAL MEHTA

Vice President of Business and Corporate Development, Cytopia



CAMBRIDGE UNIVERSITY PRESS

Cambridge, New York, Melbourne, Madrid, Cape Town, Singapore, São Paulo, Delhi

Cambridge University Press

The Edinburgh Building, Cambridge CB2 8RU, UK

Published in the United States of America by Cambridge University Press, New York

www.cambridge.org

Information on this title: www.cambridge.org/9780521870986

© S. S. Mehta 2008

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2008

Printed in the United Kingdom at the University Press, Cambridge

A catalog record for this publication is available from the British Library

ISBN 978-0-521-87098-6 hardback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

To Gauri, whose continuing support and encouragement, whose patience and willingness to shoulder my share of parenting when necessary, and more, made the completion of this book possible. Without your help, there would have been no book.

Contents

	<i>Foreword by F. L. Douglas</i>	<i>page xv</i>
	<i>Preface</i>	<i>xix</i>
	<i>Acknowledgements</i>	<i>xxii</i>
1	The biomedical drug, diagnostic, and devices industries and their markets	1
	1.1 The healthcare industry	1
	1.2 Biomedical technology – definition and scope; applications	2
	1.3 Drugs and biotechnology – definition and scope	4
	1.4 Devices and diagnostics – definition and scope	8
	1.4.1 Medical devices industry	8
	1.4.2 Diagnostics – IVD industry	9
	1.5 Industry analysis	10
	1.6 Biomedical industry clusters	11
	1.6.1 Biopharmaceutical and biotechnology concentration in clusters	11
	1.6.2 Biomedical device clusters	13
	1.7 Competitive analysis of an industry or sector with Porter’s five forces model	13
	1.7.1 Competitiveness summary for the pharmaceutical industry	14
	1.7.2 Competitiveness summary for the biomedical devices industry	15
	1.7.3 Competitiveness summary for the diagnostics market	15
	1.8 Industrial value chains	17
	1.8.1 Drug development process	20
	1.8.2 Biomedical device and diagnostic development process	23
	1.9 Technology trends in biomedical device and drug development	24
	1.9.1 Drug development technology trends	24
	1.9.2 Medical device and diagnostics technology trends	27
	1.9.3 Emerging technologies and materials in the nucleic acid diagnostics field	27
	1.10 Convergence of technologies in biotechnology	29
	1.11 Summary	31
	Appendix 1.1 Industry classification system for government and other databases	33

2	Markets of interest and market research steps	36
2.1	Introduction	36
2.2	General market research methodology	37
2.2.1	Reports, projections, and historical data	37
2.2.2	Experimental	37
2.2.3	Observational	38
2.2.4	Survey	39
2.2.5	Primary sources of information in biomedical market research	39
2.2.6	Secondary sources of information	40
2.3	Sizing and segmenting the markets (a stepwise approach)	40
2.3.1	Market size segmented by application	40
2.3.2	Market size segmented by geography for drugs, devices, and IVD	41
2.3.3	How big is the market for my technology or innovation?	42
2.4	Drivers and hurdles	44
2.4.1	Drivers	45
2.4.2	Hurdles	46
2.5	The referral chain – developing market context and understanding customer needs	47
2.5.1	Market context – insight into biology or disease pathology	47
2.5.2	Market context – the referral chain	48
2.5.3	What competitive or alternate products exist?	50
2.5.4	Defining the end user	50
2.5.5	Defining the indication	53
2.6	Market research in the context of medical device design and development	60
3	Intellectual property, licensing, and business models	63
3.1	Types of intellectual property	63
3.2	Patents and patent rights	64
3.2.1	Patent rights	64
3.3	Types of patent	65
3.3.1	Utility patents	65
3.3.2	Design patents	66
3.3.3	Plant patents	66
3.4	What can and cannot be patented?	66
3.4.1	What cannot be patented (from the US PTO website)	66
3.4.2	Can living things be patented?	66
3.4.3	What type of invention or discovery is patentable?	68
3.5	Protecting intellectual property by filing a patent	68
3.5.1	How long do issued patents last in the USA?	68
3.5.2	How much does it cost to get a patent?	68

3.5.3	Considerations before filing a patent	69
3.5.4	Steps to prepare a patent filing	70
3.5.5	What is in a patent? How to read an issued patent	70
3.5.6	Provisional patent application	73
3.5.7	Priority date and publicizing inventions	73
3.5.8	International patent filings and the Patent Cooperation Treaty (PCT) process	76
3.5.9	Patent prosecution process	76
3.5.10	Rough estimate of patent costs for project budgets	78
3.6	Patent infringement and freedom to operate	78
3.6.1	Patent infringement and protecting your rights	78
3.6.2	“Freedom to practice” or “freedom to operate”	80
3.7	Trademarks	82
3.7.1	Why register your trademark?	83
3.7.2	Filing a trademark with the US PTO	83
3.7.3	International filing of trademarks	84
3.8	Copyrights	84
3.9	Trade secrets	84
3.10	Intellectual property commercialization and technology transfer	85
3.10.1	Commercial use of intellectual property	85
3.10.2	Technology transfer in academic research institutions	86
3.10.3	The Bayh–Dole Act	86
3.11	Licensing	88
3.11.1	Key non-financial terms of license agreements	88
3.11.2	Financial terms in a license	90
3.11.3	“Boilerplate” clauses in the license agreement	95
3.12	Biotech business models and IP management strategies	95
3.12.1	What is a business model?	97
3.12.2	Practical note on business models for drug, device, and diagnostic innovator companies	98
3.12.3	Emergent dominant business models among biotechnology (drug) companies	99
3.13	Summary	101
4	New product development (NPD)	104
4.1	Why have a new product development (NPD) process – just get it done!	105
4.2	Planning and preparing an NPD process for biomedical technologies (drugs, devices, and diagnostics)	106
4.2.1	The project proposal document	106
4.2.2	Strategy and competency of the company and goal of the project	107
4.2.3	Product life cycle planning	108

4.2.4	Market research	108
4.2.5	Identify key unknowns and risks	109
4.2.6	Build a milestone-based plan for product development	109
4.2.7	Specific risks known to occur frequently during the development of biomedical products	109
4.3	Kill the project early or try some more?	110
4.3.1	Early failure is better than late failure in biomedical product development	110
4.3.2	When to kill a project	113
4.4	Uncertainty-based view of product development processes	115
4.5	Stage-gate approach	118
4.5.1	Stages and gates	118
4.5.2	How to configure a stage-gate process plan for my biomedical product	119
4.5.3	Unique features of biomedical development	119
4.6	Ethical requirements in biomedical product development	120
4.6.1	Institutional Animal Care and Use Committee (IACUC)	121
4.6.2	Institutional Review Board (IRB)	121
4.7	Define the product and process – indications and endpoints	121
4.8	Typical drug development process	124
4.8.1	Discovery and pre-clinical testing	124
4.8.2	Distinctions in pre-clinical development of biotechnology drugs (large molecule biologics)	132
4.8.3	Drug candidate clinical testing to market approval	132
4.8.4	Manufacturing, marketing, sales, and reimbursement	137
4.8.5	Keeping a record for the FDA	138
4.8.6	General stage-gate process for new drug development	138
4.9	Typical diagnostics development process	138
4.10	Typical device development process	144
4.10.1	Discovery, feasibility, and optimization – design and pre-clinical testing	145
4.10.2	Special considerations for device clinical trial design	150
4.10.3	Device manufacturing	153
4.10.4	Keeping records for the FDA	154
4.10.5	Device development stage-gate process	154
4.11	A few general notes on biomedical product development	154
4.12	Project management	156
4.12.1	Project management tools – Gantt charts and critical path	156
4.12.2	Team composition	158
4.12.3	Team management in a matrix environment	159
4.13	Formulating budgets	160
4.14	How to get your project funded in a larger organization	162
4.14.1	The art of persuasion	162
4.14.2	Business case	162

4.14.3	Valuation decision – net present value (NPV)	162
4.14.4	Stakeholders	164
4.15	Outsourcing product development	166
4.16	Summary of pre-clinical certifications and laboratory regulations	168
4.17	Summary	170
5	The regulated market: gateway through the FDA	172
5.1	The FDA: its role and significance for biomedical product development	172
5.1.1	Introduction and history	172
5.1.2	Role of the FDA and significance for product development	174
5.2	Organization and scope of the FDA	174
5.2.1	Divisions of the FDA	174
5.2.2	What the FDA does not regulate	175
5.2.3	What does the FDA regulate?	176
5.2.4	Friends not foe	176
5.2.5	Science rules – most of the time	178
5.2.6	International harmonization	179
5.3	Regulatory pathways for drugs (biologicals or synthetic chemicals)	179
5.3.1	Pre-clinical studies regulated by the FDA	181
5.3.2	Filing an investigational new drug application (IND; or form FDA 1571)	183
5.3.3	Working with the FDA in formally arranged meetings	185
5.3.4	New drug application submission	185
5.3.5	Clinical trials done in foreign countries	187
5.3.6	Drug master files	187
5.3.7	Regulatory pathway for copies of already approved drugs (generic or biosimilar drugs)	188
5.3.8	Regulatory pathway for OTC (over-the-counter) drugs	188
5.3.9	Post-market clinical studies (Phase IV) and safety surveillance by FDA	189
5.3.10	Schematics of IND, NDA, and ANDA review processes	190
5.3.11	Speeding up access to drugs	192
5.3.12	Market exclusivity for new drugs and the Hatch Waxman Act 1984	195
5.3.13	Drugs: helpful FDA websites and the Electronic Orange Book	195
5.4	Orphan drugs	196
5.5	Devices: regulatory pathways and NPD considerations	196
5.5.1	Step 1: determine the jurisdiction of the FDA center – is it a device?	197
5.5.2	Step 2: classify the medical device – what controls and regulations apply?	198

5.5.3	Step 3: determine marketing application required to be submitted	199
5.5.4	Working with the FDA in formal meetings	200
5.5.5	General controls and exempt devices	201
5.5.6	Pre-clinical considerations – special controls and QSR for Class II and III devices	201
5.5.7	The use of master files (MAF)	204
5.5.8	510(k) submission type and content	204
5.5.9	PMA submission content	206
5.5.10	Types of PMA submission	206
5.5.11	Humanitarian use devices (HUDs)	207
5.6	Diagnostics: regulatory pathways and NPD considerations	207
5.6.1	In vitro devices – regulatory clearance or approval steps to market	209
5.6.2	Pre-clinical and clinical considerations for in vitro devices	210
5.6.3	Clinical Laboratory Improvement Amendments program	212
5.6.4	Analyte-specific reagents or “home-brew” tests	212
5.7	Emerging regulatory guidelines for co-development of pharmacogenomic diagnostic tests and drugs	215
5.8	Combination products, genetic material, and tissues	217
5.8.1	Cellular, tissue, and gene therapies	219
5.9	Summary	224
6	Manufacturing	226
6.1	Introduction	226
6.2	Technology transfer to manufacturing operations (drugs, devices, and diagnostics)	227
6.3	Regulatory compliance in manufacturing	228
6.3.1	Current good manufacturing practices	228
6.3.2	Validation	230
6.3.3	Drug manufacture regulations – control systems reviewed for compliance	230
6.3.4	Device and diagnostic manufacture regulations – control systems reviewed for compliance	231
6.4	Manufacturing standards	233
6.4.1	What are standards and what is their purpose?	233
6.4.2	Who sets standards?	235
6.4.3	Which of the thousands of standards apply to my product?	236
6.4.4	What are “clean room” standards?	236
6.5	Manufacturing in drug development	237
6.5.1	Process validation before approval	240
6.5.2	Bulk drug scale-up and production stages	242
6.5.3	Commercial manufacturing planning	243

6.6	Manufacturing in devices and diagnostics	245
6.6.1	Design for manufacturability	247
6.6.2	Design for assembly	247
6.7	Manufacturing in diagnostics	247
6.7.1	Labeling requirements for in vitro devices	250
6.8	Buy or build	250
6.9	Summary	252
Appendix 6.1	Compliance to pharmaceutical GMP	254
Appendix 6.2	Compliance to device and diagnostic GMP	258
7	Reimbursement, marketing, sales, and product liability	264
7.1	Introduction	264
7.2	Healthcare system in the USA	265
7.2.1	Economic impact of the healthcare system	265
7.2.2	Insurance coverage of the US population	265
7.2.3	Who pays for the national healthcare costs?	266
7.3	Flow of payments and distribution models for products and services	269
7.4	Distribution and payment flow for biomedical product types	271
7.4.1	Drugs and biologics: product payment and distribution model	271
7.4.2	Devices and diagnostics: product payment and distribution model	273
7.5	Components of the reimbursement process	274
7.5.1	Coverage	276
7.5.2	Coding	282
7.5.3	Payment	284
7.6	Reimbursement planning activities	291
7.7	Reimbursement path for self-administered drugs (mostly pills)	292
7.8	Reimbursement path for devices and infused drugs	293
7.8.1	Reimbursement path for physician-administered drugs (continued)	294
7.8.2	Reimbursement path for devices (continued)	296
7.9	Reimbursement pathway for in vitro diagnostics (IVDs)	302
7.10	Major differences among selected national healthcare and reimbursement systems	304
7.11	Marketing	305
7.12	Sales	307
7.13	Product liability	309
Appendix 7.1	Technology assessment center for coverage determination	313
	<i>Glossary and acronyms</i>	317
	<i>Index</i>	330

Foreword

The deciphering of the human genome at the dawn of our twenty-first century not only fueled expectation of an increase in speed of developing therapies for many diseases but also exploded some cherished myths. Among the myths exploded was the belief that there were about 100 000 genes in the human genome and that this would lead to thousands of new ‘targets’ (receptors, enzymes, transporters, ion channels, etc.) for the discovery of new drugs. Although still somewhat in question, the number of genes in the human genome is felt to be about 30 000, thus dampening considerably some of the initial euphoria over the anticipated results of this outstanding achievement: the deciphering of the human genome. Another disappointing projection is that the number of druggable targets will only increase some threefold, from about 550 to 1500. Nonetheless, this incredible achievement, enabled by many technologies associated with genome sequencing, has fueled additional technologies, such as proteomics and metabolomics, for the innovation of new drugs and diagnostics.

The dawn of this century has also seen an increase in awareness of the importance of unwanted side effects in marketed drugs and safety issues in device usage. This debate has not only captured the attention of the public, as some widely used drugs, such as Vioxx and Pergolide, have been removed from the market, but also that of the Congress. Members of Congress have questioned whether there should be an agency separate from the Food and Drug Administration (FDA) to assess and monitor the safety of marketed drugs and devices.

In addition to the discussion of benefit and risk of new therapies, the cost of drugs is an increasingly popular topic of debate, along with the overall rapid rise of healthcare costs. The cost for major medical coverage has increased 124 percent above the consumer price index (CPI) every year since 1957. Meanwhile, the fully loaded cost of bringing a new drug to the market is over a billion dollars and only about one third of these drugs make more than \$300 000 in sales per year.

Another challenge facing the industry, as the first decade of the twenty-first century ends, is the number of innovative drugs that will lose patent status and be converted to generics. Although this is good news for the consumer, this will be a challenge for the companies who innovated many of these drugs. For example, between 2004 and 2012, the top 15 pharmaceutical companies will see 95 of their drugs converted to generics. Thus in this first decade, these companies will lose billions of dollars in revenues.

It should be noted that manufacturing in devices and drugs has also had its challenges. Manufacturing problems at Chiron led to a potential shortage of flu vaccines in 2004 and manufacturing problems at Schering Plough led to significant loss of sales for their introduction of Clarinex. In fact, the FDA has had only modest success with their Process and Analytical Technology (PAT) initiative in their attempts to improve good manufacturing processes in the companies. Thirty-two serious Class I device recalls in the first six months of 2007 and 56 class I recalls in all of 2006 show that quality assurance and other manufacturing issues in the device industry continue. Thus, manufacturing remains an area for significant improvement and cost reduction in the industry.

Where then are the opportunities?

The first two decades of the twenty-first century will undoubtedly see the fulfillment of the hopes that genomic-based technologies, predictive modeling, automation, and miniaturization will revolutionize the way drugs are discovered, manufactured, and marketed. Two streams of importance will be the ability to identify that subset of patients that will best respond to a therapy and those patients who are likely to experience unwanted effects from that therapy. This will be the coming of age of “stratified medicine.” Presently, Herceptin, for the treatment of a subset of breast cancers, is the best example. In this example, patients whose breast cancer is found to have HER2/neu receptors respond better to a regimen including Herceptin than to other regimens. Thus the diagnosis of the type of cancer and best therapy for that person are linked by a diagnostic. To be sure, not every therapy will lend itself to this unique constellation of diagnostic enabling therapy, as it is clear that at least three specific criteria will be necessary for this to occur. These criteria include the presence of: differential biological mechanisms, many treatment options, and a biological marker or diagnostic. The biological marker might be genomic-based, clinical observation, or imaging (M. R. Trusheim, E. R. Berndt, F. L. Douglas; Strategic and economic implications of stratified medicine, *Nature Reviews Drug Discovery*, April, 2007).

Another opportunity will be the combination of devices and therapy. A good example of this is the drug-eluting stent for the treatment of occluded coronary arteries. Other applications wait in areas such as diabetes, with the measurement of glucose accompanied by the release of the appropriate amount of insulin from an indwelling insulin reservoir. Other examples exist in cardiology and rheumatology, where measurement of arrhythmia or acute changes in an analyte by indwelling devices can lead to an appropriate release of drug to normalize the condition.

When stratified medicine becomes a standard part of the approach to health-care, changes in the manner of commercialization will occur. It is quite likely that new commercialization paradigms that focus on specialists as opposed to the general practitioners will be associated with this approach. The supply chain issues will also be affected and perhaps there will be more opportunities for “just-in-time”

type approaches in the biopharmaceutical industry. The PAT initiative of the FDA may very well benefit this area.

A final area of progress will be in organizations and this is an arena where Dr Mehta's book will make a major contribution. Because of the complexity and the long times (8–15 years) involved with bringing a biomedical product (drugs, novel devices) from idea to market, few employees enter the industry with an appreciation of the pre-clinical, clinical, manufacturing, commercial and regulatory issues, and expertise needed to achieve this noble task of making novel medicines and devices accessible to patients. Dr Mehta's book not only introduces the reader to the nomenclature and issues but, through problem discussions, he gives the reader (student or industry employee) a sense of the complexity, the creativity as well as the regulatory requirements that must be satisfied to achieve the task. This book should improve the public's understanding of the challenge of innovating devices and drugs and thus improve the dialogue of benefit and risk decisions associated with the approval and marketing of devices and drugs.

Frank L Douglas Ph.D., M.D.

Former Executive Vice President, member of Board of Management and Chief Scientific Officer of Aventis Pharmaceutical, Former Professor of the Practice and Executive Director of the MIT Center for Biomedical Innovation and Partner at Pure Tech Ventures.

Preface

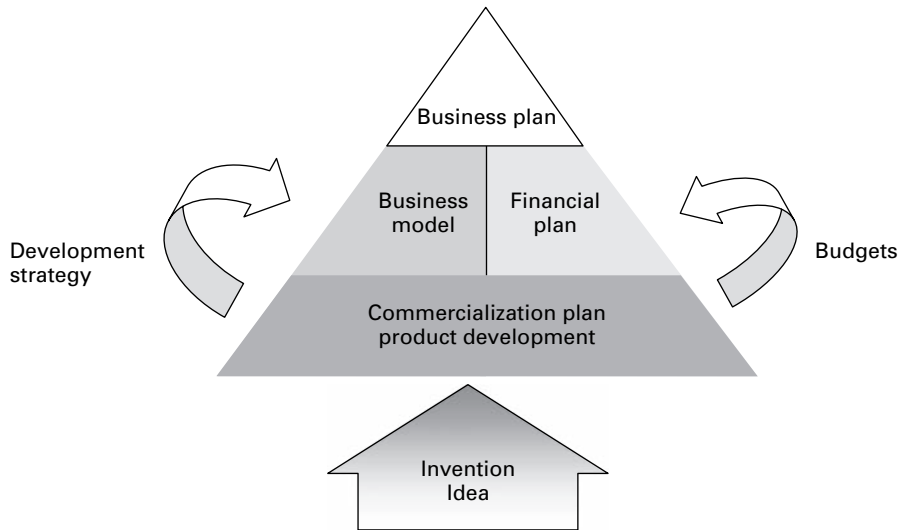
This book will help readers draw a roadmap of the process of taking a biomedical invention and creating a product that can pass regulatory approval to be successfully commercialized. The regulated products included in this context are drugs (both small molecules and biologics), medical devices, diagnostics, and their combination products, as defined by the Food and Drug Administration (FDA) – the regulatory agency that is responsible for overseeing the world’s single largest healthcare market, the United States. The term “biomedical technologies” refers to the collective technologies underlying these FDA-regulated products: biotechnology, various engineering technologies, chemistry and materials science, etc.

The book highlights key issues that might help improve chances of success through the complete commercialization process for biomedical technologies and products. This text started as an expansion of a series of lectures given to students at the Lally School of Management and Technology, Rensselaer Polytechnic Institute in Troy, NY as part of a class called “Commercializing biomedical technology.” However, going beyond the classroom in writing this book, information has been taken from many sources and experienced people from industry have contributed to add current and practical information to various segments of the book.

This book could be used to bring science and engineering students together with business and law students, and show them the benefits of approaching this complex process as a team. Many of these students have found the information useful in job interviews and in planning careers in the biotech industry and its service sectors.

This book has a practical perspective, so that current scientists, engineers and managers in the industry can apply these concepts, issues, and exercises within the context of their job functions in the industry. What’s more, aspiring entrepreneurs may seek to apply these concepts to their invention or idea; walking through all the steps and exercises to create a sound commercialization plan that can form the basis for a business plan for a new venture (see figure).

Business models and financial plans vary with the economic or personal context and the goals of the founders. However, any business model, to be successful, must come from an understanding of the complete commercialization path for the regulated product. The linear roadmap shows the components that must be assessed to build a sound commercialization plan, but the processes are all carried out in parallel, with shifting emphasis on each component as one proceeds down the plan. The sequence of components is mirrored in the sequence of chapters in the



First you have to understand how your idea will be developed into a product and reach the paying customers; then you can choose one of many successful business models in the biomedical industry and prepare a business or financial plan to execute that development strategy.

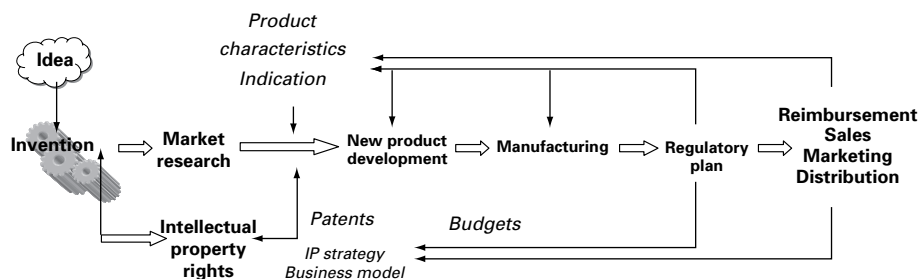
Components of a product commercialization plan and roadmap

Plan	Position	Patent	Product	Pass!	Production	Profits
Industry context	Market research	Intellectual property rights	New product development (NPD)	Regulatory plan	Manufacture	Reimbursement
Technology positioning and strategy, corporate portfolio strategy, industrial value chain context	Market need, Specific indication of interest, market size and segments, product characteristics	Intellectual property management and licensing strategy, Patent content for market protection, Business models	Stage gate new product testing and development plan, budget, Gantt chart	Regulatory strategy – working with FDA towards approval	Production planning	Coverage, Coding, Payment, Distribution, Marketing and sales planning
↓	↓	↓	↑	↓	↓	↓

Roadmap to create a commercialization plan. The linear stages shown here reflect the layout of the book.

book. The arrows below the components in the roadmap illustrate the fact that all these components must be kept in mind to achieve a successful commercial and product development plan.

The process of doing science and also the process of building commercial entities can be represented as a linear thought process, but the practice of both is a



Successful development of new biomedical products for a competitive and regulated marketplace requires a full and thorough understanding of specific issues in the full value chain, discussed in the book. As feedback from various areas is defined for the specific product concept, the commercialization and product development plan will be revised (indicated by thinner feedback arrows above).

path-dependent, iterative process, where learning and understanding grow by doing each experiment or building each step of a commercialization plan. The schematic (above) illustrates, with arrows, the process of feedback between the various components of a commercialization process. As an example, the regulatory process influences the product development plan and also defines the markets accessed by the product. Likewise, access to intellectual property rights influences the direction of development and access to specific markets. Thus, iterative feedback from evaluating the specific regulatory pathways or intellectual property rights might require reconfiguration of the product characteristics or might require choosing a different application from that conceived during original invention.

The process for planning new product development might, for instance, follow the steps:

Idea – invention – market research – intellectual property search – define product and indications of interest – plan the key product development steps – check on regulatory strategy – revise product development plan and characteristics – check on reimbursement strategy – revise product characteristics and product development plan.

The result will be a comprehensive product development and commercialization plan with a timeline and budget. The exercises at the end of the chapters will help guide the reader through these steps.

While the original multidisciplinary (scientists, engineers, management, and other humanities students) course continues as a graduate-level course, much of the developed material has been incorporated into the Biomedical Engineering undergraduate capstone design course at Rensselaer Polytechnic Institute (RPI) as part of the core curriculum, hopefully creating a more conscious and self-aware breed of product development scientist and engineer.

Finally, it is my hope that better thinking and planning in the development of regulated products will help improve the efficiency, success, and quality of biomedical technology commercialization, increasing the number of innovative products that can be delivered to help people.

Acknowledgements

The contributions and suggestions of friends and colleagues who shared their time, their insights from years of industry experience, their editorial suggestions, and specific case studies, have significantly improved this book. I would particularly like to recognize the formative early discussions and exchanges with my colleague Dr Jan Stegemann during the creation of the eponymous class that we co-taught at Rensselaer Polytechnic Institute (RPI).

Contributors and reviewers

Jim Greenwood, President of Biotechnology Industry Organization, USA
Christoph Hergersberg, Global Head of Bioscience Technology, GE
Mark Leahy, President of Medical Device Manufacturers Association, USA
Andrew Marshall, Editor, *Nature Biotechnology*
Parashar Patel, Vice President of Health Economics and Reimbursement,
Boston Scientific; and past Deputy Director of Hospital and Ambulatory
Payment Group, Centers for Medicare and Medicaid Services
Kim Popovits, Chief Operating Officer and President, Genomic Health
Tony Rao, Principal, Stantec
Dan Recinella, Vice President of Product Development, Angiodynamics Inc.
Phil Roberts, Head of Process Development, Nektar Therapeutics
Lawrence Roth, Vice President of Product and Business Development,
Percardia Inc.
Randall Rupp, Sr., Vice President of Manufacturing, Regeneron
Robert Schaffer, Partner, Darby and Darby PC
Jayson Slotnick, Director of Medicare Reimbursement and Economic Policy at
the Biotechnology Industry Organization (BIO)
Jo Ellen Slurzberg, Vice President of Reimbursement and Health Policy,
Almyra, Inc. and Chair of Medical Device Manufacturers Association
Reimbursement Task Force
Mitchell Sugarman (and colleagues), Director of Health Economics, Policy, and
Payment, Medtronics
Lawrence Zisman, Vice President of Cardiovascular Research, Cytopia Inc.

Acknowledgements

xxiii

Reviewers

Jori Frahler, Director of Federal Affairs, Medical Device Manufacturers Association

Mary Pendergast, Principal, Pendergast Consulting and past Assistant Commissioner of FDA

Hanson Gifford, Founder and CEO, The Foundry Inc.

Tanvi Mehta, freelance editor