CONTENTS

Contents iii
Preface xi
List of Abbreviations xiii

1. Technology Transfer Introduction and Objectives 1
   Mark Gibson

   Purpose of the Book 1
   Technology Transfer and the Drug Discovery and Development Process 1
   Why is Technology Transfer Important? 6
   Scope of the Book 7
   References 11

2. Technology Transfer: The Regulatory and Business Perspective 13
   Alan Harris and Siegfried Schmitt

   Introduction 13
   Regulatory Requirements for Technology Transfer 13
   Safety, Health and Environmental (SHE) Regulations 15
   General Safety and Health Considerations 16
   Waste Disposal 16
   POTENTIAL IMPACT OF NOTIFICATION OF NEW SUBSTANCES (NONS) REGULATIONS 17
   Economic Factors 18
   Technology 19
   Social Aspects and the Impact on Technology Transfer 20
   Language 20
   Culture 21
   Team Building 22
   Conclusions 23
   References 24
3. Technology Transfer: Organisation Strategy and Planning 25

Steve Burns and Mark Gibson

Introduction 25
Stages of the Technology Transfer Process 26
Stage 1: Pre-technology Transfer Preparation 26
Technology Transfer Strategies 29
Stage 2: Scale-up and Establish Process at Commercial Scale 32
Stage 3: Plan and Perform Process Validation 33
Management of Change 34
Organisation 34
Teams Supporting the Technology Transfer Process 36
Global Technology Transfer Management Team (GTTMT) 36
Sending Site (R&D) Drug Substance Project Team 38
Sending Site (R&D) Drug Product Project Team 38
Receiving Sites(s) Project Teams 40
Documentation Required to Support Technology Transfer 41
Planning 42
Timings 44
References 46
Acknowledgements 46

4. Training: An Essential Element of Technology Transfer 47

Siegfried Schmitt

Introduction 47
Learning from Technology Transfer 48
Developing a Training Strategy 48
Scope of Training 49
Prioritisation and Context of Training Needs 49
Detailed Contents of Training Programmes 50
Methods and Tools for Delivering Training 51
Management of Training Programmes 52
Trainers 52
Templates and Style Guidelines 53
Training Documentation 53
Language Used for Training Programmes 53
Measuring the Success of Training 54
Auditing of Training 54
Conclusions 54
5. **Drug Substance Development and Technology Transfer**
   *Alan Harris*

Introduction 57

THE DRUG SUBSTANCE DEVELOPMENT PROCESS 57

Introduction to Drug Substance Process Research and Development 57

The Role of Process R&D 59

Good Process Design 60

Introduction to Technology Transfer for API 63

Aims of Technology Transfer 65

The Impact of Technology Transfer Issues on Process Development Strategies 66

*Early Development Decisions* 66

*Route Selection, Regulatory and Sourcing Strategies* 67

*Process Freeze* 68

Potential Impact of Notification of New Substances (NONS) Regulations 68

Applying Risk Analysis and Risk Management to Technology Transfer Decisions 69

Managing the Technology Transfer Programme 70

*Principles for Technology Transfer* 70

*The Technology Transfer Team* 71

Documentation to be Transferred or Generated during Technology Transfer and Establishment of the Process 72

SUCCESS CRITERIA FOR TECHNOLOGY TRANSFER 73

Process Validation 74

Case Study 1: Remacemide Hydrochloride 75

*Early Process Evaluation* 75

*Process Research and Development Work* 77

*Early Technology Transfer of the Process for DPAP* 77

Second Source for DPAP 80

Technology Transfer of the Final Stages of the Process 81

Salt Selection, Polymorphism and Particle Size 81

*Lessons from Case Study 1* 82

Case Study 2: Sibenadet Hydrochloride 83

Synthesis and Technology Transfer of the Benzothiazolone Amine Intermediate 84

*Synthesis and Technology Transfer of the Intermediate Benzoate Ester* 86

Technology Transfer of the Final Steps 88

Control of Physical Form 89

Crystallisation/Drying Issues 90

*Overall Lessons from Case Study 2* 90

FUTURE DIRECTIONS FOR PROCESS DEVELOPMENT AND THE IMPACT ON TECHNOLOGY TRANSFER 92

Biopharmaceuticals 92
6. Drug Product Development and Technology Transfer  

Mark Gibson

Introduction 99
Product Design 100
Product Optimisation 105
Process Design and Optimisation 107
Process Capability and Robustness 111
Use of PAT to Aid Process Optimisation and Understanding 111
Scale-Up and Technology Transfer 114
Process Validation 116
Clinical Trials Process Validation 116
Cleaning Validation 117
Process Validation of the Commercial Process: Acceptance by Production 119
Post-Validation and Post-Regulatory Approval Changes 122
Documenting the Drug Development Process 124
Drug Product Technology Transfer Case Studies 126
Case Study 1 126
Learning Points from Case Study 1 130
Case Study 2 130
Learning Points from Case Study 2 132
Case Study 3 132
Learning Points from Case Study 3 134
References 135

7. Analytical Methodology and Specifications  

Kevin McKiernan and Mark Hindle

Introduction 137
Analytical Technology Transfer: What to do before Formal Transfer Starts 138
Production QC Involvement during Method Validation 140
Production QC Involvement Post Validation 141
Analytical Technology Transfer: When does it Start and When does it Finish 142
Principles of Analytical Methodology Transfer 144
Comparative Testing 145
Covalidation between Two Laboratories 145
Method Validation at the Receiving Site 145
Completion and Timing 146
THE TECHNOLOGY TRANSFER PROCESS FOR ANALYTICAL METHODOLOGY AND SPECIFICATIONS 146
Stage 1: Analytical Strategy 147
Stage 2: Knowledge and Information Transfer 147
Stage 3: Transfer Protocol 148
Stage 4: Analytical Testing 148
Stage 5: Summary Report 148
STAGE 1: ANALYTICAL STRATEGY 150
Analytical Method Transfer Team 150
Analytical Transfer Strategy Document 151
STAGE 2: KNOWLEDGE AND INFORMATION TRANSFER 153
Information Package 154
Knowledge Transfer 155
Method Discussion and Review 155
Training and Familiarisation 156
Approval of Information Transfer Package 157
STAGE 3: METHOD TRANSFER PROTOCOL 157
Testing Design 159
Analytical Sample Identification and Transportation 159
Acceptance Criteria 161
Use of Statistics 163
Approval of Method Transfer Protocol 165
STAGE 4: ANALYTICAL TESTING 165
STAGE 5: SUMMARY REPORT 166
Transfer Approval 167
Post-Approval Changes 167
Method Transfer: Potential Problems and How to Avoid Them 168
A Good Quality Method 168
Language and Culture 169
Communication 170
Documentation 171
Procedures 172
Timescales 172
Practical Problems 173
Acceptance Criteria 174
Summary 174
References 175
List of Figures

Figure 1.1 The Drug Discovery and Development Process and Technology Transfer 3
Figure 3.1 Stages of Technology Transfer 27
Figure 3.2 High Level Documentation to Support Technology Transfer 43
Figure 5.1 The Process R&D Contribution to the Development Process 60
Figure 5.2 Hypothetical Process for API Manufacture 64
Figure 5.3 Medicinal Chemistry Synthesis of Remacemide Hydrochloride 76
Figure 5.4 Final Manufacturing Process for Remacemide Hydrochloride 78
Figure 5.5 Sibenadet Hydrochloride 84
Figure 5.6 Synthesis of the Benzothiazalone Intermediate for Sibenadet Hydrochloride 85
Figure 5.7 Technology Transfer Process for Intermediate (2) 86
Figure 5.8 The Synthesis of the Benzoate Intermediate for Sibenadet Hydrochloride 87
Figure 5.9 The Final Steps of the Sibenadet Hydrochloride Process 89
Figure 6.1 Stages of Product Development and Technology Transfer 101
Figure 6.2 Manufacturing Process for IR Film Coated Tablet 129
Figure 6.3 Manufacturing Process for Ophthalmic Solution 131
Figure 6.4 Manufacturing Process for Metered Dose Inhaler 133
Figure 7.1 Options for Involvement of QC Group in Technology Transfer 141
Figure 7.2 Flow Diagram of the Analytical Process 149
In the early 1980's when I started my career in the pharmaceutical industry, I recall that Technology Transfer from R&D to Production did not attract the attention that it does today. This could be partly because the R&D and Production facilities were co-located on the same site for the majority of transfers in which I was involved. Pilot scale batches were made in the R&D facilities on one day and products requiring scale-up and commercial scale manufacture were undertaken in the Production plant on another. Technology transfer was a very informal process with few written guidelines and procedures. R&D and Production personnel were able to develop very good working relationships because they could easily spend a lot of time together and get to know each other well.

A few years later, on moving to another pharmaceutical company the circumstances had changed. The R&D site I worked at was in an isolated location and technology transfers were to distant Production sites, often overseas. Establishing good communication and planning were essential for success. With the plethora of company acquisitions and mergers over the past 15 to 20 years resulting in fewer, but much larger pharmaceutical companies, there has been an increased need to transfer technology between R&D and Production sites across the globe in a cost efficient and effective way. Pharmaceutical companies have been under increasing pressure to speed products from R&D to the market. At the same time, the drug development and regulatory hurdles have increased, including the need to pass an FDA pre-approval inspection if the product was destined for the United States market. The timely and successful technology transfer of new Drug Substances, Drug Products and Analytical Tests between these sites is a prerequisite to product registration, approval and launch and so the importance of having a structured approach to drug development and technology transfer has become paramount.

This book is intended to give a comprehensive overview and guide to the technology transfer process for pharmaceutical Drug Substance, Drug Product and the corresponding analytical tests and methods from R&D to Production. Each of the contributors has extensive personal knowledge and experience in this field and they
have provided practical examples to explain the critical factors involved in achieving successful and effective technology transfers. Several of the contributors are from AstraZeneca, including myself, but the reader must not assume that this book only reflects the AstraZeneca way of doing technology transfer. Many of the contributors have worked for different pharmaceutical companies; have been involved in developing and reviewing internal company guidelines and in giving seminars and presentations externally on technology transfer. I am indebted to each of the contributors for giving up so much of their time to produce the specialist chapters in this book.

This book should benefit practitioners working in the pharmaceutical and related industries from R&D, commercial Production and various other areas of responsibility such as; Project Management, Clinical, Regulatory Affairs and Quality Assurance.

Finally, I would like to thank my wife Alison and three children, Laura, Joanna and David, for their patience and understanding whilst I have been preparing this book and for not being able to spend so much time with over the past few months.

Mark Gibson

December, 2004
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ANDA</td>
<td>Abbreviated New Drug Application</td>
</tr>
<tr>
<td>API</td>
<td>Active Pharmaceutical Ingredient</td>
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<td>BIRA</td>
<td>Business Interruption Risk Assessment</td>
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<tr>
<td>BPC</td>
<td>Bulk Pharmaceutical Chemical</td>
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<tr>
<td>C of A</td>
<td>Certificate of Analysis</td>
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<tr>
<td>CBZ</td>
<td>Benzyloxycarbonyl</td>
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<td>CD</td>
<td>Candidate Drugs</td>
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<td>CBER</td>
<td>Center for Biologic Evaluation and Research</td>
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<td>CDER</td>
<td>Center for Drug Evaluation and Research</td>
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<td>CDS</td>
<td>Chromatography Data System</td>
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<tr>
<td>CDTP</td>
<td>CD Target Profile</td>
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<td>CFR</td>
<td>Code of Federal Regulations</td>
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<td>cGMP</td>
<td>Current Good Manufacturing Practice</td>
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<td>Clean-In-Place</td>
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<td>COG</td>
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<td>CMC</td>
<td>Chemistry, Manufacturing and Controls</td>
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<td>CMC</td>
<td>Contract Manufacturing Organisation</td>
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<td>COPD</td>
<td>Chronic Pulmonary Obstructive Disease</td>
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<td>COSHH</td>
<td>Control of Substances Hazardous to Health</td>
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<td>CpK</td>
<td>Process Capability Index</td>
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<td>CPMP</td>
<td>Committee for Proprietary Medicinal Products</td>
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<td>CRO</td>
<td>Contract Research Organisation</td>
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<td>CTA</td>
<td>Clinical Trial Application</td>
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<td>CTD</td>
<td>Common Technical Document</td>
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<td>DCC</td>
<td>Dicyclohexyl Carbodiimide</td>
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<td>DMF</td>
<td>Drug Master File</td>
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<td>Diphenylpropylamine</td>
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<td>DPD</td>
<td>Drug Product Device</td>
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<td>DQ</td>
<td>Design Qualification</td>
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<tr>
<td>EEC</td>
<td>European Economic Community</td>
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<td>EGMP</td>
<td>European Good Manufacturing Practice</td>
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<td>EINECS</td>
<td>European Inventory of Existing Commercial Chemical Substances</td>
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<td>EMEA</td>
<td>European Agency for the Evaluation of Medicinal Products</td>
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<td>EP</td>
<td>European Pharmacopoeia</td>
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<tr>
<td>ER</td>
<td>Electronic Record</td>
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<tr>
<td>ES</td>
<td>Electronic Signature</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FIP</td>
<td>International Pharmaceutical Federation</td>
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<tr>
<td>FP</td>
<td>Finished Pack</td>
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<tr>
<td>FTIM</td>
<td>First Time In Man Studies</td>
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<tr>
<td>GAMP</td>
<td>Good Automated Manufacturing Practice</td>
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<tr>
<td>GC</td>
<td>Gas Chromatography</td>
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<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>GLP</td>
<td>Good Laboratory Practice</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
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<td>Global Technology Transfer Management Team</td>
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<tr>
<td>GxP</td>
<td>European Good Practice</td>
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<td>HAZOP</td>
<td>Hazard and Operability Studies</td>
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<td>HPLC</td>
<td>High Performance Liquid Chromatography</td>
</tr>
<tr>
<td>HSE</td>
<td>Health and Safety Executive</td>
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<tr>
<td>ICH</td>
<td>International Conference on Harmonisation</td>
</tr>
<tr>
<td>IMP</td>
<td>Investigative Medicinal Product</td>
</tr>
<tr>
<td>IND</td>
<td>Investigational New Drug</td>
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<tr>
<td>INDA</td>
<td>Investigational New Drug Application</td>
</tr>
<tr>
<td>IP</td>
<td>Intellectual Property</td>
</tr>
<tr>
<td>IQ</td>
<td>Installation Qualification</td>
</tr>
<tr>
<td>ISPE</td>
<td>International Society of Pharmaceutical Engineers</td>
</tr>
<tr>
<td>ISO</td>
<td>International Organisation for Standardisation</td>
</tr>
<tr>
<td>JNDA</td>
<td>Japanese New Drug Application</td>
</tr>
<tr>
<td>JP</td>
<td>Japanese Pharmacopoeia</td>
</tr>
<tr>
<td>LIMS</td>
<td>Laboratory Information Management Systems</td>
</tr>
<tr>
<td>LOD</td>
<td>Limit of Detection</td>
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<tr>
<td>LOQ</td>
<td>Limit of Quantification</td>
</tr>
<tr>
<td>M&amp;A</td>
<td>Mergers and Acquisitions</td>
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<tr>
<td>MA</td>
<td>Marketing Authorisation</td>
</tr>
<tr>
<td>MAA</td>
<td>Marketing Authorisation Application</td>
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<tr>
<td>MBR</td>
<td>Master Batch Record</td>
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<tr>
<td>MCA</td>
<td>Medicines Control Agency</td>
</tr>
<tr>
<td>MDI</td>
<td>Metered Dose Inhaler</td>
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</table>
MHRA  Medicines and Healthcare Products Regulatory Agency
MRA  Mutual Recognition Agreement
MSDS  Material Safety Data Sheets
NCE  New Chemical Entity
NDA  New Drug Application
NIR  Near Infrared
NME  New Molecular Entity
NMR  Nuclear Magnetic Resonance
NONS  Notification of New Substances
OEL  Occupational Exposure Limit
OOS  Out of Specification
OP  Operational Qualification
PAI  Pre-approval Inspection
PAT  Process Analytical Technologies
PDA  Parenteral Drug Association
PIC  Pharmaceutical Inspection Convention
pMDI  Pressurised Metered Dose Inhaler
POC  Proof of Concept
POP  Proof of Principle
PPE  Personal Protective Equipment
PQ  Performance Qualification
PQ  Process Qualification
PV  Process Validation
PVC  Polyvinylchloride
PVdC  Polyvinylidichloride
QA  Quality Assurance
QC  Quality Control
QMS  Quality Management System
QP  Qualified Person
REACH  Registration, Evaluation and Authorisation of Chemicals
SHE  Safety, Health and Environmental Regulations
SM  Starting Material
SMB  Simulated Moving Bed Chromatography
SMP  Stability Master Plan
sNDA  Supplementary New Drug Application
SOP  Standard Operating Procedure
SST  System Suitability Testing
SUPAC  Scale-up Post-Approval Changes
TPP  Target Product Profile
TT  Technology Transfer
USP  United States Pharmacopoeia
List of Abbreviations

VMP  Validation Master Plan
WFI  Water for Injection