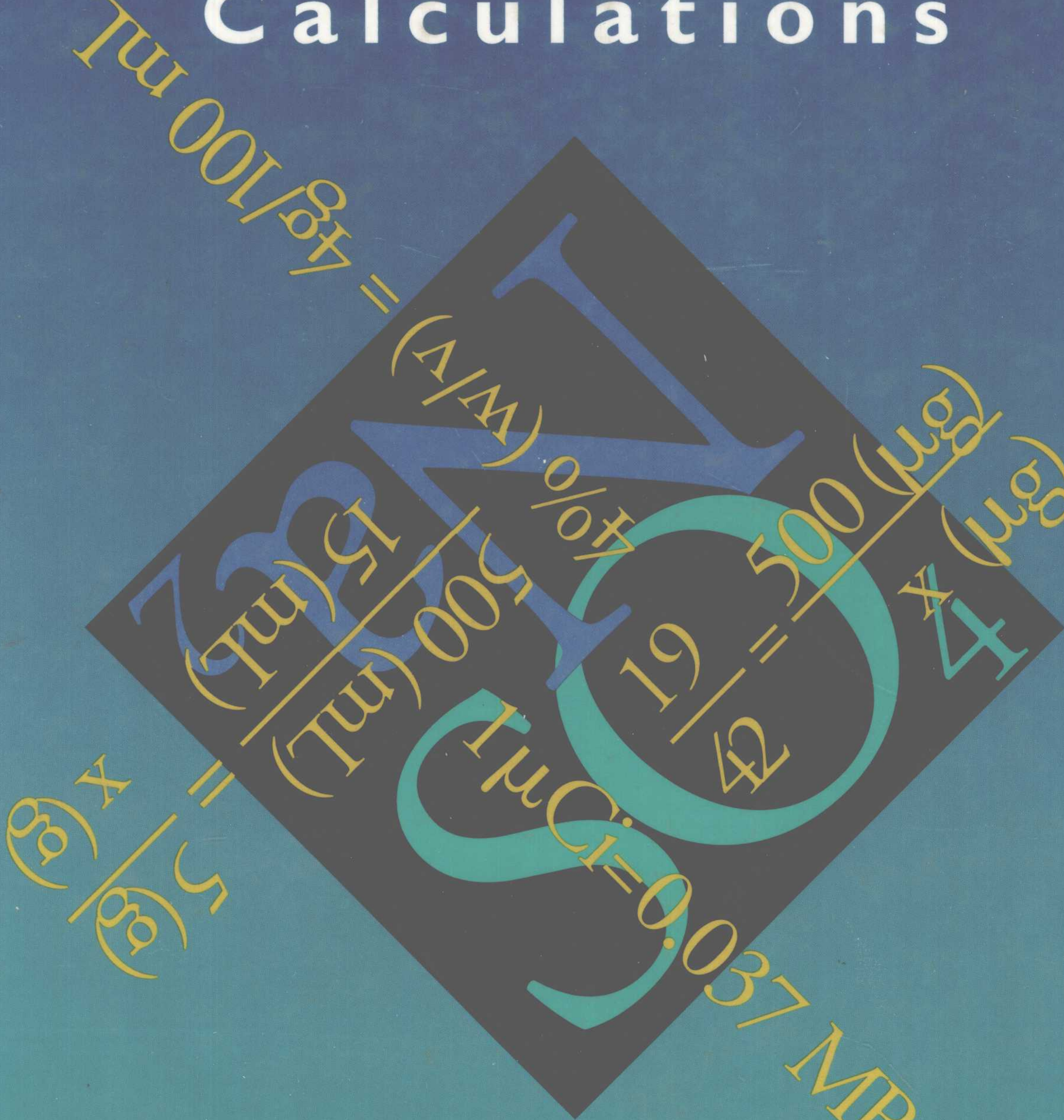
TENTH EDITION

Pharmaceutical Calculations



Mitchell J. Stoklosa

Howard C. Ansel

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Pharmaceutical Calculations

Mitchell J. Stoklosa, A.M., Sc.D.
Professor of Pharmacy Emeritus
Massachusetts College of Pharmacy
and Allied Health Sciences,
Boston, Massachusetts

Howard C. Ansel, Ph. D.
Professor of Pharmacy
College of Pharmacy
The University of Georgia
Athens, Georgia

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Accurate indications, adverse reactions, and dosage schedules for drugs are provided in this book, but it is possible they may change. The reader is urged to review the package information data of the manufacturers of the medications mentioned.

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Preface

This Tenth Edition of *Pharmaceutical Calculations* represents the most complete revision of this widely used textbook in its fifty-year history. Each chapter has been revised completely to reflect the dramatic changes in the practice of pharmacy and the requirements of today's and tomorrow's students and practitioners.

Among the changes, and the most significant, is the elimination of the apothecaries' system from the body of the text and the use throughout of the metric system. This is in recognition of contemporary practice in the United States and throughout the world and is in conformance with the new edition of the *United States Pharmacopeia*. For reference, the apothecaries' and avoirdupois systems and factors for intersystem conversion appear in an Appendix chapter along with the recommendation to convert to metric quantities in problem-solving.

Another new and useful reference Appendix chapter includes definitions and brief descriptions of the various pharmaceutical dosage forms and drug delivery systems. This is intended to assist the beginning pharmacy student in understanding the terminology and the purpose of calculations in the preparation of extemporaneously compounded and prefabricated dosing forms. A new section on the techniques of pharmaceutical measurement also has been included to assist beginning students, and may be of special benefit to those programs in which instruction in calculations is integrated with an initial pharmacy laboratory experience.

The introduction of *dimensional analysis* as a problem-solving technique has been added to the traditional approach of using ratio and proportion. A retitled chapter "Constituted Solutions, Intravenous Admixtures, and Rate of Flow Calculations," offers a new array of calculations for the constitution of dry powders for oral solution or suspension, for pediatric drops, and for parenteral use. A completely revised section on total parenteral nutrition includes standard formulas, parameters for use, and new and expanded treatment of problems involving electrolyte and caloric requirements. Another retitled chapter, "Some Calculations Involving Use of Prefabricated Dosage Forms in Compounding Procedures," presents a variety of problems involving the use of tablets, capsules, and injections as the drug-source in the extemporaneous compounding of prescriptions and medication orders.

Other changes include: an expanded discussion and related dosage problems for the pediatric and elderly patient; new material on the use of creatinine clearance dosage tables and the adjustment of dosage based on body surface area; a new section covering calculations based on parts-per-million; additional treatment of millimoles; the introduction of freezing-point data in solving isotonicity problems; and, the introduction of problems involving *tissue culture infectious dose* ($TCID_{50}$), *flocculating units (Lf)* and other measures of potency used in the dosing of biologic products. Where applicable, the International System (SI) of units of measure is integrated in the text and in problem sets.

As is the case with each of the primary chapters of the text, the Appendix chapters have been thoroughly evaluated and retained when considered useful, excluded when not, revised as needed, and new chapters added as noted. Throughout the text, new example and practice problems have replaced older ones and the comprehensive section of review problems has been completely revised to reflect modern therapies.

On this, the golden anniversary of this textbook, the authors acknowledge the wonderful heritage to this work provided by Professors Willis T. Bradley and Carroll B. Gustafson, and express with gratitude the many helpful comments and suggestions of colleagues and students so thoughtfully and generously provided during the preparation of this revision.

Special appreciation is extended to Keith N. Herist for his contributions in the area of dimensional analysis.

Boston, Massachusetts Mitchell J. Stoklosa
Athens, Georgia Howard C. Ansel

Introduction

SCOPE OF PHARMACEUTICAL CALCULATIONS

The use of calculations in pharmacy is varied and broad-based. It encompasses calculations performed by pharmacists in traditional as well as in specialized practice settings and within operational and research areas in industry, academia, and government.

In the broad context, the scope of pharmaceutical calculations includes computation of:

- Chemical purity, physical characteristics, and biological parameters of drug substances, pharmaceutical ingredients, dosage forms and drug delivery systems;
- Drug stability, rates of drug degradation, and shelf-life of pharmaceutical preparations;
- Rates of drug absorption, bodily distribution, metabolism, and elimination;
- Dosage, based on individual patient characteristics;
- Pharmaceutical formulations of various production batches;
- Individual prescriptions and medication orders requiring extemporaneous compounding;
- Various parameters of drug dynamics, clinical effectiveness, and safety in patient populations; and,
- Epidemiologic, sociologic, and economic impact of drugs and drug therapy, with statistical presentation and analysis.

For each of these, there is a body of knowledge upon which the premise and understanding of the calculation is based. Certain of these areas are more specialized or advanced than others and constitute separate and distinct areas of study. Others are more foundational, providing the basic underpinnings of pharmacy practice. It is upon the latter that this textbook is based.

The chapters and appendices in this text present an array of pharmaceutical calculations which have direct application to pharmacy practice in a variety of practice settings, including community, institutional, and industrial pharmacy.

In each of these settings, pharmacists provide for the medication needs of patients. In the community pharmacy, this is accomplished through the filling of a *prescription,* written by a physician or other authorized health care professional, and through the provision of appropriate clinical information to assure the safe and effective use of the medication. The prescription may call for a *prefabricated* pharmaceutical product manufactured in industry, or, the prescription may be written for individual components to be weighed or measured by the pharmacist and *compounded* extemporaneously into a finished product. In the hospital and other institutional settings, a *medication order* entered on the patient's chart constitutes the prescription.

Whether the pharmaceutical product provided to a patient is produced in the industrial setting or prepared in a community or institutional pharmacy, pharmacists engage in calculations to determine quantities of the various ingredients used to achieve standards of quality and proper dosage upon administration. The difference between industrially prepared pharmaceuticals and those extemporaneously compounded by the pharmacist is the *quantity* of product prepared. In the community and institutional pharmacy, prescriptions and medication orders call for relatively small quantities of medications for individual patients. In the hospital setting, the pharmacy may additionally engage in the *small-scale* manufacture of frequently prescribed medications for institutional use. However, in industry, there is the routine *large-scale* production to meet the requirements of pharmacists and their patients on a national and even international basis. This involves the production of hundreds of thousands or even millions of dosage units (e.g. tablets) of a given drug product during a production cycle. The calculations involved in the compounding of a single prescription to the large-scale production of pharmaceuticals is an important component of pharmacy calculations and of this textbook.

In the preparation of prescriptions or product formulations various medicinal and non-medicinal *(pharmaceutic)* materials are used. Some are solid materials, as powders, which are accurately weighed on a pharmaceutical balance prior to use. Other materials are liquids, which are usually measured volumetrically prior to use, although they may also be weighed. The primary components of any prescription or pharmaceutical product are the *active ingredients* or the *medicinal substances,* which provide the basis for the product in preventing, treating, or curing the target illness or disease. Other components are *inactive ingredients* which are included in a formulation to produce the desired physical form, for convenience and safety of dosage administration, and the desired pharmaceutical qualities, including chemical and physical stability, rates of drug release, product appearance, taste, and smell. Active and inactive ingredients are obtained in *bulk* quantities for use in the pharmaceutical manufacture of *finished pharmaceuticals,* that is, *dosage forms* (e.g. tablets) and *drug delivery systems* (e.g. transdermal skin patches). In the extemporaneous filling of compounded prescriptions in the community pharmacy, in instances in which the active ingredient is unavailable in bulk, pharmacists may utilize prefabricated dosage forms as tablets, capsules, or injections of the drug as the source of active ingredient.

With very few exceptions, drugs are prepared and administered to patients in various dosage forms and drug delivery systems to assure accurate dosing. It is important for the pharmacy student to have an appreciation for the various dosage forms and drug delivery systems utilized in patient care. Calculations common to each involve the determination of the quantities of active and inactive ingredients required to achieve the desired strength, concentration, or quantity of drug per dosage unit. Additionally, there are calculations which are specific to particular dosage forms, pharmaceutical techniques, and patient requirements. The various types of pharmaceutical dosage forms and drug delivery systems are briefly defined and described in Appendix M, "Glossary of Pharmaceutical Dosage Forms and Drug Delivery Systems."

Contents

1 Some Fundamentals of Measurement and Calculation

NUMBERS AND NUMERALS

A *number* is a total quantity, or amount, of units. A *numeral* is a word or sign, or a group of words or signs, expressing a number. For example, *3, 6,* and *48* are Arabic numerals expressing numbers that are, respectively, *3 times, 6 times,* and 48 times the unit *1*.

KINDS OF NUMBERS

In *arithmetic,* the science of calculating with positive, real numbers, a number is usually (a) a natural or *whole* number, or *integer,* such as *549;* (b) a *fraction,* or subdivision of a whole number, such as $\frac{4}{7}$; or (c) a *mixed* number, consisting of a whole number plus a fraction, such as $3\frac{7}{8}$.

A number such as *4, 8,* or *12,* taken by itself, without application to anything concrete, is called an *abstract* or *pure* number. It merely designates how many times the unit *1* is contained in it, without implying that anything else is being counted or measured. An abstract number may be added to, subtracted from, multiplied by, or divided by any other abstract number. The result of any of these operations is always an abstract number designating a new total of units.

A number that designates a quantity of objects or units of measure, such as *4 grams, 8 ounces, or 12 grains,* is called a *concrete* or *denominate* number. It designates the total quantity of whatever has been measured. A denominate number may be added to or subtracted from any other number of the same denomination, but a denominate number may be multiplied or divided only by a pure number. The result of any of these operations is always a number of the same denomination.

Examples:

$$10 \text{ grams} + 5 \text{ grams} = 15 \text{ grams}$$
$$10 \text{ grams} - 5 \text{ grams} = 5 \text{ grams}$$
$$300 \text{ grains} \times 2 = 600 \text{ grains}$$
$$12 \text{ ounces} \div 3 = 4 \text{ ounces}$$

If any one rule of arithmetic may take first place in importance, this is it: *Numbers of different denominations have no numeric connection with each other and cannot be used together in any direct arithmetical operation.* We will see again and again that if quantities are to be added, or if one quantity is to be subtracted from another, they must be expressed in the same denomination. When we apparently multiply or divide a denominate number by a number of different denomination, we are in fact using the multiplier or divisor as an abstract number. If, for example, *1 ounce* costs *5¢* and we want to find the cost of *12 ounces,* we do not multiply *5¢* by *12 ounces,* but by the abstract number 12.

ARABIC NUMERALS

The so-called "Arabic" system of notation is properly called a *decimal system.* With only *10 figures—a zero* and *nine digits* (1,2,3,4,5,6,7,8,9)—any number can be expressed by an ingenious system in which different values are assigned to the digits according to the *place* they occupy in a row. The central place in the row is usually identified by a sign placed to its right called the *decimal point.* Any digit occupying this place expresses its own value—in other words, a certain number of *ones.* The former value of a digit is increased 10-fold each time it moves one place to the left, and, conversely, its value is one-tenth of its preceding value each time it moves one place to the right. *Zero* marks a place not occupied by one of the digits.

The simplicity of the system is further demonstrated by the fact that these *10 figures* serve all our needs in dealing with positive integers, and with the aid of a few signs, are adequate for expressing fractions, negative numbers, and irrational and imaginary numbers.

The practical range of the system is represented by the following scheme (which can be extended to the left or right into even higher or lower reaches):

Scheme of the decimal system:

	millions	*hundred thousands*	*ten thousands*	*thousands*	*hundreds*	*tens*	*ones*	*tenths*	*hundredths*	*thousandths*	*ten thousandths*	*hundred-thousandths*	*millionths*	
Etc. ←	o	o	o	o	o	o	o	o	o	o	o	o	o	→ Etc.

The total value of any number expressed in the Arabic (decimal) system, then, is the sum of the values of its digits as determined by their position.

Example:

5,083.623 means:
5,000.000 or 5 thousands
\+ 000.000 plus 0 hundreds
\+ 080.000 plus 8 tens
\+ 003.000 plus 3 ones
\+ 000.600 plus 6 tenths
\+ 000.020 plus 2 hundredths
\+ 000.003 plus 3 thousandths

The universal use of this system has resulted from the ease with which it can be adapted to the various purposes of arithmetical calculations.

ROMAN NUMERALS

The Roman system of notation expresses a fairly large range of numbers by the use of a few letters of the alphabet in a simple "positional" notation indicating adding to or subtracting from a succession of bases extending from 1 through *5, 10, 50, 100*, and *500* to *1000*. Roman numerals merely record quantities: they are of no use in computation.

To express quantities in the Roman system, eight letters of fixed values are used:

ss	=	½
I or i	=	1
V or v	=	5
X or x	=	10
L or l	=	50
C or c	=	100
D or d	=	500
M or m	=	1000

Other quantities are expressed by combining these letters by the general rule that when the second of two letters has a value equal to or smaller than that of the first, their values are to be added; when the second has a value greater than that of the first, the smaller is to be subtracted from the larger. This rule may be illustrated as follows:

1. Two or more letters express a quantity that is the *sum* of their values *if they are successively equal or smaller in value:*

ii	= 2	xv	= 15	lxxvii	= 77	dv	= 505	mc	= 1100
iii	= 3	xx	= 20	lxxxviii	= 88	dx	= 510	md	= 1500
vi	= 6	xxii	= 22	ci	= 101	dl	= 550	mdclxvi	= 1666
vii	= 7	xxxiii	= 33	cv	= 105	dc	= 600	mm	= 2000
viii	= 8	li	= 51	cx	= 110	mi	= 1001		
xi	= 11	lv	= 55	cl	= 150	mv	= 1005		
xii	= 12	lx	= 60	cc	= 200	mx	= 1010		
xiii	= 13	lxvi	= 66	di	= 501	ml	= 1050		

2. Two or more letters express a quantity that is the *sum* of the values remaining *after the value of each smaller letter has been subtracted from that of a following greater letter:*

iv	= 4	xxiv	= 24	xliv	= 44	cdi	= 401	cm	= 900
ix	= 9	xxxix	= 39	xc	= 90	cdxl	= 440	cmxcix	= 999
xiv	= 14	xl	= 40	xcix	= 99	cdxliv	= 444	MCDXCII	= 1492
xix	= 19	xli	= 41	cd	= 400	cdxc	= 490	MCMXCV	= 1995

Roman numerals are used in pharmacy only occasionally on prescriptions: (1) to designate the number of dosage units prescribed (e.g., *capsules no. C*), (2) to indicate the quantity of medication to be administered (e.g., *teaspoonfuls ii*), and (3) in rare instances in which the common or apothecaries' systems of measurement are used (e.g., *grains iv*).[1]

Practice Problems

1. Write the following in Roman numerals:
   (*a*) 18 (*f*) 37
   (*b*) 64 (*g*) 84
   (*c*) 72 (*h*) 48
   (*d*) 126 (*i*) 1989
   (*e*) 99

[1] On prescriptions, physicians tend to use capitals except for the letter *i*, which they dot for the sake of clarity; they may use *j* for a final *i*. Following the Latin custom, they put the symbol for the denomination first and the Roman numeral second (e.g., gr iv). Dates are customarily expressed in capitals.

2. Write the following in Arabic numerals:
   (*a*) Part IV
   (*b*) Chapter XIX
   (*c*) MCMLIX
   (*d*) MDCCCXIV

3. Interpret the *quantity* in each of these phrases taken from prescriptions:
   (*a*) Caps. no. xlv
   (*b*) Gtts. ij
   (*c*) Tabs. no. xlviii
   (*d*) Pil. no. lxiv
   (*e*) Pulv. no. xvi
   (*f*) Caps. no. lxxxiv

4. Interpret the *quantities* in each of these prescriptions:

(*a*)	℞	Zinc Oxide	parts v
		Wool Fat	parts xv
		Petrolatum	parts lxxx
		Disp. ℥iv	
		Sig. Apply.	
(*b*)	℞	Dilaudid	gr iss
		Ammonium Chloride	gr xl
		Syrup ad	℥vi
		Sig. ʒss pro tuss.	

COMMON AND DECIMAL FRACTIONS

The arithmetic of pharmacy requires facility in the handling of common fractions and decimal fractions. Even if the student already has a good working knowledge of their use, the following brief review of certain principles and rules should be helpful, and the practice problems should provide a means of gaining accuracy and speed in their manipulation.

Common Fractions

A number in the form $\frac{1}{8}$, $\frac{3}{16}$, and so on, is called a *common fraction,* or often simply a *fraction.* Its *denominator,* or second or lower figure, always indicates the number of aliquot parts into which *1* is divided; its *numerator*, or first or upper figure, specifies the number of those parts with which we are concerned.

The *value* of a fraction is the *quotient* (i.e., the result of dividing one number by another) when its numerator is divided by its denominator. If the numerator is smaller than the denominator, the fraction is called *proper,* and its value is less than *1.* If the numerator and denominator are alike, its value is *1.* If the numerator is larger than the denominator, the fraction is called *improper,* and its value is greater than *1.*

Two principles must be understood by anyone attempting to calculate with common fractions. In the **first principle,** multiplying the numerator increases the value of a fraction, and multiplying the denominator decreases the value, but *when both numerator and denominator are multiplied by the same number, the value does not change.*

$$\frac{2}{7} = \frac{3 \times 2}{3 \times 7} = \frac{6}{21}$$

This principle allows us to reduce two or more fractions to a common denomination when necessary. We usually want the *lowest common denominator,* which is the smallest number divisible by all the other given denominators. It is found most easily by testing successive multiples of the largest given denominator until we reach a number divisible by all the other given denominators. Then we multiply both numerator and denominator of each fraction by the number of times its denominator is contained in the common denominator.

Example:

Reduce the fractions ¾, ⅘, and ⅓ to a common denomination.

By testing successive multiples of 5, we discover that 60 is the smallest number divisible by 4, 5, and 3; 4 is contained 15 times in 60; 5, 12 times; and 3, 20 times.

$$\left.\begin{aligned} \frac{3}{4} &= \frac{15 \times 3}{15 \times 4} = \frac{45}{60}, \\ \frac{4}{5} &= \frac{12 \times 4}{12 \times 5} = \frac{48}{60}, \\ \frac{1}{3} &= \frac{20 \times 1}{20 \times 3} = \frac{20}{60}, \end{aligned}\right\} \textit{answers}$$

In the **second principle**, dividing the numerator decreases the value of a fraction, and dividing the denominator increases the value, but ***when both numerator and denominator are divided by the same number, the value does not change.***

$$\frac{6}{21} = \frac{6 \div 3}{21 \div 3} = \frac{2}{7}$$

This principle allows us to reduce an unwieldy fraction to more convenient lower terms, either at any time during a series of calculations or when recording a final result. To reduce a fraction to its *lowest terms,* divide both the numerator and the denominator by the largest common divisor.

Example:

Reduce ³⁶⁄₂₈₈₀ to its lowest terms.

The largest common divisor is 36.

$$\frac{36}{2880} = \frac{36 \div 36}{2880 \div 36} = \frac{1}{80}, \textit{ answer.}$$

In addition to developing a firm grasp of these two principles, the student should follow two rules before indulging in any short cuts.

Rule 1. Before performing any arithmetical operation involving fractions, ***reduce every mixed number to an improper fraction.*** To do so, multiply the integer, or whole number, by the denominator of the fractional remainder, add the numerator, and write the result over the denominator. For example, before attempting to multiply ¾ by 1⅕, first reduce the 1⅕ to an improper fraction:

$$1\tfrac{1}{5} = \frac{(1 \times 5) + 1}{5} = \tfrac{6}{5}$$

If the final result of a calculation is an improper fraction, you may, if you like, reduce it to a mixed number. To do so, simply divide the numerator by the denominator and express the remainder as a common, not a decimal fraction:

$$\tfrac{6}{5} = 6 \div 5 = 1\tfrac{1}{5}$$

Rule 2. When performing an operation involving a fraction and a whole number, *express (or at least visualize) the whole number as a fraction having 1 for its denominator.*

Think of 3, as $\frac{3}{1}$, 42 as $\frac{42}{1}$, and so on. This visualization is desirable when a fraction is subtracted from a whole number, and it is necessary when a fraction is divided by a whole number.

Adding Fractions. To add common fractions, reduce them to a common denomination, add the numerators, and write the sum over the common denominator. If whole and mixed numbers are involved, the safest (although not the quickest) procedure is to apply *Rules 1 and 2*. If the sum is an improper fraction, you may want to reduce it to a mixed number.

Example:

In preparing batches of a formula, a pharmacist used $\frac{1}{4}$ ounce, $\frac{1}{12}$ ounce, $\frac{1}{8}$ ounce, and $\frac{1}{6}$ ounce of a chemical. Calculate the total quantity of chemical used.

The lowest common denominator of the fractions is 24.

$$\frac{1}{4} = \frac{6}{24},\ \frac{1}{12} = \frac{2}{24},\ \frac{1}{8} = \frac{3}{24}, \text{ and } \frac{1}{6} = \frac{4}{24}$$

$$\frac{6 + 2 + 3 + 4}{24} \text{ ounce} = \frac{15}{24} \text{ ounce}$$

$$\frac{15}{24} \text{ ounce} = \frac{5}{8} \text{ ounce, } \textit{answer.}$$

Subtracting Fractions. To subtract one fraction from another, reduce them to a common denomination, subtract, and write the difference over the common denominator. If a whole or mixed number is involved, first apply *Rule 1 or 2*. If the difference is an improper fraction, you may want to reduce it to a mixed number.

Examples:

A hospitalized patient received $\frac{7}{12}$ liter of a prescribed intravenous infusion. If he had not received the final $\frac{1}{8}$ liter, what fraction of a liter would he have received?

The lowest common denominator is 24.

$$\frac{7}{12} = \frac{14}{24} \text{ and } \frac{1}{8} = \frac{3}{24}$$

$$\frac{14 - 3}{24} \text{ liter} = \frac{11}{24} \text{ liter, } \textit{answer.}$$

If 3 fl. oz. of a liquid mixture are to contain $\frac{1}{24}$ fl. oz. of ingredient A, $\frac{1}{4}$ fl. oz. of ingredient B, and $\frac{1}{3}$ fl. oz. of ingredient C, how many fluidounces of ingredient D are required?

The lowest common denominator is 24.

$$\frac{1}{24} = \frac{1}{24},\ \frac{1}{4} = \frac{6}{24}, \text{ and } \frac{1}{3} = \frac{8}{24}$$

$$\frac{1 + 6 + 8}{24} \text{ fl. oz.} = \frac{15}{24} \text{ fl. oz.} = \frac{5}{8} \text{ fl. oz.}$$

Interpret the given 3 fl. oz. as $\frac{3}{1}$ fl. oz., and reduce it to a fraction with 8 for a denominator:

$$\frac{3}{1} \text{ fl. oz.} = \frac{24}{8} \text{ fl. oz.}$$

Subtracting:

$$\frac{24 - 5}{8} \text{ fl. oz.} = \frac{19}{8} \text{ fl. oz.}$$