

Pharmaceutical and Biopharmaceutical Manufacturing: Understanding Your Process Series

Risk Management Library, Volume 7

Risk Problem Solvers: Inadequate Facilities, Procedures and Process Control



Edited by
Russell E. Madsen and Maik W. Jornitz

Risk Management Library, Volume 7

**Risk Problem Solvers:
Inadequate Facilities,
Procedures and Process
Control**

Russell E. Madsen and Maik W. Jornitz

**PDA
Bethesda, MD, USA**

**DHI Publishing, LLC
River Grove, IL, USA**

www.pda.org/bookstore

10 9 8 7 6 5 4 3 2 1

ISBN: 978-1-942911-24-1

**Copyright © 2018 Russell E. Madsen and Maik W. Jornitz
All rights reserved.**

All rights reserved. This book is protected by copyright. No part of it may be reproduced, stored in a retrieval system or transmitted in any means, electronic, mechanical, photocopying, recording, or otherwise, without written permission from the publisher. Printed in the United States of America.

Where a product trademark, registration mark, or other protected mark is made in the text, ownership of the mark remains with the lawful owner of the mark. No claim, intentional or otherwise, is made by reference to any such marks in the book. Websites cited are current at the time of publication. The authors have made every effort to provide accurate citations. If there are any omissions, please contact the publisher.

While every effort has been made by the publisher and the authors to ensure the accuracy of the information expressed in this book, the organization accepts no responsibility for errors or omissions. The views expressed in this book are those of the editors and authors and may not represent those of either Davis Healthcare International or the PDA, its officers, or directors.



Connecting People, Science and Regulation®



This book is printed on sustainable resource paper approved by the Forest Stewardship Council. The printer, Gasch Printing, is a member of the Green Press Initiative and all paper used is from SFI (Sustainable Forest Initiative) certified mills.

PDA Global Headquarters
Bethesda Towers, Suite 150
4350 East-West Highway
Bethesda, MD 20814
United States
www.pda.org/bookstore
001-301-986-0293

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

www.pda.org/bookstore

ABOUT THIS BOOK

This book is about failure in pharmaceutical manufacturing — its causes, detection, correction and the teachings and lessons implicit in it.

No human endeavor is perfect and the manufacture of pharmaceuticals is no exception. People simply make mistakes and even well-conceived systems occasionally fail. As evidenced by the examples in this book, when errors occur pharmaceutical manufacturing systems are usually robust enough to detect them and prevent defective products from reaching consumers, but not always.

The errors that occur can provide valuable information to improve imperfect systems and lessons to improve personnel performance and understanding. Often these lessons provide the foundational “why” that is so necessary to put into perspective for manufacturing and quality control personnel the need for a particular practice or procedure. People learn best when they understand why a procedure or practice is important and what can happen if it isn’t followed.

This book provides many examples of failures that have actually happened. Careful study of these failures will lead to better understanding of why they occurred and what might have been done to prevent them. The “lessons” in this book can be used, through training and systems review, to prevent these types of failures.

Many thanks to the people who contributed to this book. Their insights and investigations into the causes of failure are invaluable. We have chosen not to link the lessons to their authors to preserve anonymity and to “protect the innocent” so to speak. Further, we believe candid presentation and discussion of these lessons increases their value and may encourage others to share their experiences.

One final thought before you begin your journey through these lessons: “Murphy” is always watching.

CONTENTS

1	White Precipitate	3	1
2	I've Got It! ...You Take It!	5	5
3	Bioburden Contamination in a Contained Water System	9	9
4	Cleaning Validation	13	13
5	Material Decontamination Failure	23	23
6	An Aseptic Processing Intervention to Avoid	27	27
7	It's a Like for Like Replacement	29	29
8	Not Invented Here	31	33
9	Bury my Heart in the SOP	35	35
10	The Complaint is Unjustified	41	41
11	The Nitrogen Delivery Wasn't Made: Or Was It?	47	47

vi	<i>Risk Problem Solvers: Inadequate Facilities, Procedures, Process</i>	
12	Used the Right Gas? Are You Sure?	49
13	How to Train a Body Builder	53
14	Viral Contamination of Bioreactors used to Produce Enzyme Replacement Therapy	59
15	Fungal Problems Sideline Vaccine Manufacturer	63
16	Blue Sky	67
17	Technology Transfer	69
18	You See What You Want to See	73
19	Not Invented Here 3	77
20	A 12-step Program for CGMPs: Lessons of a Pharmaceutical Lifetime	81
21	Is Anybody Listening?	93
22	The Troublesome Media Fill	97
23	Contamination of an Aseptic Fill	101
24	The Green Blob	107
	Current Regulations, Guidances, Technical Reports and Texts Useful For Further Reference	111