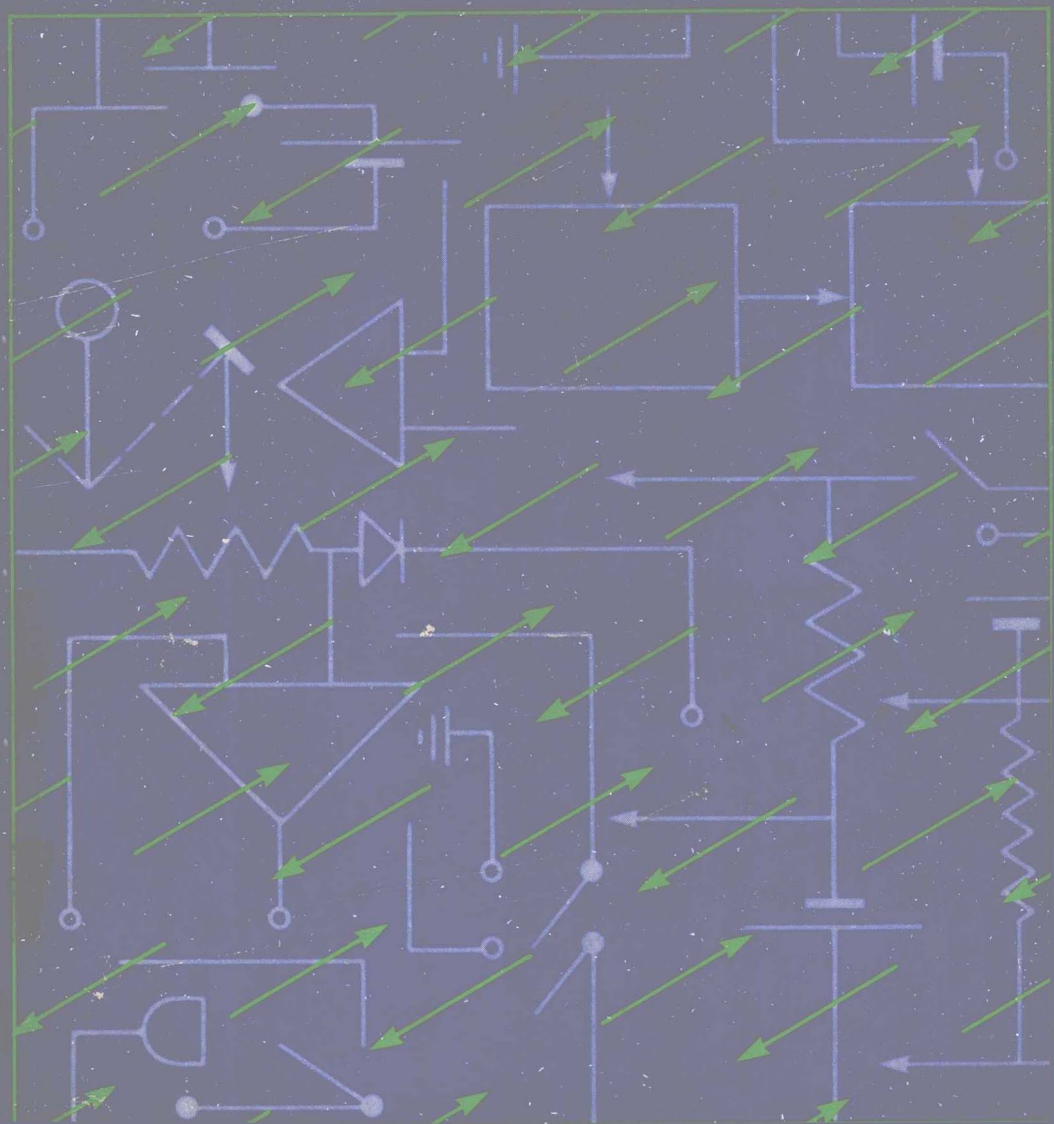


# GUIDE TO MEDICAL LABORATORY INSTRUMENTS

Clifford D. Ferris, D.Sc., P.E.



# Guide to Medical Laboratory Instruments

---

Clifford D. Ferris, D.Sc., P.E.

Professor and Director,  
Bioengineering Program,  
University of Wyoming, Laramie

Little, Brown and Company, Boston

Copyright © 1980 by Little, Brown and Co., (Inc.)

First Edition

All rights reserved. No part of this book may be reproduced in any form or by any electronic or mechanical means, including information storage and retrieval systems, without permission in writing from the publisher, except by a reviewer who may quote brief passages in a review.

Library of Congress Catalog Card No. 80-80585

ISBN 0-316-28127-1

Printed in the United States of America

HAL

## Preface

---

This book has evolved from a course taught during the past 6 years to second-semester, junior-year students in the Medical Technology Program at the University of Wyoming. The purpose of the course and this text is to familiarize students with the operating principles of various classes of electronic instruments used in the clinical laboratory before they enter their year of clinical training. Electronic equipment is now used extensively in clinical chemistry laboratories. In most programs, unfortunately, much, if not all, of the training during the internship year is devoted to chemistry, hematology, and microbiology. The little training given in the operation of electronic equipment is frequently provided only as an afterthought. Many of the instruments and applications described in this book are equally useful in research laboratories. Thus, the book should prove valuable to workers outside of hospital clinical laboratories.

The book is divided into four subject areas. The first two chapters provide the basic electrical “vocabulary” necessary for intelligent reading of equipment instruction and operation manuals, as well as the elementary principles of electricity and electronics. Chapter 3 describes some of the many optical devices used in clinical laboratory instruments. Chapters 4 to 12 cover the design and operation of various classes of equipment. With only a few exceptions, there is no mention of specific models or suppliers of commercial equipment. This policy was adopted for two reasons: First, model changes occur annually—more often in some cases. Basic design philosophy, however, remains relatively stable. Second, differences among different instrument models usually relate to user convenience features, measurement range, sensitivity, and degree of automation, while the physical principles of operation are very similar, if not identical. Thus, our approach is to emphasize certain design techniques common to a specific class of instruments. With this type of background, the reader should then be able to operate any model of that class of instrument with only a brief reading of the operation manual.

It should be pointed out that the occasional reference to a commercial product of a particular manufacturer does not constitute an endorsement of the product or lack of endorsement of other such products.

The subject of Chapter 13 is general laboratory safety, especially the hazard of electric shock and its prevention. Various regulations and regulatory bodies that affect laboratory operation are described briefly. While possible device malfunctions and operator errors are stressed throughout the instrument descrip-

tion chapters, Chapter 14 focuses specifically on troubleshooting procedures. The emphasis is placed on those procedures that the technologist can carry out in the laboratory environment.

The final chapter examines several matters related to the use of equipment and general laboratory operation. Included are instrument accuracy and precision, calibration, quality control, data reporting, record keeping, liability, and licensing.

The Appendix provides a review of basic exponential and logarithmic functions. Techniques for graphic presentation of data are included, with emphasis on instrument calibration curves.

A set of 10 exercise problems is included at the end of each chapter (including the Appendix), some of which require outside work on the student's part. These include checking instrument specifications and other matters that would normally occur in practice.

For the most part, the International System of Units (SI units) has been used in the text. Where medical convention differs from general scientific convention, the medical units are used. An example is the use of millimeters of mercury for pressure measurements, rather than kilopascals.

The book has been designed for readers with varying degrees of mathematical background. A knowledge of basic algebra, logarithms, and scientific notation is assumed. When the book is used as a class text, certain sections may be omitted at the discretion of the instructor. These sections are designated by an asterisk preceding the section heading.

Preparation of the first draft of the book was conducted while the author was on sabbatical leave from the University of Wyoming and serving as a Visiting Professor at the University of Colorado Medical School, in the Department of Biophysics, Biochemistry and Genetics. Mr. Kingsley C. Rock, Director of Bioengineering, kindly provided office space in his facility and made initial arrangements for the author to visit various laboratory facilities. Dr. J. Richard Pearson, Director of the Clinical Chemistry Laboratory, and Dr. Yasuhiko Takeda, Director of the Immunoassay Laboratory, willingly provided access to their respective laboratories and discussed operation of their facilities at Colorado General Hospital.

The author would also like to acknowledge with thanks the many courtesies provided, during visits to their institutions, by the following: Dr. Edward M. Lonsdale, Head, Biomedical Engineering and Communication Services, St. Joseph's Hospital, Tucson, Arizona; Dr. Loren P. McRae, Director of Bioengineering, Tucson Medical Center, Tucson, Arizona; Emanuel F. Furst, Director, Biomedical Engineering Division, Arizona Health Sciences Center, University of Arizona, Tucson, Ari-

zona. The author also acknowledges the many helpful suggestions made by his students during the class-testing phase of the manuscript, especially those made by Alonna S. Widdoss. Special thanks are due Gerry Eisenhower, Karen Nickerson, Liz Czapla, and Velma Vialpando, who produced the typed manuscript.

C.D.F.

# Symbols, Units, and Definitions

1. <i>Physical Quantity</i>	<i>Name of Unit</i>	<i>Unit Symbol</i>
mass	kilogram (gram)	kg (g)
length	meter	m
time	second	s, sec
electric charge	coulomb	C
amount of substance	mole	mol
energy	joule	J
force	newton	N
power	watt	W
pressure	millimeters of mercury or pounds per square inch	mm Hg, psi
temperature	degrees Kelvin or Celsius	K, °C
volume	liter	l
frequency	hertz	Hz
radian frequency	radians/second	rad/sec, rad s <sup>-1</sup>
osmolality	osmol	Osm
atomic mass unit	dalton	D
electric current	ampere	A
electric potential (voltage)	volt	V
electrical conductivity	siemen/meter	S/m, S m <sup>-1</sup>
electrical capacitance	farad	F (C <sup>2</sup> J <sup>-1</sup> )
electrical inductance	henry	H (J C <sup>-2</sup> s <sup>2</sup> )
electrical resistance	ohm	Ω (J s C <sup>-2</sup> )
gamma*	microgram	μg

\*This is an old term; we have restricted its use to fluorescent materials.

2. <i>Symbol</i>	<i>Definition</i>	<i>Symbol for Physical Unit</i>
<i>A</i>	area	m <sup>2</sup>
<i>A</i>	optical absorbance	—
<i>C</i>	electrical capacitance	F
<i>E</i>	electric field intensity	V m <sup>-1</sup> , V/m
<i>F</i>	Faraday constant	96,495 C mol <sup>-1</sup>
<i>F</i>	force	N
<i>H</i>	amount of heat	J (calorie)
<i>H</i>	heat flux	W m <sup>-2</sup>
<i>I, I</i>	electric current	A
<i>I</i>	light intensity	W m <sup>-2</sup>
<i>L</i>	electrical inductance	H
<i>P</i>	power	W
PCO <sub>2</sub>	partial pressure of carbon dioxide	mm Hg
PO <sub>2</sub>	partial pressure of oxygen	mm Hg
<i>Q</i>	electric charge	C
<i>Q</i>	figure of merit	—
<i>R</i>	electrical resistance	Ω

<i>Symbol</i>	<i>Definition</i>	<i>Symbol for Physical Unit</i>
$R$	universal gas constant	8.315 kJ kg <sup>-1</sup> mol deg K
$T$	temperature	K, °C
% $T$	optical percent transmittance	—
$U$	particle mobility	m <sup>2</sup> V <sup>-1</sup> s <sup>-1</sup> , m <sup>2</sup> C J <sup>-1</sup> s <sup>-1</sup>
$V, V$	electrical potential, voltage	V
$W$	energy	J
$X$	electrical reactance (AC resistance)	$\Omega$
$Z$	electrical impedance	$\Omega$
$Z$	valence	—
$c$	speed of light	$\sim 3 \times 10^8$ m s <sup>-1</sup>
$d$	length	m
dB	decibel	—
$e$	electronic charge	$1.6 \times 10^{-19}$ C
$f$	frequency	Hz
g%	concentration	g/100 ml
g/dl	concentration	g/100 ml
$h$	Planck's constant	$6.625 \times 10^{-34}$ J s
$i$	electric current	A
$j$	unit imaginary $\sqrt{-1}$	—
mEq/l	number of milliequivalents per liter	—
$P$	pressure	mm Hg
$q$	electric charge	C
$t$	time	s, sec
$u$	particle velocity	m s <sup>-1</sup> , m/s
$v$	electric potential, voltage	V
$x$	distance	m, cm
$\epsilon$	dielectric permittivity	F m <sup>-1</sup>
$\epsilon_r$	dielectric constant	—
$\eta$	dynamic viscosity	N s m <sup>-2</sup>
$\theta$	geometric angle	degrees, radians
$\lambda$	optical wavelength	nm, m
$\mu$	charge mobility	m <sup>2</sup> V <sup>-1</sup> s <sup>-1</sup> , m <sup>2</sup> C J <sup>-1</sup> s <sup>-1</sup>
$\mu$	magnetic permeability	H m <sup>-1</sup>
$\pi$	physical constant	3.1416
$\sigma$	electrical conductivity	S m <sup>-1</sup>
$\omega$	radian frequency	rad/sec, rad s <sup>-1</sup>
$O$	osmolality	Osm
$\kappa$	osmotic coefficient	—

### 3. Mathematical Symbols

=	equality
~	proportional to
>	greater than ( $\geq$ greater than or equal to)
<	less than ( $\leq$ less than or equal to)
$\infty$	infinity
	absolute value, magnitude
$\sqrt{\quad}$	square root
!	factorial
log	logarithm to the base 10
ln	logarithm to the base $e$
$e$	physical constant = 2.718



4. Multiples and Scientific Notation (S.N.)

<i>Factor</i>	<i>S.N.</i>	<i>Prefix</i>	<i>Symbol</i>
million millionth	$10^{-12}$	pico	p
thousand millionth	$10^{-9}$	nano	n
millionth	$10^{-6}$	micro	$\mu$
thousandth	$10^{-3}$	milli	m
hundredth	$10^{-2}$	centi	c
tenth	$10^{-1}$	deci	d
ten	$10^1$	deca	da
hundred	$10^2$	hecto	h
thousand	$10^3$	kilo	k
million	$10^6$	mega	M

# Guide to Medical Laboratory Instruments

---

# Contents

---

Preface	v
Symbols, Units, and Definitions	xvii

---

1 Basic Electricity	1
---------------------	---

---

1.1 Introduction	1
1.2 Basic Electrical Quantities	1
1.3 Time Variation of Voltage and Current	4
1.4 Some Practical Electrical Devices	9
1.4.1 Resistors	9
1.4.2 Inductors	14
1.4.3 Capacitors	17
1.5 Auxiliary Devices	22
1.6 Semiconductors and Integrated Circuits (Solid-State Devices)	22
1.7 Printed Circuit Boards	26
1.8 Summary	27
1.9 Problems	27

---

2 Instrumentation Systems: Modular Approach	29
---	----

---

2.1 Basic Systems	29
2.2 Some Electronic Circuits from the Functional Point of View	31
2.2.1 Attenuation	31
2.2.2 Signal Detection	32
2.2.3 Amplification	32
2.2.4 Feedback	33
2.2.5 Filters	34
2.2.6 Oscillators	34
2.3 Elementary Circuit Analysis	35
2.4 Electronic Bridges	39
2.5 Summary	40
2.6 Problems	41

---

3 Light Sources and Sensors	43
-----------------------------	----

---

3.1 Introduction	43
3.2 Light Sources	45
3.2.1 Incandescent Lamps	45
3.2.2 Gas-Discharge Lamps	47
3.2.3 Fluorescent Lamps	49
3.2.4 Solid-State Light Sources	50
3.3 Wavelength Selection: Monochromators	50
3.3.1 Filters	51
3.3.2 Prisms and Diffraction Gratings	52

- 3.3.3 Monochromators 54
- 3.4 Cuvet Design 56
- 3.5 Optical Detectors 57
  - 3.5.1 Phototubes 57
  - 3.5.2 Light-Detecting Diodes (Photodiodes) 58
  - 3.5.3 Photomultiplier Tubes 58
  - 3.5.4 Other Devices 59
  - 3.5.5 Dark Current 60
- 3.6 Displays 60
- 3.7 Bandwidth and Spectral Response 61
- 3.8 Summary 63
- 3.9 Problems 64

---

## 4 Instruments That Use Exciter Lamps

---

65

- 4.1 Introduction 65
- 4.2 Spectrophotometers 65
  - 4.2.1 General Considerations 65
    - 4.2.1.1 Beer-Lambert Law 65
    - 4.2.1.2 Light Sources 67
    - 4.2.1.3 Split-Beam Design 69
    - 4.2.1.4 Light Choppers 70
    - 4.2.1.5 Scanning Instruments 71
    - 4.2.1.6 Additional Factors 72
    - 4.2.1.7 Beer's Law Derivation 73
  - 4.2.2 Operating Techniques 74
  - 4.2.3 Operator Errors 77
- 4.3 Photofluorometers 77
  - 4.3.1 General Considerations 77
  - 4.3.2 Operating Techniques 78
  - 4.3.3 Operator Errors 79
  - 4.3.4 Quenching 79
- 4.4 Spectrofluorometers 80
- 4.5 Some General Considerations in the Use of Photometric Instruments 81
- 4.6 Special-Purpose Instruments 82
- 4.7 Nephelometers and Related Instruments 83
  - 4.7.1 Introduction 83
  - 4.7.2 Nephelometers 84
  - 4.7.3 Typical Nephelometer Protocol (Urine Protein Analysis) 85
- 4.8 Summary 86
- 4.9 Problems 86

---

## 5 Instruments That Use Flame Excitation

---

87

- 5.1 Introduction 87

5.2 Flame Photometers	87
5.2.1 Operating Techniques and Precautions	89
5.2.2 Operator Errors	92
5.3 Atomic Absorption-Emission Instruments	92
5.3.1 Emission Mode	93
5.3.2 Absorption Mode	93
5.3.3 General Considerations	94
5.3.3.1 Graphite-Tube Atomizer	95
5.3.3.2 Vapor Generation Assembly	96
5.3.4 Operator Errors	96
5.4 User Convenience Features	97
5.5 Carry-over	97
5.6 Summary	98
5.7 Problems	98
 6 Measurement of Electrolyte and Water Balance	 99
6.1 Introduction	99
6.2 Conductivity Measurements	99
6.2.1 Conductivity Bridge	99
6.3 Osmolality Measurements	101
6.3.1 Freezing-Point Osmometers	102
6.3.2 Calibration of Freezing-Point Osmometers	104
6.3.3 Operator Errors	105
6.3.4 Vapor-Pressure Osmometers	105
6.3.4.1 Colloid Osmometers	107
6.3.5 Osmolality Measurement Correlation	107
6.4 Discussion	107
6.5 Summary	108
6.6 Appendix: Thermocouples	108
6.7 Problems	109
 7 Ion-Selective Electrodes	 111
7.1 Introduction	111
7.2 Reference Electrodes	112
7.2.1 Silver-Silver Chloride Electrode	112
7.2.2 Calomel Electrode	113
7.2.3 General Considerations	113
7.3 Membrane Electrodes	114
7.3.1 pH Electrodes	114
7.3.2 Correction for Interfering Ions	116
7.3.3 Calibration	116
7.3.4 Care of Ion-Selective Electrodes	117
7.3.5 Solid-State Ion-Selective Electrodes	119
7.4 pH and Ion-Selective-Electrode Meters	119
7.4.1 Instrument Calibration and Use	120

7.4.2 Instrument Functions	121
7.5 Combination Electrodes	123
7.6 Polarographic Electrodes (Oxygen Measurement)	124
7.7 Carbon Dioxide Electrodes	125
7.8 Measurement of Chloride Ion	127
7.8.1 Chloride-Ion Electrodes	127
7.8.2 Coulometric Titration	127
7.8.3 Other Techniques	128
7.9 Glucose Determination	128
7.10 Blood Urea Nitrogen Determination	129
7.11 Summary	129
7.12 Problems	130

---

8 Particle Counters	131
---------------------	-----

---

8.1 Introduction	131
8.2 Blood-Cell Counters: Coulter Principle	131
8.2.1 Operating Problems	133
8.3 Optoelectronic Blood-Cell Counters	134
8.3.1 Errors and Problems	135
8.4 Cell-Counter Shutdown	136
8.5 Colony Counters	136
8.6 Other Applications	137
8.7 Summary	138
8.8 Appendix: Normal Adult Ranges for Hematological Parameters	138
8.9 Problems	139

---

9 Nuclear Counting	141
--------------------	-----

---

9.1 Introduction	141
9.2 Scintillation Counters (Crystal)	143
9.3 Scintillation Counters (Liquid)	145
9.4 Other Radioactivity Detectors	145
9.4.1 Geiger Counters	145
9.4.2 Film Badges	146
9.4.3 Ionization Chambers	147
9.4.4 Semiconductor Sensors	147
9.5 Summary	147
9.6 Problems	148

---

10 Automated Chemistry Analyzers	149
----------------------------------	-----

---

10.1 Introduction	149
10.1.1 Basic Concepts	150
10.1.2 Sequential and Parallel Operation	152
10.1.3 Design Philosophies	152
10.2 Flow Instruments	153

10.3 Discrete Analyzers	155
10.4 Centrifugal Analyzers (Centrifugally Operated Discrete Analyzers)	156
10.5 Summary	158
10.6 Problems	158
 11 Chromatography	 159
11.1 Introduction	159
11.2 Paper Chromatography	159
11.2.1 Substrate Selection	161
11.2.2 Solvent Selection	161
11.2.3 Two-Dimensional Paper Chromatography	162
11.2.4 Descending Chromatography	162
11.2.5 Development Time	163
11.2.6 Visualizing the Fractions	163
11.2.7 Identifying the Sample Fractions ( $R_f$ Numbers)	163
11.3 Thin-Layer Chromatography	164
11.3.1 Visualization in Thin-Layer Chromatography Plates	167
11.3.2 Toxicology Systems	167
11.4 Problems in Paper and Thin-Layer Chromatography Methods	168
11.4.1 Errors in Technique	168
11.5 Liquid Chromatography	168
11.5.1 High-Pressure Liquid Chromatography	170
11.5.1.1 Innovations in Column Chromatography	172
11.5.2 Portable Drug-Detection System	173
11.6 Gas Chromatography	174
11.6.1 Thermal-Conductivity Detectors	175
11.6.2 Flame Ionization Detectors	176
11.6.3 Electron-Capture Detectors	177
11.6.4 Other Detectors	178
11.6.5 Summary: Gas Chromatography	178
11.7 Summary	179
11.8 Problems	179
 12 Electrophoresis	 181
12.1 Basic Principles	181
12.2 Producing an Electrophoresis Record	182
12.2.1 Substrate Material	182
12.2.2 Buffer	183
12.2.3 The Chamber (Cell)	184
12.2.4 Power Supply	184
12.2.5 Running the Electrophoresis Separation	185
12.2.6 Summary: Serum-Protein Electrophoresis Plate Preparation	186
12.2.7 Stains	186

12.3	Errors in Technique and Other Problems	187
12.3.1	Endosmosis	188
12.4	Reading the Electrophoresis Plate: Densitometers	189
12.5	Interpreting the Electrophoretogram	190
12.6	System Errors	193
12.6.1	Dye Error	193
12.6.2	Albumin Tailing	193
12.6.3	Deviation from Beer's Law	194
12.7	Immunoelectrophoresis	194
12.8	Summary	194
12.9	Appendix: Mathematical Analysis of Electrophoresis	194
12.10	Problems	196

---

13	Laboratory Safety	197
----	-------------------	-----

---

13.1	Introduction	197
13.2	Basic Considerations	198
13.3	Fire	200
13.4	Chemicals and Compressed Gases	200
13.5	Biohazards	201
13.6	Other Hazards	203
13.7	Electrical Safety	203
13.7.1	Grounding	203
13.7.2	Electric Shock	205
13.7.3	Ground-Potential Differences	207
13.7.4	Some Electrical Safety Guidelines	207
13.8	Summary	209
13.9	Problems	209

---

14	Troubleshooting	211
----	-----------------	-----

---

14.1	Introduction	211
14.2	General Troubleshooting	211
14.2.1	Does the Instrument Have Power?	212
14.2.2	Instrument Pilot Lights	214
14.3	Instrument Has Power But Functions Poorly	215
14.3.1	Fuse Blows Repetitively	215
14.4	Optical Instruments—Nonflame	216
14.5	Optical Instruments—Flame	218
14.6	Conductivity Bridges	218
14.7	Osmometers	219
14.8	pH and Ion-Selective-Electrode Meters	220
14.9	Particle Counters	220
14.10	Scintillation Counters	221
14.11	Automated Chemistry Equipment	222
14.12	Chromatography	223
14.13	Electrophoresis Apparatus	223



14.14 Summary 224

14.15 Problems 225

---

15 Accuracy, Standards, and Related Matters 227

---

15.1 Introduction 227

15.1.1 Preventive Maintenance 228

15.2 Instrument Accuracy 228

15.2.1 Linearity 229

15.3 Standards 231

15.4 Quality Control 231

15.4.1 The Gaussian Distribution 235

15.5 Record Keeping, Test Reporting, and Liability 236

15.6 Licensing and Liability 237

15.7 Actions of The Food and Drug Administration 238

15.8 Summary 239

15.9 Problems 240

---

Appendix: Exponentials, Logarithms, and Graphs 241

---

A.1 Exponential Functions 241

A.2 Logarithms 241

A.3 Graphs 243

A.4 Problems 246

Bibliography 249

Index 251