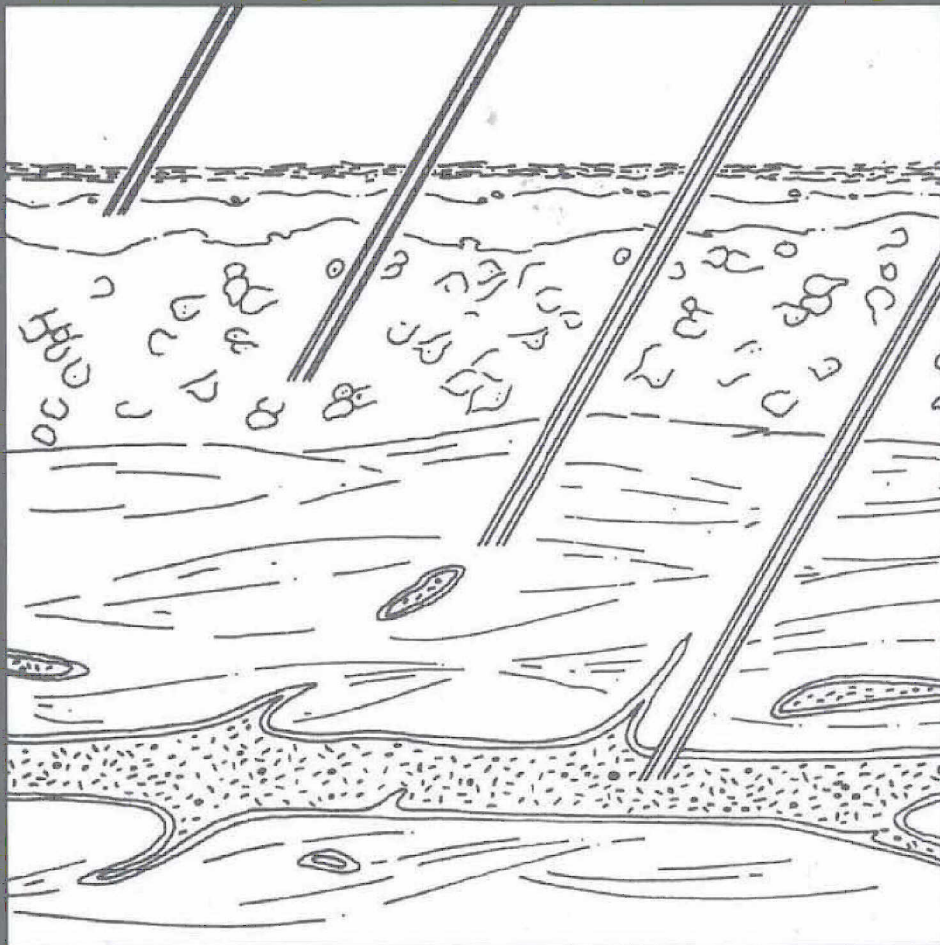


# *Parenteral Technology Manual*



**Michael J. Groves**



**Interpharm Press**

**SECOND EDITION**

# *PARENTERAL TECHNOLOGY MANUAL*

AN INTRODUCTION TO  
FORMULATION, PRODUCTION AND QUALITY  
ASPECTS OF PARENTERAL PRODUCTS

SECOND EXPANDED EDITION

---

*Michael J. Groves*

College of Pharmacy  
University of Illinois at Chicago

Printing History:

Parenteral Technology Manual — First Edition, 1985

Reprinted, 1986

Second Edition, 1988

Second Edition ISBN: 0-935184-10-4

©Copyright, January 1989 by Interpharm Press Inc.,

P.O. Box 530,

Prairie View, IL 60069, USA

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 form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without written permission from the publisher. Made in the United States of America.

Where a product trademark, registration mark or other protected mark is made in the text, the ownership of the mark remains with the lawful owner of the mark. No claim of ownership, intentional or otherwise, is made by reference to any such marks in this book.

While every effort has been made by Interpharm Press Inc. to ensure the accuracy of the information contained in this book, this organization accepts no responsibility for errors or omissions.

# PARENTERAL TECHNOLOGY MANUAL

## SECOND EDITION

---

<i>Chapter 1</i>	
Overview .....	1
<i>Chapter 2</i>	
Perspectives on the Use and Essential Requirements of Parenteral Products .....	3
<i>Chapter 3</i>	
Water .....	17
<i>Chapter 4</i>	
Electrolytes and Adjuvants .....	37
<i>Chapter 5</i>	
Non-Aqueous Systems, Dispersions and Emulsions .....	49
<i>Chapter 6</i>	
Hyperalimentation Solutions and Admixtures .....	63
<i>Chapter 7</i>	
Dry Powders .....	73
<i>Chapter 8</i>	
Filtration .....	83
<i>Chapter 9</i>	
Containers and Their Seals .....	99
<i>Chapter 10</i>	
Sterilization and Depyrogenation .....	119
<i>Chapter 11</i>	
Sterility Testing, Pyrogens and Pyrogen Testing .....	145
<i>Chapter 12</i>	
Particulate Contamination and Testing .....	159
<i>Chapter 13</i>	
The Production Environment .....	183
<i>Chapter 14</i>	
The Quality of Injectable Products .....	195
<i>Chapter 15</i>	
Regulation Issues Affecting the Parenteral Industry .....	209
<i>Index</i> .....	225

## FIGURES

---

### Chapter 2

1. Injection routes into and through the skin . . . . . 7
2. Intrathecal injection routes into the subarachnoid space surrounding the spinal cord . . . . . 8
3. Intracisternal route for withdrawing cerebrospinal fluid . . . . . 9
4. The effect of route of injection on the intensity of action of a hypothetical drug as measured by the blood level–time curve . . . . . 10

### Chapter 3

5. Preparation of Water for Injection (WFI) . . . . . 19
6. A simple water still . . . . . 20
7. Temperature/energy diagram for water . . . . . 21
8. Multiple effect stills with boilers and condensers connected in series . . . . . 21
9. Vapor compression still . . . . . 23
10. Relationship between temperature and pressure of water vapor . . . . . 24
11. Principle of Reverse Osmosis (RO) . . . . . 25
12. Water storage system . . . . . 29
13. Pure steam generator . . . . . 31

### Chapter 5

14. Preparation of a sterile suspension . . . . . 52
15. Production flow diagram for a hypothetical intravenous emulsion . . . . . 57

### Chapter 7

16. Preparation of a crystalline powder fill . . . . . 74
17. Freeze drying as applied with a powder fill or an *in situ* lyophilization . . . . . 75
18. Water vapor pressure vs temperature curve for water . . . . . 77
19. Phase equilibrium diagram for a typical salt water system . . . . . 78
20. Preparation of a sterile spray dried powder . . . . . 80

### Chapter 8

21. Mechanisms for particles to impinge on a capturing surface . . . . . 87

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.