

Contents

PHARMACEUTICAL DEVELOPMENT

| | |
|---------------------------------|------|
| <i>Table of Contents</i> | VII |
| <i>Acronyms - Abbreviations</i> | XIII |
| Introduction | XIV |
| Preface | XV |
| Forward | XVI |

Chapter 1

| | |
|--|-----|
| Regulatory | 1.1 |
| - Pre-formulation checklist | 1.3 |
| Documentation | 1.4 |
| - SOP Control checklist | 1.5 |
| Development Notebooks | 1.6 |
| - Development Notebooks checklist | 1.7 |
| - SOP Control and Development Notebooks SOPs | 1.8 |

Chapter 2

| | |
|---|------|
| Developing the Formula -an Overview | 2.1 |
| - Formulation checklist | 2.2 |
| - Development formulations | 2.3 |
| Drug Development Checklist | 2.4 |
| Development Formula SOPs | 2.5 |
| Developing the Formula | 2.6 |
| Product Development Flow Chart | 2.11 |
| Product Development Guide | 2.13 |
| Direct Compression Tablet Development | 2.21 |
| Direct Compression Flow Charts | 2.26 |
| Direct Compression Master Formula | 2.29 |
| Wet Granulation Development | 2.31 |
| Wet & Direct Compression Flow Charts | 2.26 |
| Wet Granulation Manufacturing Flow Charts | 2.41 |
| Wet Granulation Master Formula (aqueous granulation) | 2.42 |
| Wet Granulation Master Formula (alcoholic granulation) | 2.44 |

Contents



Chapter 2

| | |
|---|------|
| Purified Water - an essential ingredient | 2.45 |
| Do and Don'ts in Development | 2.48 |
| Purified Water - Checklist | 2.49 |

Chapter 3

| | |
|---|-----|
| Active Ingredients & Alternative API Sources | 3.1 |
| -Do's and Don'ts | 3.2 |
| -Active checklist | 3.3 |
| -Approved Suppliers Checklist | 3.5 |
| -Standard Operating Procedures, Actives | 3.6 |

Chapter 4

| | |
|--|-----|
| Semi active ingredients | 4.1 |
| -Validating the Semi-active ingredients, Checklist | 4.2 |
| Qualifying the Antioxidant | 4.4 |
| Antioxidant Tabulations | 4.5 |

Chapter 5

| | |
|---|-----|
| Non active materials (excipients) | 5.1 |
| -Checklist non active ingredient | 5.2 |
| -Standard Operating Procedures, Non actives | 5.3 |

Chapter 6

| | |
|--|------|
| Container closure systems | 6.1 |
| -Container-liner-closure systems, Checklist | 6.2 |
| -Container-liner-closure systems, SOPs | 6.3 |
| -Packaging Components | 6.5 |
| -Packaging Components Documentation Requirements SOP | 6.6 |
| -Packaging Characteristics | 6.11 |
| -Packaging Component Descriptions | 6.12 |
| -Packaging Component | 6.16 |

Chapter 7

| | |
|---|------|
| Manufacturing Instructions | 7.1 |
| - Manufacturing Instructions; Checklist | 7.4 |
| - The manufacturing Instructions and Controls | 7.5 |
| - Manufacturing Flow Charts | 7.16 |
| - Large scale manufacturing Instructions | 7.20 |
| - Large scale Master Formula | 7.24 |
| - Large scale Manufacturing Instructions | 7.27 |

Contents



Chapter 8

| | |
|---|------|
| In-process Quality Controls | 8.1 |
| -Manufacturing in-process controls; Checklist | 8.3 |
| -In-process Specifications | 8.5 |
| -Process yields | 8.8 |
| -In-process Control Specifications | 8.9 |
| -In-process Film Coating Specifications | 8.10 |

Chapter 9

| | |
|--|-----|
| Finished Product Specifications | 9.1 |
| - Finished Product Specifications Tablet & Caplets | 9.2 |
| - Finished Product Specifications; Checklists | 9.4 |
| - Finished Product Specifications; Required SOPs | 9.5 |

Chapter 10

| | |
|--|------|
| Process Optimization and Procedures | 10.1 |
| Qualification of Antioxidant and Lubricant | 10.2 |
| Qualification of Loss on Drying Limits | 10.3 |

Chapter 11

| | |
|---|------|
| Scale-up Procedures | 11.1 |
| - Scale-up procedures; checklist | 11.3 |
| - Scale-up procedures; Aqueous Film Coating | 11.6 |

Chapter 12

| | |
|--|------|
| Cleaning Limits | 12.1 |
| Cleaning Limits Procedures; Checklist | 12.6 |
| Cleaning Validation Requirements; SOPs | 12.8 |

Chapter 13

| | |
|---|-------|
| Analytical Validation Requirements | 13.1 |
| -Analytical Testing Out of Specification | 13.21 |
| -Analytical Testing Do's and Don'ts - Retesting Rules | 13.23 |
| -Out-of-Specifications Checklists | 13.24 |
| -Ruggedness and Robustness | 13.37 |
| -Impurities in Drug Substances | 13.41 |
| -Impurities Do's and Don'ts | 13.50 |
| -Impurities Glossary of terms | 13.51 |
| -Impurities Decision Trees | 13.53 |
| Analytical Post approval Changes - PAC/ALTS | 13.55 |
| PAC-ALTS Checklist | 13.58 |

Contents



Chapter 14

| | |
|---|-------|
| Process Qualification Batch | 14.1 |
| -Process Qualification Batch; Checklist | 14.2 |
| -Process Qualification Batch; SOPs | 14.3 |
| -Process Qualification Blend Analysis | 14.7 |
| -Process Qualification Blend Analysis - Do's and Don'ts | 14.7 |
| -Process Qualification Qualifying Tablet Hardness | 14.8 |
| Tablet Hardness Protocol | 14.10 |

Chapter 15

| | |
|---|------|
| Pivotal batch | |
| -The Pivotal Batch | 15.1 |
| -Pivotal batch Checklist | 15.2 |
| -Pivotal batch SOPs | 15.3 |
| -Sampling and Testing the Pivotal Batch | 15.3 |
| -Auditing the Pivotal batch | 15.4 |
| -Auditing the Pivotal batch Checklist | 15.9 |

Chapter 16

| | |
|---|--------|
| Bioequivalence vs. RLD | 16.1 |
| Test Designs - Overview | 16.2 |
| Statistical Bioequivalence | 16.13 |
| IBE Equation explained | 16.14 |
| IBE - Big Picture (Pros and Cons) | 16.15 |
| Comparing IBE and ABE | 16.16 |
| Dissolution Testing in IR Dosage Forms | 16.18 |
| Typical IVIVC Models | 16.21 |
| Choosing IVIVC levels | 16.22 |
| Dissolution Testing in IR Solid Dosage Forms | 16.23 |
| Similarity Factor in dissolution testing | 16.30 |
| Biowaivers | 16.32 |
| Overall Dissolution Picture | 16.35 |
| Biopharmaceutics Classification System | 16.36 |
| Evaluating Differences between Drug, Powder Blend, and Tablets | 16.50 |
| BA & BE Overview | 16.52 |
| Food-Effects in BA-BE Studies | 16.78 |
| Bioanalytical Methods | 16.88 |
| Performance Verification in Dissolution testing | 16.98 |
| Similarity Testing - Chow, Pitt and Others | 16.112 |

Contents



Chapter 17

| | |
|--|-------|
| Technical Transfer Documentation | 17.1 |
| -Technical Transfer Documentation; Do's and Don'ts Checklist | 17.5 |
| -Technical Transfer Documentation; Pharmaceutical Part | 17.7 |
| -Technical Transfer Documentation; Analytical Part | 17.10 |

Chapter 18

| | |
|--|------|
| Process Validation Batches | 18.1 |
| -The Process Validation Batches - Essential know-how | 18.2 |
| -Process Validation Requirements; SOPs | 18.4 |
| -Process Validation Master Plans | 18.5 |

Chapter 19

| | |
|---|-------|
| Pre--Approval Inspections | 19.1 |
| PAI Summary | 19.8 |
| Pre--Approval Inspection Audit - Team Set Up | 19.9 |
| Pre--Approval Inspection Audit - Team Activities | 19.11 |

Chapter 20

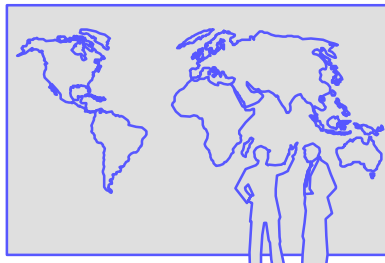
| | |
|--|-------|
| Stability Testing of Drug Substance and Drug Product I | 20.1 |
| Stability Testing of Drug Substance and Drug Product II | 20.15 |
| Stability Testing of Drug Substance and Drug Product II | 20.31 |
| Stability Testing Significant Change | 20.28 |
| Stability Storage Conditions | 20.29 |
| Photostability in Drug Substances | 20.31 |
| Setting up a Functional Stability Unit | 20.40 |
| Stability SOPs Development | 20.48 |

Chapter 21

Standard Operational Procedures

| | |
|---|-------|
| Development SOPs | 21.1 |
| Index of Pharmaceutical Standard Operating Procedures | 21.3 |
| Index of Analytical Standard Operating Procedures | 21.10 |
| Index of Microbiological Standard Operating Procedures | 21.16 |
| Index of Stability Standard Operating Procedures | 21.20 |
| Model Development Report | 22.1 |
| Experimental Development | 22.2 |
| Pre-formulation Development | 22.7 |
| Small scale Development | 22.9 |
| Scale-up | 22.14 |
| Pivotal Lot Manufacture | 22.27 |
| Model Development Report - Summary and Conclusion | 22.41 |

ISSN 0793 8632
An on-going series
Additional Volumes in Preparation
ISBN 0793 8640 - Electronic Version
Handbook Development 24 Volume Series
ISSN Series Number 0793 7792 - Electronic Version



ISSN 0793 **8632**
An on-going series

Additional Volumes in Preparation
General Drug Development Series ISSN 0973 7601
Electronic Drug Development Series ISSN 0973 **761X**



ÓšĀ
 International HPGD Print Edition
 pLocum Int. Pressp
 COPYRIGHT © All Rights Reserved
 ĩ > Đ

H P G D™

Handbook of Pharmaceutical Generic Development

Drug Development - Part I


Electronic ANDA™ - Part II

© Copyright 1995 -2005 Locum International Ltd.

2006 Update Program

Part I and Part II : HandBook Generic Development Series

| | | | |
|-------------|-------------------|-------------|-------------------|
| Ⓟ Volume 1 | Edition 07 - 2006 | Ⓟ Volume 13 | Edition 07 - 2006 |
| Ⓟ Volume 2 | Edition 07 - 2006 | Ⓟ Volume 14 | Edition 07 - 2006 |
| Ⓟ Volume 3 | Edition 07 - 2006 | Ⓟ Volume 15 | Edition 07 - 2006 |
| Ⓟ Volume 4 | Edition 07 - 2006 | Ⓟ Volume 16 | Edition 07 - 2006 |
| Ⓟ Volume 5 | Edition 07 - 2006 | Ⓟ Volume 17 | Edition 07 - 2006 |
| Ⓟ Volume 6 | Edition 07 - 2006 | Ⓟ Volume 18 | Edition 07 - 2006 |
| Ⓟ Volume 7 | Edition 07 - 2006 | Ⓟ Volume 19 | Edition 07 - 2006 |
| Ⓟ Volume 8 | Edition 07 - 2006 | Ⓟ Volume 22 | Edition 07 - 2006 |
| Ⓟ Volume 9 | Edition 07 - 2006 | Ⓟ Volume 21 | Edition 07 - 2006 |
| Ⓟ Volume 10 | Edition 07 - 2006 | Ⓟ Volume 22 | Edition 07 - 2006 |
| Ⓟ Volume 11 | Edition 07 - 2006 | Ⓟ Volume 23 | Edition 07 - 2006 |
| Ⓟ Volume 12 | Edition 07 - 2006 | Ⓟ Volume 24 | Edition 07 - 2006 |

| | | | |
|-----------------|---|---|--|
| Initiation Date | : | January 2006 |  |
| Expiration Date | : | January 2008 | |
| No of Years | : | THREE (3) | |
| Update Period | : | January 2006; January 2007; January 2008. | |
| | | | |

This Print or CD ROM Edition of the Drug Development Series has been updated to current Office of Generic Drug's requirements. Handbook clients requiring to continue this annual ONGOING service require to become members of the Drug Development Association (I.A.G.I.M.) for the period of the update service as required by the firm, starting from date of purchase. The Drug Development Update Program is renewed in December each year as a function of the firms requirements. New Drug Formula and Manufacturing Procedures are added annually All updates are on CD ROM in PDF™. Warning: Copyright © 1985 -2005 Locum Publishing House Inc.-All Rights Reserved.

COPYRIGHT

Neither this information or nor any part of the data contained therein may be reproduced, copied or transmitted in any form, modification or merged portion or by any means, electronic or mechanical, including printing photocopying, microfilming and recording, or by any information storage and retrieval system, without the prior written permission of the publishers. ™ Trademark - Locum Corporation, ™ Locum International Group.

<http://www.locum.co.il>
info@locumusa.com
<http://www.locumusa.com>

info@locumeuro.com
<http://www.locumeuro.com>

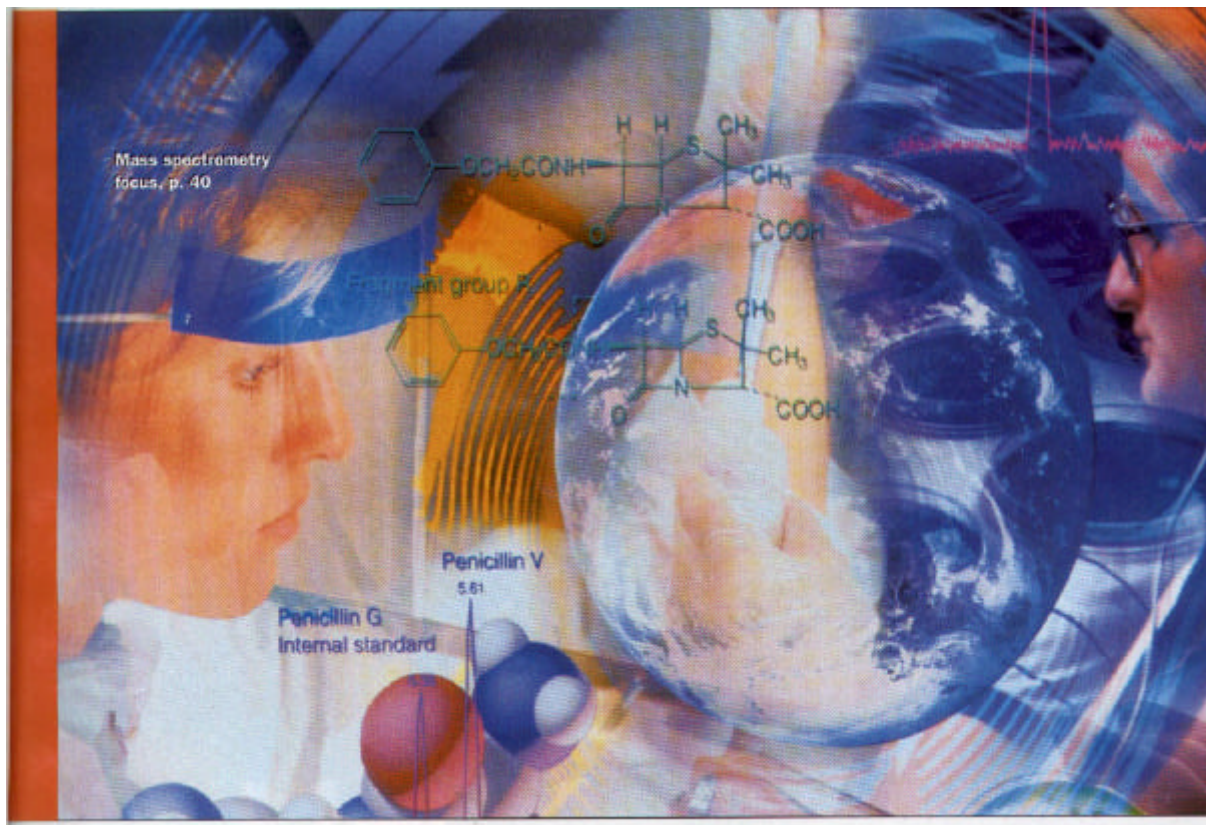
(See web site for IAGIM Application Membership Forms)

info@iagim.org

<http://www.iagim.org>

The Secret of Success is Making your Vocation your Vacation.

All of these achievers are driven by a passion for what they do, an overpowering feeling that compels them to do their best. Without passion, the visions of youth are only daydreams. Passion gave these men and women the drive to turn their dreams into reality. They all love their chosen professions and have devoted their loves to the pursuit of excellence. - Mark Twain



Additional Handbooks in preparation on drug specific dosage forms
in the title series 120+ Ready-To-Go Series

view at <http://www.locumusa.com/2go>

Available either in Print on CD ROM or On-line

An on-going electronic and print series
Additional Volumes in Preparation

info@locumusa.com
<http://www.locumusa.com>

info@locumGroup.org
<http://www.locumeuro.com>

(See web site for IAGIM Application Membership Forms)

info@iagim.org
<http://www.iagim.org>