



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 delievery 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
```

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
Acknov	vledgments	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



ix

Contents

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	



DISPERSE SYSTEMS

Chapter at a Glance

Suspensions

Reasons for Suspensions

Features Desired in a Pharmaceutical

Suspension

Physical Features of the Dispersed Phase of

a Suspension Dispersion Medium

Preparation of Suspensions

Sustained-Release Suspensions

Extemporaneous Compounding of

Suspensions

Packaging and Storage of Suspensions

Examples of Oral Suspensions

Antacid Oral Suspensions

Antibacterial Oral Suspensions

Examples of Other Suspensions

Otic Suspensions

Rectal Suspensions

Dry Powders for Oral Suspension

Emulsions

Purpose of Emulsions and of

Emulsification

Theories of Emulsification

Preparation of Emulsions

Emulsifying Agents

The HLB System

Methods of Emulsion Preparation

Continental or Dry Gum Method

English or Wet Gum Method

Bottle or Forbes Bottle Method

Auxiliary Methods

In Situ Soap Method

Microemulsions

Stability of Emulsions

Aggregation and Coalescence

Examples of Oral Emulsions

Mineral Oil Emulsion

Castor Oil Emulsion

Simethicone Emulsion

Gels and Magmas

Colloidal Dispersions

Terminology Related to Gels

Classification and Types of Gels

Preparation of Magmas and Gels

Examples of Gelling Agents

Gel Formulation Considerations

Examples of Magmas and Gels

Bentonite Magma, NF

Aluminum Hydroxide Gel, USP

Milk of Magnesia, USP

Starch Glycerite

Lubricating Jelly Formula

Clear Aqueous Gel with Dimethicone

Poloxamer Gel Base

Proper Administration and Use of

Disperse Systems

Aerosols

Advantages of the Aerosol Dosage

Form

The Aerosol Principle

Aerosol Systems

Two-phase Systems

Three-phase Systems

Compressed Gas Systems

Aerosol Container and Valve Assembly

Containers

Valve Assembly

Metered Dose Inhalers (MDIs)

Filling Operations

Cold Filling

Pressure Filling

Testing the Filled Containers

Packaging, Labeling, and Storage

Proper Administration and Use of

Pharmaceutical Aerosols

Topical Aerosols

Vaginal and Rectal Aerosols



346

DOCKET

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.

