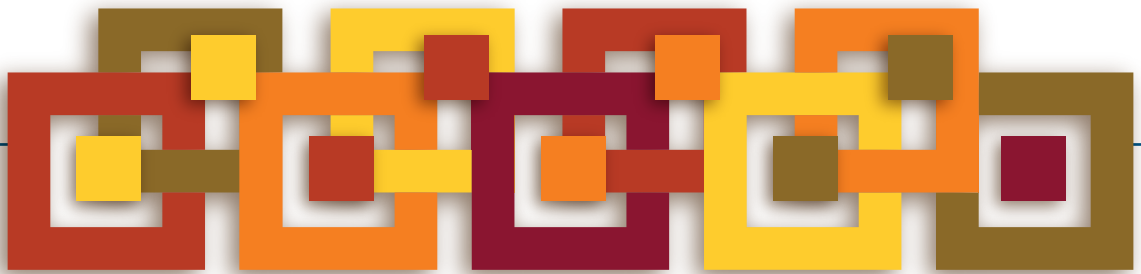


COMBINATION PRODUCTS

IMPLEMENTATION OF cGMP REQUIREMENTS



Lisa A. Hornback
Editor

www.pda.org/bookstore

CONTENTS

FOREWORD	viii
<i>Richard Levy</i>	
1 INTRODUCTION	1
<i>Lisa A. Hornback</i>	
References	6
About the Author	6
2 QUALITY SYSTEM DEVELOPMENTS TO MEET COMBINATION PRODUCT REQUIREMENTS	7
<i>Lisa A. Hornback</i>	
Introduction	7
21 CFR4 Applicability	8
Quality Systems — Bridging the Gaps between Requirements	10
21 CFR 820 as Primary cGMP	11
21 CFR 211.84 Testing of Material	11

21 CFR 211.103 Yield calculation	17
21 CFR 211.132 Tamper-evident packaging	17
21 CFR 211.137 Expiration dating	18
21 CFR 211.166 Stability testing	19
21 CFR 211.165 Testing/release for distribution	22
21 CFR 211.167 Special testing requirements	25
21 CFR 211.170 Reserve samples	26
21 CFR 211 as Primary cGMP	30
21 CFR 820.20 Management responsibility	30
21 CFR 820.30 Design controls	34
21 CFR 820.50 Purchasing controls	41
21 CFR 820.100 Corrective and preventive actions	42
21 CFR 820.170 Installation	44
21 CFR 820.200 Servicing	45
Risk Management in cGMP	46
Conclusion	46
References	48
About the Author	49
3 RISK MANAGEMENT FOR COMBINATION PRODUCTS	51
<i>Edwin Bills</i>	
Introduction	51
Complications for Combination Products	52
Risk Definition	54
Medical Devices	54
Pharmaceuticals and Biologics	55
Health Product Risk Management	58
The Risk Management Process	58
Hazard Identification	62
Hazardous Situation	65
Risk Estimation	65
Risk Control	71
Overall Residual Risk Evaluation	76
Risk Management Report	78
Production and Post-Production	79
Summary	82
References	83
About the Author	85

4	DESIGN INPUTS AND ASSOCIATED DESIGN VERIFICATION AND VALIDATION — A PRIMER ON APPLYING HUMAN FACTORS ENGINEERING	87
	<i>Edwin Israelski</i>	
	Introduction	87
	HFE Process Details	89
	System/Product Definition	91
	Contextual Inquiry	91
	Use Scenarios	94
	Use Error Risk Analysis	94
	Usability Objectives/Goals	96
	Usability Objectives Planning	97
	Customer Confirmation of Usability Objectives	98
	Reporting of Usability Objectives	98
	Iterative Design	99
	Usability Evaluation and Testing	99
	Formative testing	99
	Summative testing	100
	Post Implementation Analysis	101
	Regulatory Body Expectations	101
	The Future of HFR for Combination Products	103
	References	106
	About the Author	
5	PURCHASING CONTROLS AND SUPPLIER RELATIONSHIPS	107
	<i>Lisa Hornback</i>	
	Introduction	107
	Purchasing Control Process	108
	Planning	111
	Selection of Potential Suppliers	114
	Supplier Evaluation and Control	115
	Finalization of Controls	118
	Delivery, Measurement and Monitoring	121
	Feedback and Communication	122
	Conclusion	123
	References	123
	About the Author	124

6	CROSS LABELED COMBINATION PRODUCTS	125
	<i>Suzanne O'Shea</i>	
	Introduction	125
	What are Cross Labeled Products?	126
	Differences from General Use Devices	128
	Marketing Applications	129
	Mutually Conforming Labelling	130
	Intent to Cross Label	132
	Cross Labeling Challenges	133
	Conclusion	134
	References	135
	About the Author	136
7	REGULATORY STRATEGIES FOR COMBINATION PRODUCTS	137
	<i>William D'Agostino</i>	
	US FDA Regulatory Process	139
	PMOA and Project Risks	140
	Strategies for Development and Launch	141
	Fast-Track Drug-Device Approval	142
	PMOA Roadmap	143
	European Union	149
	EU products with device PMOA	149
	EU products with drug PMOA	150
	Combination Product Intellectual Property	152
	Summary	152
	References	152
	About the Author	154
8	DEVELOPMENT OF A DRUG/AUTOINJECTOR COMBINATION PRODUCT: A CASE STUDY	155
	<i>Mark A. Chipperfield, Ruby Gulati and Jennifer Mercer</i>	
	Introduction	155
	cGMP for Combination Products	156
	Development of a Combination Product	157
	Case Study Background	157
	Development of the autoinjector	159
	Quality systems	160
	Risk management	161

Facility inspections	162
Human factors engineering	162
Outcome	163
Business process	163
Terminology Considerations	164
Quality system development	164
Development process	165
Unique testing requirements	166
Stability	167
Risk management	167
Quality plan	168
Conclusion	168
References	169
About the Authors	170
APPENDIX	
FEDERAL REGISTER: COMBINATION	
PRODUCT FINAL RULE (WITH PREAMBLE)	171
INDEX	189