

2 0 T H E D I T I O N

---

# Remington: The Science and Practice of Pharmacy

**ALFONSO R GENNARO**

Chairman of the Editorial Board  
and Editor

*Editor:* Daniel Limmer  
*Managing Editor:* Matthew J. Hauber  
*Marketing Manager:* Anne Smith

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*

Entered according to Act of Congress, in the year 1885 by Joseph P Remington, in the Office of the Librarian of Congress, at Washington DC

Copyright 1889, 1894, 1905, 1907, 1917, by Joseph P Remington

Copyright 1926, 1936, by the Joseph P Remington Estate

Copyright 1948, 1951, by the Philadelphia College of Pharmacy and Science

Copyright 1956, 1960, 1965, 1970, 1975, 1980, 1985, 1990, 1995, by the Philadelphia College of Pharmacy and Science

Copyright 2000, by the University of the Sciences in Philadelphia

*All Rights Reserved*  
Library of Congress Catalog Card Information is available  
ISBN 0-683-306472

*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 structural formulas from USAN and the USP Dictionary of Drug Names is by permission of The USP Convention. The Convention is not responsible for any inaccuracy contained herein.*

*Notice—This text is not intended to represent, nor shall it be interpreted to be, the equivalent of or a substitute for the official United States Pharmacopeia (USP) and/or the National Formulary (NF). In the event of any difference or discrepancy between the current official USP or NF standards of strength, quality, purity, packaging and labeling for drugs and representations of them herein, the context and effect of the official compendia shall prevail.*

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

# Table of Contents

<b>Part 1 Orientation</b>		49 Biotechnology and Drugs . . . . .	944
1 Scope of Pharmacy . . . . .	3	50 Aerosols . . . . .	963
2 Evolution of Pharmacy . . . . .	7	51 Quality Assurance and Control . . . . .	980
3 Ethics and Professionalism . . . . .	19	52 Stability of Pharmaceutical Products . . . . .	986
4 The Practice of Community Pharmacy . . . . .	28	53 Bioavailability and Bioequivalency Testing . . . . .	995
5 Pharmacists in Industry . . . . .	33	54 Plastic Packaging Materials . . . . .	1005
6 Pharmacists in Government . . . . .	38	55 Pharmaceutical Necessities . . . . .	1015
7 Pharmacists and Public Health . . . . .	47	<b>Part 6 Pharmacodynamics</b>	
8 Information Resources in Pharmacy and the Pharmaceutical Sciences . . . . .	60	56 Diseases: Manifestations and Pathophysiology . . . . .	1053
9 Clinical Drug Literature . . . . .	70	57 Drug Absorption, Action, and Disposition . . . . .	1098
10 Research . . . . .	81	58 Basic Pharmacokinetics . . . . .	1127
<b>Part 2 Pharmaceutics</b>		59 Clinical Pharmacokinetics . . . . .	1145
11 Pharmaceutical Calculations . . . . .	91	60 Principles of Immunology . . . . .	1156
12 Statistics . . . . .	124	61 Adverse Drug Reactions . . . . .	1165
13 Molecular Structure, Properties, and States of Matter . . . . .	159	62 Pharmacogenetics . . . . .	1169
14 Complex Formation . . . . .	183	63 Pharmacological Aspects of Substance Abuse . . . . .	1175
15 Thermodynamics . . . . .	198	<b>Part 7 Pharmaceutical and Medicinal Agents</b>	
16 Solutions and Phase Equilibria . . . . .	208	64 Diagnostic Drugs and Reagents . . . . .	1185
17 Ionic Solutions and Electrolytic Equilibria . . . . .	227	65 Topical Drugs . . . . .	1200
18 Tonicity, Osmoticity, Osmolality, and Osmolarity . . . . .	246	66 Gastrointestinal and Liver Drugs . . . . .	1219
19 Chemical Kinetics . . . . .	263	67 Blood, Fluids, Electrolytes, and Hematological Drugs . . . . .	1243
20 Interfacial Phenomena . . . . .	275	68 Cardiovascular Drugs . . . . .	1274
21 Colloidal Dispersions . . . . .	288	69 Respiratory Drugs . . . . .	1297
22 Coarse Dispersions . . . . .	316	70 Sympathomimetic Drugs . . . . .	1305
23 Rheology . . . . .	335	71 Cholinomimetic Drugs . . . . .	1314
<b>Part 3 Pharmaceutical Chemistry</b>		72 Adrenergic and Adrenergic Neuron Blocking Drugs . . . . .	1322
24 Inorganic Pharmaceutical Chemistry . . . . .	359	73 Antimuscarinic and Antispasmodic Drugs . . . . .	1328
25 Organic Pharmaceutical Chemistry . . . . .	385	74 Skeletal Muscle Relaxants . . . . .	1333
26 Natural Products . . . . .	409	75 Diuretic Drugs . . . . .	1344
27 Drug Nomenclature—United States Adopted Names . . . . .	441	76 Uterine and Antimigraine Drugs . . . . .	1354
28 Structure-Activity Relationship and Drug Design . . . . .	458	77 Hormones and Hormone Antagonists . . . . .	1358
29 Fundamentals of Radionuclides . . . . .	469	78 General Anesthetics . . . . .	1395
<b>Part 4 Pharmaceutical Testing, Analysis and Control</b>		79 Local Anesthetics . . . . .	1400
30 Analysis of Medicinals . . . . .	485	80 Sedative and Hypnotic Drugs . . . . .	1407
31 Biological Testing . . . . .	540	81 Antiepileptic Drugs . . . . .	1421
32 Clinical Analysis . . . . .	552	82 Psychopharmacologic Agents . . . . .	1429
33 Chromatography . . . . .	587	83 Analgesic, Antipyretic, and Anti-Inflammatory Drugs . . . . .	1444
34 Instrumental Methods of Analysis . . . . .	614	84 Histamine and Antihistaminic Drugs . . . . .	1464
35 Dissolution . . . . .	654	85 Central Nervous System Stimulants . . . . .	1471
<b>Part 5 Pharmaceutical Manufacturing</b>		86 Antineoplastic and Immunoactive Drugs . . . . .	1477
36 Separation . . . . .	669	87 Anti-Infectives . . . . .	1507
37 Powders . . . . .	681	88 Parasiticides . . . . .	1562
38 Preformulation . . . . .	700	89 Immunizing Agents and Allergenic Extracts . . . . .	1567
39 Solutions, Emulsions, Suspensions, and Extracts . . . . .	721	<b>Part 8 Pharmacy Practice</b>	
40 Sterilization . . . . .	753	<b>Part 8A Pharmacy Administration</b>	
41 Parenteral Preparations . . . . .	780	90 Laws Governing Pharmacy . . . . .	1595
42 Intravenous Admixtures . . . . .	807	91 Pharmacoeconomics . . . . .	1625
43 Ophthalmic Preparations . . . . .	821	92 Marketing Pharmaceutical Care Services . . . . .	1634
44 Medicated Topicals . . . . .	836	93 Documenting and Billing for Pharmaceutical Care Services . . . . .	1640
45 Oral Solid Dosage Forms . . . . .	858	94 Community Pharmacy Economics and Management . . . . .	1650
46 Coating of Pharmaceutical Dosage Forms . . . . .	894	95 Product Recalls and Withdrawals . . . . .	1666
47 Controlled-Release Drug-Delivery Systems . . . . .	903	<b>Part 8B Fundamentals of Pharmacy Practice</b>	
48 The Introduction of New Drugs . . . . .	930	96 Drug Education . . . . .	1677

97	The Prescription	1687
98	Extemporaneous Prescription Compounding	1706
99	Poison Control	1716
100	Nutrition in Pharmacy Practice	1725
101	Self-Care/Diagnostic Products	1738
102	Drug Interactions	1746
103	Complementary and Alternative Medical Health Care	1762
104	Nuclear Pharmacy Practice	1781
105	Enzymes	1792
106	Vitamins and Other Nutrients	1796
107	Pesticides	1825
108	Surgical Supplies	1846
109	Health Accessories	1857

**Part 8C Patient Care**

110	Ambulatory Patient Care	1893
111	Institutional Patient Care	1911
112	Long-Term Care Facilities	1932

113	The Patient: Behavioral Determinants	1948
114	Patient Communication	1957
115	Patient Compliance	1966
116	Pharmacoepidemiology	1980
117	Integrated Health-Care Delivery Systems	1990
118	Home Health Patient Care	2012
119	Aseptic Technology for Home-Care Pharmaceuticals	2020

**Appendixes**

Dose Equivalents	2033
Periodic Chart	2034
Logarithms	2036

**Glossary and Index**

Glossary	2037
Index	2039

# Ophthalmic Preparations

## Gerald Hecht, PhD

Senior Director, Pharmaceutical Sciences  
Alcon Laboratories  
Fort Worth, TX 76101

Ophthalmic preparations are sterile products essentially free from foreign particles, suitably compounded and packaged for instillation into the eye. Ophthalmic preparations include solutions, suspensions, ointments, and solid dosage forms. The solutions and suspensions are, for the most part, aqueous. Ophthalmic ointments usually contain a white petrolatum-mineral oil base.

Ophthalmic preparations can be grouped broadly into two divisions of major significance to the pharmacist. These include single or multidose prescription products and the category described as OTC or over-the-counter ophthalmic products. The latter group has been subjected to a searching review and analysis by a body of experts as a part of the Food and Drug Administration's (FDA) OTC Drug Review process.

The single dominant factor characteristic of all ophthalmic products is the specification of sterility. Any product intended for use in the eye regardless of form, substance, or intent must be sterile. This requirement increases the similarity between ophthalmic and parenteral products; however the physiology of the human eye in many respects imposes more rigid formulation requirements. This is considered in the following discussion.

Preparations intended for the treatment of eye disorders can be traced to antiquity. Egyptian papyri writings describe eye medications. The Greeks and Romans expanded such uses and gave us the term *collyria*. Collyria refers collectively to materials that were dissolved in water, milk, or egg white for use as eyedrops. In the Middle Ages collyria included mydriatic substances to dilate the pupils of milady's eyes for cosmetic purposes, thus the term *belladonna*, or *beautiful lady*.

From the time of belladonna collyria, ophthalmic technology progressed at a pharmaceutical snail's pace well into modern times. It was not until after World War II that the concept of sterility became mandatory for ophthalmic solutions. Prior to World War II and continuing into the 1940s very few ophthalmic preparations were available commercially or were described officially. The USP XIV, official in 1950, included only three ophthalmic preparations, and all three were ointments.

Preparations to be used in the eye, either solutions or ointments, invariably were compounded in the community or hospital pharmacy and were intended for immediate (prescription) use. Such preparation and prompt use is reflected in the pharmaceutical literature of the times. The stability of ophthalmic preparations is discussed in terms of days or a few months.

One of the most important attributes of ophthalmic products is the requirement of sterility. Even that, however, is a surprisingly recent event. The USP XV in 1955 was the first official compendium to include a sterility requirement for ophthalmic solutions. The FDA in 1953 adopted the position that a nonsterile ophthalmic solution was adulterated. Sterile ophthalmic products were, of course, available prior to the mid-1950s; however the legal requirement of sterility dates only from 1955.

The sterility requirements for ophthalmic ointments appeared first in the USP XVIII, *Third Supplement* (1972). Prior to that date there was no legal requirement for a sterile ophthalmic ointment. This probably was due to the difficulty (at that time) of testing for sterility in such nonaqueous systems and also the anticipated difficulties in sterilizing and maintaining sterile conditions during the manufacture and filling of ointments on a large scale.

## ANATOMY AND PHYSIOLOGY OF THE EYE

The human eye is a challenging subject for topical administration of drugs. The basis of this can be found in the anatomical arrangement of the surface tissues and in the permeability of the cornea. The protective operation of the eyelids and lacrimal system is such that there is rapid removal of material instilled into the eye, unless the material is suitably small in volume and chemically and physiologically compatible with surface tissues. Figures 43-1<sup>1</sup> and 43-2<sup>1</sup> include pertinent anatomy of the human eye.

**EYELIDS**—The eyelids serve two purposes: mechanical protection of the globe and creation of an optimum milieu for the cornea. The eyelids are lubricated and kept fluid-filled by secretions of the lacrimal glands and specialized cells residing in the bulbar conjunctiva. The antechamber has the shape of a narrow cleft directly over the front of the eyeball, with pocket-like extensions upward and downward. The pockets are called the superior and inferior fornices (vaults), and the entire space, the cul-de-sac. The elliptical opening between the eyelids is called the palpebral fissure.

**EYEBALL**—The wall of the human eyeball (bulbus, globe) is composed of three concentric layers.

1. The outer fibrous layer.
2. A middle vascular layer—the uvea or uveal tract, consisting of the choroid, the ciliary body, and the iris.
3. A nervous layer—the retina.

The outer layer is tough, pliable, but only slightly stretchable. In its front portion—the portion facing the outside world—the fine structure of the outer layer is so regular and the water content so carefully adjusted that it acts as a clear, transparent window (the cornea). It is devoid of blood vessels. Over the remaining two-thirds the fibrous coat is opaque (the *white* of the eye) and is called the sclera. It contains the microcirculation, which nourishes the tissues of this anterior segment, and is usually white except when irritated and vessel dilatation occurs.

The eyeball houses an optical apparatus that causes inverted reduced images of the outside world to form on the retina, which is a thin translucent membrane. The optical apparatus consists, in sequence, of the precorneal film, the cornea, the aqueous humor, the pupil, the crystalline lens, the

# 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.