

SEVENTH EDITION
**PHARMACEUTICAL
DOSAGE FORMS
AND DRUG
DELIVERY SYSTEMS**

Howard C. Ansel

Loyd V. Allen, Jr.

Nicholas G. Popovich



Editor: Donna Balado
Managing Editor: Jennifer Schmidt
Marketing Manager: Christine Kushner

Copyright © 1999 Lippincott Williams & Wilkins

351 West Camden Street
Baltimore, Maryland 21201-2436 USA

227 East Washington Square
Philadelphia, PA 19106

All rights reserved. This book is protected by copyright. No part of this book may be reproduced in any form or by any means, including photocopying, or utilized by any information storage and retrieval system without written permission from the copyright owner.

The publisher is not responsible (as a matter of product liability, negligence, or otherwise) for any injury resulting from any material contained herein. This publication contains information relating to general principles of medical care which should not be construed as specific instructions for individual patients. Manufacturers' product information and package inserts should be reviewed for current information, including contraindications, dosages, and precautions.

Printed in the United States of America

Library of Congress Cataloging-in-Publication Data

Ansel, Howard C., 1933–
Pharmaceutical dosage forms and drug delivery systems / Howard C.
Ansel, Loyd V. Allen, Jr., Nicholas G. Popovich. — 7th ed.
p. cm.
Includes bibliographical references and index.
ISBN 0-683-30572-7
1. Drugs—Dosage forms. 2. Drug delivery systems. I. Allen, Loyd V.
II. Popovich, Nicholas G. III. Title.
[DNLM: 1. Dosage Forms. 2. Drug Delivery Systems. QV 785 A618i 1999]
RS200.A57 1999
615'.1—dc21
DNLM/DLC
for Library of Congress

99-17498
CIP

The publishers have made every effort to trace the copyright holders for borrowed material. If they have inadvertently overlooked any, they will be pleased to make the necessary arrangements at the first opportunity.

The use of portions of the text of USP23/NF18, copyright 1994, is by permission of the USP Convention, Inc. The Convention is not responsible for any inaccuracy of quotation or for any false or misleading implication that may arise from separation of excerpts from the original context or by obsolescence resulting from publication of a supplement.

To purchase additional copies of this book call our customer service department at (800) 638-3030 or fax orders to (301) 824-7390. International customers should call (301) 714-2324.

99 00 01 02
1 2 3 4 5 6 7 8 9 10



Contents

Preface	v
Acknowledgments	vii
Section I. PRINCIPLES OF DOSAGE FORM DESIGN AND DEVELOPMENT	
1 Introduction to Drugs and Pharmacy	1
2 New Drug Development and Approval Process	23
3 Dosage Form Design: Pharmaceutic and Formulation Considerations	60
4 Dosage Form Design: Biopharmaceutic and Pharmacokinetic Considerations	101
5 Current Good Manufacturing Practices and Good Compounding Practices	142
Section II. SOLID DOSAGE FORMS AND MODIFIED-RELEASE DRUG DELIVERY SYSTEMS	
6 Powders and Granules	164
7 Capsules and Tablets	179
8 Modified-Release Dosage Forms and Drug Delivery Systems	229
Section III. SEMI-SOLID AND TRANSDERMAL SYSTEMS	
9 Ointments, Creams, and Gels	244
10 Transdermal Drug Delivery Systems	263

Section IV. PHARMACEUTICAL INSERTS	
11 Suppositories and Inserts	279
Section V. LIQUID DOSAGE FORMS	
12 Solutions	296
13 Disperse Systems	346
Section VI. STERILE DOSAGE FORMS AND DELIVERY SYSTEMS	
14 Parenterals	397
15 Biologicals	450
16 Ophthalmic Solutions and Suspensions	469
Section VII. NOVEL AND ADVANCED DOSAGE FORMS, DELIVERY SYSTEMS, AND DEVICES	
17 Radiopharmaceuticals	487
18 Products of Biotechnology	503
19 Novel Dosage Forms and Drug Delivery Technologies	535
Appendix	
Systems and Techniques of Pharmaceutical Measurement	552
Index	563

PARENTERALS

Chapter at a Glance

Injections

Parenteral Routes of Administration

- Intravenous Route
- Intramuscular Route
- Subcutaneous Route
- Intradermal Route
- Specialized Access

Official Types of Injections

Solvents and Vehicles for Injections

Nonaqueous Vehicles

Added Substances

Methods of Sterilization

- Steam Sterilization
- Dry-Heat Sterilization
- Sterilization by Filtration
- Gas Sterilization
- Sterilization by Ionizing Radiation

Validation of Sterility

- Pyrogens and Pyrogen Testing

The Industrial Preparation of Parenteral Products

Packaging, Labeling, and Storage of Injections

Quality Assurance for Pharmacy-Prepared Sterile Products

Available Injections

Small Volume Parenterals

Insulin Injection (Regular)

Human Insulin

Lispro Insulin Solution

Isophane Insulin Suspension (NPH Insulin)

Isophane Insulin Suspension and Insulin Injection

Insulin Zinc Suspension

Extended Insulin Zinc Suspension

Prompt Insulin Zinc Suspension

Insulin Infusion Pumps

Large Volume Parenterals (LVPs)

Maintenance Therapy

Replacement Therapy

Water Requirement

Electrolyte Requirement

Caloric Requirements

Parenteral Hyperalimentation

Enteral Nutrition

Intravenous Infusion Devices

Special considerations associated with parenteral therapy

Adsorption of Drugs

Handling/Disposal of Chemotherapeutic Agents for Cancer

Other Injectable Products—Pellets or Implants

Levonorgestrel Implants

Irrigation and Dialysis Solutions

Irrigation Solutions

Dialysis Solutions

CONSIDERED IN this chapter are important pharmaceutical dosage forms that have the common characteristic of being prepared to be sterile; that is, free from contaminating microorganisms. Among these sterile dosage forms are the various small- and large-volume injectable preparations, irrigation flu-

ids intended to bathe body wounds or surgical openings, and dialysis solutions. Biological preparations as vaccines, toxoids, and antitoxins are also among this group and discussed in Chapter 15. Sterility in these preparations is of utmost importance because they are placed in direct contact with

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.