TECHNOLOGY TRANSFER:

AN INTERNATIONAL GOOD PRACTICE GUIDE FOR PHARMACEUTICALS AND ALLIED INDUSTRIES

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PDA
Bethesda, MD, USA
DHI Publishing, LLC
River Grove, IL, USA

10 9 8 7 6 5 4 3 2 1

ISBN: x-xxxxxx-xx-x

PDA
3 Bethesda Metro Center
Suite 1500
Bethesda, MD 20814
United States
301-986-0293

Davis Healthcare International Publishing, LLC
2636 West Street
River Grove
IL 60171
United States
www.DHIBooks..com

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PREFACE

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

LIST OF ABBREVIATIONS

ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredient
BIRA	Business Interruption Risk Assessment
BPC	Bulk Pharmaceutical Chemical
C of A	Certificate of Analysis
CBZ	Benzyloxycarbonyl
CD	Candidate Drugs
CBER	Center for Biologic Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDS	Chromatography Data System
CDTP	CD Target Profile
CFR	Code of Federal Regulations
cGMP	Current Good Manufacturing Practice
CIP	Clean-In-Place
COG	Cost of Goods
CMC	Chemistry, Manufacturing and Controls
CMC	Contract Manufacturing Organisation
COPD	Chronic Pulmonary Obstructive Disease
COSHH	Control of Substances Hazardous to Health
CpK	Process Capability Index
CPMP	Committee for Proprietary Medicinal Products
CRO	Contract Research Organisation
CTA	Clinical Trial Application
CTD	Common Technical Document
DCC	Dicyclohexyl Carbodiimide
DMF	Drug Master File
DP	Drug Product
DPAP	Diphenylpropylamine
DPD	Drug Product Device
DQ	Design Qualification
DS	Drug Substance

EEC	European Economic Community
EGMP	European Good Manufacturing Practice
EINECS	European Inventory of Existing Commercial Chemical Substances
EMEA	European Agency for the Evaluation of Medicinal Products
EP	European Pharmacopoeia
ER	Electronic Record
ES	Electronic Signature
FDA	Food and Drug Administration
FIP	International Pharmaceutical Federation
FP	Finished Pack
FTIM	First Time In Man Studies
GAMP	Good Automated Manufacturing Practice
GC	Gas Chromatography
GCP	Good Clinical Practice
GI	Gastrointestinal
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GTTMT	Global Technology Transfer Management Team
GxP	European Good Practice
HAZOP	Hazard and Operability Studies
HPLC	High Performance Liquid Chromatography
HSE	Health and Safety Executive
ICH	International Conference on Harmonisation
IMP	Investigative Medicinal Product
IND	Investigational New Drug
INDA	Investigational New Drug Application
IP	Intellectual Property
IQ	Installation Qualification
ISPE	International Society of Pharmaceutical Engineers
ISO	International Organisation for Standardisation
JNDA	Japanese New Drug Application
JP	Japanese Pharmacopoeia
LIMS	Laboratory Information Management Systems
LOD	Limit of Detection
LOQ	Limit of Quantification
M&A	Mergers and Acquisitions
MA	Marketing Authorisation
MAA	Marketing Authorisation Application
MBR	Master Batch Record
MCA	Medicines Control Agency
MDI	Metered Dose Inhaler

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	Polyvinyldichloride
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

VMP	Validation Master Plan
WFI	Water for Injection