

CDC A4P051

Pharmacy Journeyman

Volume 4. Pharmaceutical Calculations, Chemistry, and Sterile Compounding

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Career Development Course 4P051A, Pharmacy Journeyman, is designed to satisfy the 5-skill level CDC subject and task knowledge requirements specified in the Specialty Training Standard. This is the last volume for this set of the Pharmacy Journeyman course. The concepts covered in this volume, along with the information that you received in Volumes 1 thru 3 will help you understand how your pharmacy is operated and aid you becoming a better pharmacy technician in the United States Air Force. This final volume has three units and is set up as follows.

Unit 1, Pharmaceutical Calculations, introduces you basic mathematical conversions to include: whole numbers, fractions, ratios, percentages, Arabic and Roman numerals, plus conversion of measurement units and systems. We will also discuss pharmaceutical dosage calculations and intravenous administration rate calculations. The unit will end with formulas for reducing and enlarging compounding formulas. These math skills are very important to your understanding of pharmaceutical dosages and both sterile and non-sterile compounding.

Unit 2, Pharmaceutical Chemistry, covers a basic chemistry concepts and chemical bonding. The second section of the unit discusses solutions and chemical solubility. Balance of acids and bases closes out this short but important pharmaceutical unit.

Unit 3, Sterile Pharmaceutical Compounding, reinforces the operations and requirements of sterile compounding learned during your pharmacy technical training. The unit will cover principles of intravenous admixtures, aseptic technique, sources of contamination, and maintain an aseptic environment. We will closed this last volume with information on adverse events reporting, compatibilities and stability principals, requirements for compounding cytotoxic and biological agents, and common pharmaceutical references.

A glossary is included for your use.

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NOTE:

In this volume, the subject matter is divided into self-contained units. A unit menu begins each unit, identifying the lesson headings and numbers. After reading the unit menu page and unit introduction, study the section, answer the self-test questions, and compare your answers with those given at the end of the unit. Then complete the unit review exercises.

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THE DAILY ACTIVITIES of pharmacy technicians center around the care of our patients. For most of you, this activity will focus on dispensing outpatient prescriptions. For others, it will involve compounding certain medications and/or preparing sterile products. Although the trend in our pharmacies has moved away from daily compounding of pharmaceutical products, you must possess the skills to provide this service when necessary.

Compounding pharmaceutical products requires precise calculations and measurements. Therefore, it is essential you understand the different measurement systems used within the pharmacy career field, the different formulas and conversions used to calculate a desired equation, and how to apply this knowledge. To ensure you develop this firm foundation of knowledge, we will begin with a review of conversion fundamentals. Then we will move on to pharmacy-specific topics such as dosage calculations, drug administration rates, concentration and dilution of preparations, percentage solution by percentage preparation, and alligations.

1–1. Converting Units/Systems of Weights and Measurements

Measurement is the process of obtaining quantitative information about the physical world. This section discusses the different systems of pharmaceutical notations, weights and measures, and how to perform conversions between the different systems. You will learn the metric, apothecary, avoirdupois, and household systems of measurement. In addition, you will also learn how to convert between those systems and some accepted methods for rounding numerical values.

Before you begin your study of the different types of calculations necessary to determine medication dosages, you need to look at the conversions between systems of measurement common to pharmacy. Nearly all medication orders written today use the metric system. However, there are still some orders being written using avoirdupois and apothecary notations. You will also see both Arabic and Roman numerals on prescriptions. As a technician, you must be able to read either type of numeral and convert the weights and measures between all three systems.

601. Numbers, fractions, and metric conversions

If you recall, pharmaceutical calculations was covered during technical training, so let's review the information, beginning with differentiating between whole numbers and fractions.

Whole numbers

Whole numbers are positive integers to include zero.

Examples: 0, 1, 2, 3, 4, 5, and so forth.

Fractions

Fractions are parts of whole numbers.

Examples: $\frac{1}{3}, \frac{2}{6}, \frac{7}{9}, \frac{8}{12}$

Always express a fraction in its simplest form.

Examples: $\frac{3}{6} = \frac{1}{2}, \frac{4}{12} = \frac{1}{3}, \frac{5}{20} = \frac{1}{4}$

The upper whole number of a fraction is called the numerator and the lower number of a fraction is called the denominator.

$$\frac{\text{Numerator}}{\text{Denominator}}$$

Mixed numbers

Mixed numbers contain both whole numbers and fractions. You may also see mixed numbers referred to as compound fractions.

Examples: $1\frac{1}{2}, 11\frac{2}{3}, 20\frac{7}{8}, 3\frac{5}{6}$

Types of fractions

There are four basic types of fractions:

1. Proper fractions.
2. Improper fractions.
3. Simple fractions.
4. Complex fractions.

Proper fractions

Proper fractions have a numerator that is smaller than the denominator. The overall value of a proper fraction is always less than one.

Example: $\frac{1}{8}$

Improper fractions

Improper fractions have a numerator that's larger than the denominator. The overall value of an improper fraction is always greater than one.

Example: $\frac{6}{5}$

Dividing the numerator by the denominator reduces improper fractions.

Example: $\frac{6}{5} = 6 \div 5 = 1\frac{1}{5}$

Simple fractions

A simple fraction is a proper fraction that has been reduced to its lowest terms, and cannot be reduced further.

Example: $\frac{6}{18}$ is a proper fraction, but once reduced to its lowest terms, equals $\frac{1}{3}$.

$$\text{Example: } \frac{6}{18} = \frac{6 \div 6}{18 \div 6} = \frac{1}{3}$$

Complex fractions

Complex fractions have a numerator and a denominator that are both fractions. Dividing the numerator by the denominator will reduce the complex fraction.

$$\text{Example: } \frac{1/3}{3/4} = \frac{1}{3} \div \frac{3}{4} = \frac{1}{3} \times \frac{4}{3} = \frac{4}{9}$$

Rules for calculating fractions

There are four basic rules to follow in calculating fractions.

Rule 1

Multiplying the numerator increases the value of the fraction, whereas multiplying the denominator decreases the value of the fraction. The value of a fraction does not change if the same number multiplies both the numerator and denominator.

$$\frac{3 \times 2}{4} = \frac{6}{4} = \frac{3}{2} \text{ which is greater than } \frac{3}{4}$$

$$\frac{3}{4 \times 2} = \frac{3}{8} \text{ which is less than } \frac{3}{4}$$

$$\frac{3 \times 2}{4 \times 2} = \frac{6}{8} = \frac{3}{4} \text{ the value is unchanged.}$$

Rule 2

Dividing the numerator decreases the value of the fraction, whereas dividing the denominator increases the value of the fraction. The value of a fraction does not change if the same number divides both the numerator and denominator.

$$\frac{6 \div 2}{8} = \frac{3}{8} \text{ which is less than } \frac{6}{8}$$

$$\frac{6}{8 \div 2} = \frac{6}{4} \text{ which is greater than } \frac{6}{8}$$

$$\frac{6 \div 2}{8 \div 2} = \frac{3}{4} \text{ the value is unchanged.}$$

Rule 3

Change all mixed numbers to improper fractions before performing any calculations. To convert a mixed number to an improper fraction, multiply the whole number by the denominator and add the numerator to the product. Write the new number as the numerator over the old denominator.

$$1\frac{3}{4} = \frac{(4 \times 1) + 3}{4} = \frac{7}{4}$$

Rule 4

Express all whole numbers as fractions having “1” as the denominator. To multiply a fraction by a whole number, consider the whole number a fraction with the whole number as the numerator and “1” as the denominator.

$$\frac{3}{4} \times 8 = \frac{3}{4} \times \frac{8}{1} = \frac{24}{4} = 6$$

To reduce a fraction to its simplest terms, divide the numerator and denominator by the largest multiple common factor of both terms. (Two is the largest number that will divide into both 6 and 8 evenly.)

$$\frac{6 \div 2}{8 \div 2} = \frac{3}{4}$$

To add or subtract fractions, you need to change all fractions to a common denominator and then add or subtract the numerators. You will need to multiply the numerator by the common factor as shown in the following examples.

$$\frac{2}{3} + \frac{5}{6} + \frac{1}{2} = \frac{4}{6} + \frac{5}{6} + \frac{3}{6} = \frac{12}{6} = 2$$

$$\frac{3}{4} - \frac{1}{2} = \frac{3}{4} - \frac{2}{4} = \frac{1}{4}$$

To multiply fractions, multiply the numerators to get a new numerator and multiply the denominators to get a new denominator. Remember, you will need to simplify or reduce the fraction to its lowest term.

$$\frac{3}{4} \times \frac{2}{5} = \frac{6}{20} = \frac{3}{10}$$

To divide fractions, invert the divisor and multiply with the new fractions. The inverted divisor is called the reciprocal of the original fraction. Again, you will need to reduce to the lowest terms.

$$\frac{3}{4} \div \frac{1}{6} = \frac{3}{4} \times \frac{6}{1} = \frac{18}{4} = 4\frac{2}{4} = 4\frac{1}{2}$$

Decimal numbers

Decimal numbers are fractions with denominators of 10 or any multiple of 10; (10, 100, 1,000, etc.). Decimal numbers differ from common fractions by signifying the denominator with a decimal point placed at the left of the numerator. (The decimal point is the period in a decimal number.)

Examples: $\frac{1}{10}$ is written as 0.1; $\frac{65}{100}$ is written as 0.65; and $\frac{12}{1,000}$ is written as 0.012.

The value of the denominator is determined by the number of digits to the right of the decimal point as shown on the decimal line in figure 1-1. Since decimal numbers are fractions written as whole numbers—qualified by the position of the decimal point—they may be subtracted, multiplied, and divided in much the same way as a whole number.

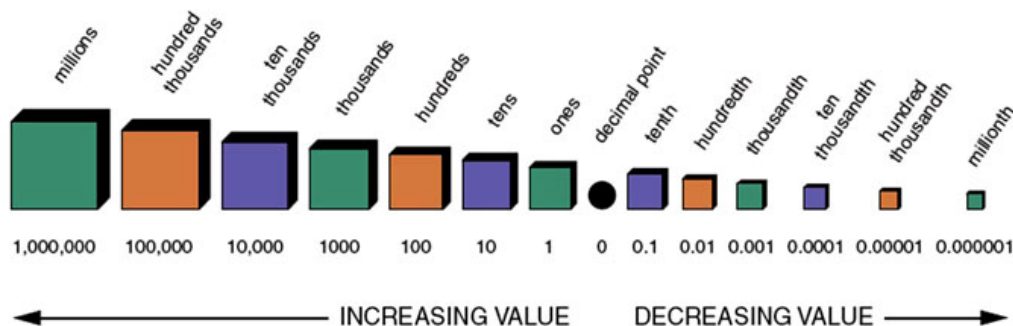


Figure 1-1. Decimal units and values.

Moving a decimal point one position to the right multiplies a number by 10. For example, 65.35 becomes 653.5; that is $65.35 \times 10 = 653.5$. Moving the decimal point one position left divides a number by 10. So, 65.35 becomes 6.535; that is $65.35 \div 10 = 6.535$. Each position is 10 times the position to the right and one-tenth the position to the left.

Decimals and Equivalent Decimal Fractions
$0.00001 = 1/100,000$
$0.0001 = 1/10,000$
$0.001 = 1/1,000$
$0.01 = 1/100$
$0.1 = 1/10$
$1 = 1/1$

The following are two rules about zeros you must know in dealing with decimal numbers.

Rule 1

Do not write whole numbers in decimal form. In other words, when you write a whole number, *never* end it with a period and a “trailing” zero. Periods can be hard to detect and may result in an error. For example, if the period in 1.0 is overlooked, the number might appear to be 10. In this case, it could cause a 10-fold dosing error, which could seriously harm or kill a patient.

Rule 2

When you write a fraction in its decimal form, *always* precede the period with a “leading” zero. Again, periods can be hard to see; for example .5 may be read as 5. But if you put a zero before the decimal point (0.5), the zero alerts the reader to look more carefully at the number. This can avoid a potentially hazardous outcome for the patient.

NOTE: Do not try to second-guess where a decimal point should or should not be. Always call the prescriber who wrote the prescription or medical order to confirm the dosage if you have any doubt about decimal point placement.

Decimal conversions

You will need to convert different kinds of numbers to decimal numbers or vice versa when filling prescriptions. This lesson will help you to refresh your memory on the conversion process.

When multiplying or dividing decimal numbers and common fractions, you must convert all terms to the same system. In other words, use all common fractions or all decimal numbers. Complete multiplication of decimal fractions as with whole numbers. To determine the position of the decimal point, count the total number of decimal places in the numbers multiplied. Then point off the answer, from right to left, the same number of places, adding zeros as necessary to make the correct number of decimal spaces.

$$\begin{array}{r}
 0.123 \times 0.012 = \\
 0.123 \\
 \times 0.012 \\
 \hline
 0246 \\
 01230 \\
 000000 \\
 \hline
 0000000 \\
 0.001476
 \end{array}$$

Dividing decimals requires that the divisor be a whole number. Convert the divisor to a whole number by moving the decimal point to the right. To maintain an equal equation, move the decimal of the dividend an equal number of places to the right.

$$\begin{aligned}0.6535 \div 0.005 &\rightarrow = 6.535 \div 0.05 \text{ (one place to the right)} \\&= 65.35 \div 0.5 \text{ (two places right)} \\&= 653.5 \div 5 \text{ (three places right).}\end{aligned}$$

The numbers are now ready to be divided, and the decimal has already been properly placed in the correct position for the answer.

$$\begin{array}{r}130.7 \\ 5 \overline{)653.5} \\ \underline{5} \\ 15 \\ \underline{15} \\ 003 \\ \underline{000} \\ 0035\end{array}$$

Converting fractions to decimal numbers

To convert a fraction to a decimal number you divide the numerator by the denominator.

Example: $\frac{1}{2} = 1 \text{ divided by } 2 = 0.5$

Converting mixed numbers to decimal numbers

There are two methods to convert mixed numbers to decimal numbers: a two-step process and a three-step process.

Method 1 – two-step process

1. Write the mixed number as a fraction. To do this, you multiply the whole number by the denominator of the fraction and add the result to the numerator of the fraction. The denominator stays the same.

Example: $2\frac{3}{4} = 4 \text{ times } 2 \text{ (8) plus } 3 \text{ (8 + 3 = 11), all over the denominator } 4 = \frac{11}{4}$.

2. Divide the numerator by the denominator.

Example: $\frac{11}{4} = 11 \text{ divided by } 4 = 2.75$

Method 2 – three-step process

1. Separate the whole number and the fraction.

Example: $2\frac{3}{4} = 2 \text{ plus } \frac{3}{4}$

2. Convert the fraction to its decimal counterpart.

Example: $\frac{3}{4} = 3 \text{ divided by } 4 = 0.75$

3. Add the whole number to the decimal number.

Example: $2 + 0.75 = 2.75$

Converting decimal numbers to mixed numbers or fractions

To convert decimal numbers to mixed numbers, you reverse the process.

1. Write the decimal number over 1. Dividing a number by 1 does not change the value of the number.

Example: $3.5 = \frac{3.5}{1}$

2. Move the decimal point the same number of places to the right in both the numerator and denominator. The number of places to move the decimal point is determined by the number of digits or numerals that follow the decimal point in the numerator.

Example: Since there is only one digit following the decimal point in 3.5, the decimal point has to be moved only one place to the right in both the numerator and the denominator:

$$\frac{3.5}{1} = \frac{35}{10}$$

The value of the number remains the same as long as you do exactly the same to both the numerator and the denominator.

3. Simplify the fraction.

Example: $\frac{35}{10} = \frac{7}{2} = 3\frac{1}{2}$

Metric system and conversions

One of the major systems of weights and measures used in medicine is the metric system. It was developed in France in the late 18th century and is based on the decimal system. In this system, everything is measured in multiples or fractions of 10. The metric system uses standard measures (meter for length, gram for weight, and liter for volume) and prefixes to describe multiples or fractions of a measure.

The metric following grid displays some common metric measurements used by the medical community. The numbers below the prefix indicates the value of each basic unit, such as meter, gram, or liter. We will only discuss grams and liters because these are the common measures that you will see as a pharmacy technician.

Kilo (k)	Hecto (h)	Deca (da)	Units (gm/L)	Deci (d)	Centi (c)	Milli (m)	Micro (mc)
1000	100	10	1	0.1	0.01	0.001	0.000001

There are two types of prefixes used to describe multiples or fractions of the standard metric measures for weight and volume.

Latin prefixes

The Latin prefixes denote *fractions*.

$$\text{micro: } \frac{1}{1,000,000} = 0.000001$$

$$\text{milli: } \frac{1}{1,000} = 0.001$$

$$\text{centi: } \frac{1}{100} = 0.01$$

$$\text{deci: } \frac{1}{10} = 0.1$$

Greek prefixes

The Greek prefixes denote *multiples*.

Deca: 10.

Hector: 100.

Kilo: 1000.

Let's look at how to apply these prefixes to metric measures for volume and weight.

Volume

The standard metric measure for volume is the *liter* (L). It is equal to 1,000 cubic centimeters of water. One cubic centimeter (cc) is considered equivalent to one milliliter (mL). Therefore, 1 L = 1,000 mL. The mathematical equivalents are provided for you in the following table.

1 milliliter (mL)	=	0.001 liter (L)
1,000 milliliters (mL)	=	1 liter (L)
1 deciliter (dL)	=	0.1 liter (L)
10 deciliters (dL)	=	1 liter (L)

NOTE: You will routinely see milliliter interchangeably abbreviated as mL (with an uppercase L) or as ml (with a lowercase l).

Weight

The standard metric measure for weight is a gram (g). The gram is defined as the weight of one cubic centimeter of distilled water at 4°C. Similar to the liter, 1 gram = 1000 milligram (mg); in other words, to convert from grams to milligrams, you would multiply milligrams by 1000, which essentially moves the decimal point three places to the right. You can also convert 1 milligram back to grams by moving the decimal point for 1 gram three places to the left; for example, 1 milligram would be written as 0.001 gram. The mathematical equivalents are provided for you in the following table.

1 kilogram (kg)	=	1,000 gram (g)
0.001 kilogram (kg)	=	1 gram (g)
1 milligram (mg)	=	0.001 gram (g)
1,000 milligram (mg)	=	1 gram (g)
1 microgram (mcg)	=	0.000001 gram (g)
1,000,000 microgram (mcg)	=	1 gram (g)

NOTE: You will routinely see gram interchangeably abbreviated as g (lowercase g only) or as gm (lower case g and lowercase m together).

602. Converting ratios, fractions, and percentages

Percent (%) means “per or out of 100.” A percent is actually a fraction, but a fraction with a specific denominator of 100.

Example: 50% means 50 in 100, or $\frac{50}{100}$, or $\frac{1}{2}$

Converting percent to a fraction

To convert a percent to a fraction, you write the number that precedes the % sign over 100. Then, simplify the resulting fraction.

Example: $25\% = \frac{25}{100} = \frac{1}{4}$

Converting a fraction to a percent

When you convert a fraction to a percent, write the fraction in a form where the denominator is 100. It is easiest when the fraction is written in the form of a decimal number.

Example: $\frac{3}{4} = 3 \text{ divided by } 4 = 0.75$

To convert a decimal value to a percent, simply multiply by 100 or move your decimal point two places right and add the percent symbol.

Example: $0.75 \times 100 = 75\%$

Converting a ratio to a percent

We use ratios to make comparisons between two numbers. Ratios can be written in different ways; for example, they can be written as a fraction, using the word “to,” or with a colon. So when you convert a ratio to a percent, you’re working the same problem as converting a fraction to a percent. All of the following ratios are equivalent:

$$\frac{3}{6}; 3 \text{ to } 6; 3:6$$

Let’s go back to the previous problem you had, “Converting a fraction to a percent.” However, this time instead of a fraction, we’ll convert using a ratio. Given the ratio of 3:6 (expressed as 3 to 6), write the ratio as a fraction.

Example: $3:6 = \frac{3}{6}$

Next, write the fraction as a decimal number.

Example: $\frac{3}{6} = 3 \text{ divided by } 6 = 0.5$

Remember, to convert a decimal value to a percent, simply multiply by 100 or move your decimal point two places right and add the percent symbol.

Example: $0.5 \times 100 = 50\%$

603. Ratios, proportions, and system conversions

Before we move further, it is imperative you know how to perform conversions needed to solve some of the pharmaceutical calculations you will encounter. You can easily accomplish these conversions

by using ratio proportion calculations. Almost every problem imaginable in calculations involving medications can be broken down into simple ratio proportions. The ability to perform these calculations is an invaluable asset in solving medication problems quickly and accurately.

Ratio

As described in the previous lesson, a ratio shows the relationship between two quantities. Ratios can be written with a colon separating the two parts, or as a fraction: $1:10 = 1/10$; $1:2 = 1/2$. To verbalize the ratio 1:10 or 1/10, you would say “one to ten, or one-tenth, or one part to ten parts.” For example, if you say there are 10 pharmacy technicians for every one pharmacy officer, then the ratio of pharmacy officers to pharmacy technicians is 1 to 10, 1:10 or 1/10.

Proportion

You can form a proportion by using two ratios that are equal (such as $1/4 = 3/12$). When two ratios or fractions are equal, their cross product is also equal. You are probably asking yourself, “What is a cross product?” A cross product is obtained by multiplying the denominator of one ratio by the numerator of the other. Look at the following example:

$$\frac{1}{4} = \frac{3}{12} \rightarrow 1 \times 12 = 4 \times 3$$

As you can see, the cross products are equal: $12 = 12$. In other words, the ratio 1/4 is equal to the ratio 3/12.

This characteristic of a proportion is extremely useful in solving problems that arise in drug administration. If any three of the values of a proportion are known, the fourth can be determined.

Dosage

Before we move forward to apply this mathematical calculation for solving proportions, you need to understand the term “dose.” Dose refers to the amount of medication that a patient must take at one time to produce the optimum therapeutic effect. The terms “average dose,” “usual dose,” and “adult dose” are based on the amount of medication needed to treat the average size adult with optimum effect. Now, let’s work through a sample problem.

Let’s say the prescriber orders 10 mg of a drug intravenously for a patient. The drug is available in a 5 ml vial, which contains 100 mg of the drug. The question here is how many milliliters are needed to supply the dose of 10 mg?

Break down the problem

First, you need to break down the problem. If you read the problem carefully, there are three pieces of information that you should be able to identify. Remember that to solve a ratio proportion, you must have three known quantities and one unknown.

1. You have a 5 mL vial.
2. There is 100 mg of the drug in the 5 mL vial.
3. 10 mg of the drug is the desired dose.

You can solve this problem by using the following ration proportion method:

$$\frac{5 \text{ mL}}{100 \text{ mg}} = \frac{X \text{ mL}}{10 \text{ mg}} \rightarrow (100 \times X) = (5 \times 10).$$

The units of this formula are labeled and like units are located in the same position in each fraction or ratio (5 mL is opposite X mL, and 100 mg is opposite 10 mg). It is imperative that you label the parts of this formula correctly.

Cross product

So how do you solve the preceding example? First you need to find the cross product and then solve for (X) or the unknown value.

$$\frac{5 \text{ mL}}{100 \text{ mg}} = \frac{X \text{ mL}}{10 \text{ mg}} \rightarrow (100 \times X = 5 \times 10) \rightarrow (100X = 50) \rightarrow X = 0.5 \text{ mL (50 divided by 100)}$$

Your problem is solved; 0.5 mL of the solution is needed for the 10 mg dose.

NOTE: Ratio proportion problems are similar to the way we think logically. Problems can be examined with the *if-then* approach.

In our example, we could say *if* we have 5 mL containing 100 mg of the drug, *then* X mL of solution would contain 10 mg of the drug.

Now that you have a firm grasp on the metric system and a fundamental understanding of ratio proportions, let's continue with the avoirdupois and apothecary systems of weight.

Avoirdupois weight conversions

The *avoirdupois system* (abbreviated as AV) is a system of weight measurement only. Its smallest unit, the grain, is the same as in the apothecary system. After the metric system, the avoirdupois system of weight (grains, ounces, and pounds) is what you'll commonly use in the pharmacy.

Conversions

The following conversion chart provides equivalent weights of measure within the avoirdupois system of weight.

Avoirdupois System of Weight	
Unit	AV Equivalent
1 gr (grain) =	65 mg
1 oz (ounce) =	437.5 gr
1 lb (pound) =	16 oz

NOTE: The pounds-to-ounce equivalent is different in the avoirdupois and apothecary systems. The avoirdupois system is most commonly used to measure weight and the apothecary system to measure volume. Be sure to make note of the difference in symbols used for the two systems. Fluid ounces (apothecary system), which measure volume, are often mistakenly changed to weighable ounces (avoirdupois system). Pay close attention to what units of measurement you are working in and convert accordingly. When converting units of measurement outside of the metric system, the ratio proportion method works well.

Example: 1 oz = 437.5 gr is a ratio and may be expressed as such: "The ratio of ounces to grains in the AV system is 1 to 437.5." This may also be written as 1:437.5 or 1/437.5.

When converting units of measurement using a ratio proportion, you must always have a known ratio. For example, we can convert any number of ounces to grains, because we know the relationship between ounces and grains.

Problem: Convert 3 oz to grains.

NOTE: In the preceding problem, you are simply asking, "How many grains are in 3 ounces?"

Known ratio between ounces and grains: 437.5 gr = 1 oz.

Unknown - how many grains are in 3 ounces? X gr = 3 oz.

Setting up the problem

Using the following ratio proportion method, you can solve this problem:

$$\frac{437.5 \text{ gr}}{1 \text{ oz}} = \frac{X \text{ gr}}{3 \text{ oz}}$$

Once your problem is set up, read the problem back to yourself as a question to see if you have the question set up properly. The preceding problem would read something like this: If we know there are 437.5 grains in 1 ounce, then how many grains are in 3 ounces?

Solving the problem


As mentioned previously, we now solve the problem using the cross product:

$$(437.5 \times 3 = 1 \times (X)) \rightarrow (1312.5 = 1X) \rightarrow X = 1312.5 \text{ gr.}$$

Apothecary weight conversions

The apothecary system was commonly used in the past by pharmacies as the system of weights and measures for prescribing and dispensing medications. Although it has largely been replaced by the metric system, you will still encounter these symbols and measures. The apothecary system of fluid measure is still used in a variety of products, both pharmaceutical and non-pharmaceutical, and you should be familiar with the fluid ounces, pints, quarts, and gallons.

The apothecary system of weights is based upon the grain, the smallest unit in the apothecary system. The grain is used in several different measurement systems, including the avoirdupois systems of weight. The origin of the grain is uncertain, but it is believed that at one time solids were weighed using grains of wheat as the standard.

Apothecary System of Weights		
lb	oz or 	gr
1 =	12 =	5,760
	1 =	480

Equivalents for Apothecary and Metric Units of Weight	
15.432 grains	= 1 gram
1 grain	= 65 milligrams*
1 ounce	= 31.1 grams
1 pound	= 373.2 grams
* Although one grain equals 65 milligrams in the apothecary system, some manufactures use 60 mg as the equivalent value instead.	

We have discussed converting within the avoirdupois system; now let's use the same ratio proportion method to solve a problem using the *apothecary system*. In this problem we will start with an apothecary measurement and convert to a metric system measurement.

Example: 1 gram = 15.432 grains is a ratio and may be expressed as such: "The ratio of grams to grains in the apothecary system is 1 to 15.432." This may also be written as 1:15.432 or 1/15.432.

We can convert apothecary system numbers to metric numbers because we know the relationship between grams and grains. Remember, when converting measures using a ratio proportion, you must always have a known ratio.

Problem: Convert 4 grains to grams (Note: You are simply asking, “How many grams are in 4 grains?”)

Known ratio between grams and grains: 1 gram = 15.432 gr.

Unknown - how many grams are in 4 grains: X grams = 4 gr.

Ratio proportion:

$$\frac{1 \text{ gm}}{15.432 \text{ gr}} = \frac{X \text{ gm}}{4 \text{ gr}}$$

Once your problem is set up, read the problem back to yourself as a question to see if you have the question set up properly. The preceding problem would read something like this: If we know there is 1 gram in 15.432 grains, then how many grams are in 4 grains? Now solve in the following manner:

$$(1 \times 4 = 15.432 \times (X)) \rightarrow (4 = 15.432X) \rightarrow X = 0.26 \text{ gm}$$

Apothecary volume conversions

The apothecary liquid measures are the same measures that you use daily (ounces, pints, quarts, and gallons). See the Apothecary System of Volume in the following table for the common units of liquid measure in the apothecary system.

Apothecary System of Volume		
1 gallon (gal) =	8 pints (pt)	128 fluid ounce (<i>f℥</i>)
	1 pt =	16 <i>f℥</i>
	1 quart (qt) =	2 pt or 32 <i>f℥</i>

There is one fluid measurement to discuss before moving on.

Fluid dram symbol

A few providers in the past, and even fewer now, use the fluid dram sign (*f℥*) to represent 1 teaspoonful or 5 mL. When our medical communities embraced the metric system for standard measures, this and other terms began to be used less. So you’re asking yourself, “If I may never see a fluid dram why bring it up?” Two reasons:

1. Notice the fluid dram symbol (*f℥*) and fluid ounces symbol (*f℥*) look a lot alike, especially when written with a sloppy hand.
2. The conversion of fluid drams to milliliters is difficult because of the conflict between references. Depending on the source you reference, you’ll see the conversion listed anywhere from 1 fluid dram (*f℥*) = 3.69 mL to 5 mL. With such a difference in conversion tables, it becomes difficult to establish a clear standard.

Fluid ounce symbol

The other apothecary symbol we just discussed is the fluid ounce (*f℥*). Unlike the fluid dram, the fluid ounce does have a clear conversion (1 fluid ounce = 29.57 mL). Since the medical community

recognizes this standard, we are able to convert to a household measurement of 2 tablespoonfuls (30 mL) when a precise measure is not required.

One-half fluid ounce symbol

For one-half fluid ounce (or 1 tablespoonful), the symbol is $\frac{1}{2}\text{ss}$. When this appears in the signa (directions for use), it is read as 1 tablespoonful or 15 mL.

Common household system of measurements and equivalents

The household system of measures is the system used in many kitchens today. This system includes teaspoons, tablespoons, cups, pints, quarts, and gallons. Look at the table below for common household measurements and their equivalents. You are probably familiar with some of these measures, but others may be new to you.

Common Household Measurements			
1 teaspoonful (tsp)	=	5 mL	
1 tablespoonful (tbsp)	=	15 mL	= 0.5 fluid ounce (fl oz)
1 cup	=	240 mL	= 8 (fl oz)
2 pt	=	1 qt	= 32 (fl oz)
4 qt	=	1 gal	= 128 (fl oz)

The term “drop” is commonly used in the pharmacy setting. Use caution with this measure, especially with potent medications. The volume of a drop depends not only on the nature of the liquid, but also on the size, shape, and position of the dropper used. For accurate measurement, use a syringe to measure milliliters.

Now that you know the measurement systems used in the pharmacy, you’re ready to handle some metric conversions between the other systems. Look at the tables of equivalents, and then read about rounding off these conversions.

Metric Equivalents for Avoirdupois Units of Weight		
1 ounce	=	30 grams*
1 pound	=	454 grams
* There are actually 28.35 grams in 1 ounce but 30 grams is the acceptable rounded quantity.		

Metric Equivalents for Apothecary Units of Volume		
1 fluid ounce	=	30 mL*
1 pint	=	480 mL
1 gallon	=	3840
* There are actually 29.57 mL in 1 fluid ounce but 30 mL is the acceptable rounded quantity.		

Approximate Metric Equivalents for Household Units of Measure			
1 tsp	=	5 mL	
1 tbsp	=	15 mL	
1 fl oz	=	30 mL*	
1 pint	=	16 fl oz	= 480 mL
1 quart	=	2 pints	= 32 fl oz = 960 mL
1 gallon	=	4 quarts	= 128 fl oz = 3840 mL
*There are actually 29.57 mL in 1 fluid ounce, but 30 mL is the acceptable rounded quantity.			

The preceding tables contain some commonly used approximate weight and measure equivalents (emphasis on *approximate*); the *approximate values are not exact equivalents*. For example, 1 gram equals 15 grains is an approximate equivalent, where 1 gram equals 15.432 grains is an exact equivalent. *When compounding medications, you must use the exact equivalents*. When calculating dosages, it may not be necessary to use exact equivalents. In fact, the exact equivalents involve many decimal places and fractional numbers. Because using exact equivalents can require awkward calculations and cause an increase in errors, approximate equivalents are often used in calculating medication dosages. The key to effectively using approximate equivalents is to “be cautious when rounding.” For example, if you round too early in a problem (i.e., on the first of four sequence steps) you may find that an error has resulted. Second, since some medications are so potent, rounding the first answer (i.e., 0.6 mg to 1.0 mg) could adversely impact the patient. These points are discussed to neither alarm nor confuse you but to make you aware that you must approach rounding with caution. The following table provides acceptable rounded-off conversions that when used with caution, do not compromise dosage accuracy.

Acceptable Rounded-Off Conversions		
1 gram	=	15 grains
1 grain	=	65 milligrams
1 ounce	=	30 grams
1 fluid ounce	=	30 milliliters
1 pint	=	480 milliliters
1 pound	=	454 grams

You’ll need to have a thorough knowledge of all the systems of weights and measures to correctly calculate and prepare medications. Determining the number of doses, the quantity to be dispensed, or the quantities of an ingredient are daily critical tasks in the pharmacy.

604. Conversion of Arabic and Roman numerals

There are two types of numerals that you’ll use quite often when performing pharmaceutical calculations; they are Arabic and Roman numerals. In this lesson, we will discuss both types, but will focus on Roman numerals since you are already familiar with Arabic numerals.

Arabic and Roman numerals

Arabic numerals are those you use every day, such as 0, 1, 2, 3, and 4. Arabic numbers can also include decimal and fraction values, such as 0.5 or 1/2.

Roman numerals are often used in writing prescriptions. They are sometimes used to specify amounts of ingredients the apothecary system has issued (e.g., “Morphine Sulfate III gr”). But more often, they are used to write the number of units (e.g., tablets, capsules, etc.) to be dispensed (e.g., “Disp. xx caps”).

Finally, Roman numerals can be used in the directions to the patient on the prescription (e.g., “take I tab now, then II q.i.d.”). Remember, q.i.d. means four times a day. Therefore, you need to be thoroughly familiar with the system of Roman numerals used in pharmacy.

Converting Roman numerals

There are seven basic numerals or symbols and four rules you need to know to correctly read these Roman symbols. The seven numerals are usually capital letters, but they can be lowercase. Their values and the rules to use Roman numerals are listed in the following table.

Roman Numeral	Value
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

Rule 1

When numerals are repeated, you add to get the value. However, *only* I, X, C, and M may be repeated, and a letter can only be repeated a maximum of three times.

$$\text{III} = (1 + 1 + 1 = 3)$$

$$\text{XX} = (10 + 10 = 20)$$

$$\text{MMM} = (1000 + 1000 + 1000 = 3000)$$

Rule 2

Add numerals when the numeral written to the right of a numeral is a *smaller* numeral. You can also think of the rule this way: If one or more numerals are placed after another numeral of greater value, add that amount.

$$\text{XII} = (10 + 1 + 1 = 12)$$

$$\text{LX} = (50 + 10 = 60)$$

$$\text{LXVI} = (50 + 10 + 5 + 1 = 66)$$

Rule 3

Subtract the value of a numeral when the numeral is written to the left of a numeral that has a larger value. You can also think of the rule this way: If a numeral is placed before another numeral of greater value, subtract that amount.

$$\text{IV} = (5 - 1 = 4)$$

$$\text{XL} = (50 - 10 = 40)$$

$$\text{XC} = (100 - 10 = 90)$$

NOTE: Only I, X, and C may be written to the left of the next two numerals of higher value. For example, only I can be written to the left of V and X—not L, C, D or M; only X can be written to the left of L and C, not D or M; and C is only written to the left of D or M. Let's review and rephrase the subtraction rule one more time to make sure you understand.

- Subtract only powers of ten, such as I, X, or C. Writing the numerals VL for 45 is not allowed: write XLV instead.
- Subtract only a single numeral from a single numeral. Write VIII for 8, not IIX; 19 is represented as XIX, not IXX.
- Don't subtract a numeral from another numeral more than 10 times greater. This means that you can only subtract I from V or X, and X from L or C, so MIM is not 1999, hence subtracting 1 from 1000 or IM breaks the rules for using Roman numerals.

Rule 4

A bar placed over a numeral means that the numeral is multiplied by 1,000.

$$\overline{C} = 100 \text{ times } 1,000 = 100,000$$

However, it is doubtful that you will see physicians use this method in prescribing amounts of medication because it may create confusion and lead to an error in filling a prescription. Remember, you need to be confident you're filling prescriptions correctly. That confidence comes from properly interpreting all written information on a prescription, to include Roman numerals.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

601. Numbers, fractions, and metric conversions

1. What is the upper whole number of a fraction called?
2. What type of fraction has a numerator that is greater than the denominator and the overall value is greater than one?
3. How are improper fractions reduced?
4. What is a simple fraction?
5. Reduce $\frac{6}{18}$ to its lowest terms.
6. What is the relationship between the numerator and denominator of a complex fraction?

7. What happens to the value of a fraction if both the numerator and denominator are divided by the same number?
8. Decimal numbers are fractions which have denominators of, or any multiple of, what number?
9. What happens to any number when you move a decimal point one position to the right?
10. What type of error can occur from using a trailing zero?
11. What type of zero should always precede the period of a decimal number?
12. When dividing decimals, what type of number must the divisor be?
13. Divide 0.6535 by 0.05.
14. How do you convert a fraction to a decimal number?
15. Express $\frac{11}{4}$ as a decimal number.
16. Convert the decimal number 3.5 to a mixed number.
17. What standard units of measure does the metric system use?
18. How many milliliters are there in 1 liter?
19. How would you convert from grams to milligrams?

602. Converting ratios, fractions, and percentages

1. What does the term “percent” mean?
2. How do you convert percentages to fractions?
3. Convert 25% to a fraction.
4. Convert $\frac{3}{4}$ to a percentage.
5. How do you convert a decimal value to a percent?

603. Ratios, proportions, and system conversions

1. What is the definition of a dose?
2. How many known quantities are needed to solve for a ratio proportion?
3. What pharmaceutical system measures only weight and uses the grain as its smallest unit of measurement?
4. What pharmaceutical system of fluid measurement includes fluid ounces, pints, quarts, and gallons?
5. How many grains are there in one apothecary gram?
6. What is the name of apothecary symbol $\mathfrak{f}\text{℥}$ and exactly how many mL does it represent?
7. Although there are 29.57 mL in 1 fluid ounce, what is the acceptable rounded quantity?

604. Conversion of Arabic and Roman numerals

1. What are the seven basic symbols for Roman numerals and their values?
2. Convert 45 to a Roman numeral.
3. Convert XIX to an Arabic numeral.
4. What does a bar written over a Roman numeral indicate?

1-2. Dosage and Administration Rate Calculations

When providers write inpatient prescriptions, chances are you may have to compound or mix several medications together in order to produce the product the doctor has ordered. To accomplish this goal, you must be able to calculate the proper doses; this includes the number of doses for each medication used, the size of each dose of medication, and the total amount for the final product. Intravenous (IV) administration is widely considered the most effective means of delivering medication to our patients. But it's also considered the most dangerous because the medication enters the bloodstream immediately with little chance for countering the effects of a miscalculated dose or wrong medication. Only skilled pharmacy personnel should perform these calculations, and they should be checked by a pharmacist. This lesson discusses the calculations skills needed to be an effective pharmacy technician regardless of practice setting.

605. Performing dosage calculations

When checking a patient's prescription dose for accuracy, first check an approved reference to see how the recommended dose is expressed. Then you will know how to proceed with checking the prescription. You learned about pharmaceutical references in the last unit; now let's look at a few questions broken down into smaller parts to make them less daunting, and work them together.

Determining the number of doses

To determine the number of doses, you divide the total amount to be dispensed by the size of each dose.

$$\text{Number of doses} = \frac{\text{Total amount}}{\text{Size of each dose}}$$

Let's work some sample problems to determine the number of doses.

First, how many 30 mL doses are contained in 480 mL of a medication?

$$\begin{aligned}\text{Number of doses} &= \frac{480 \text{ mL}}{30 \text{ mL}} \\ \text{Number of doses} &= 16.\end{aligned}$$

Secondly, how many doses are contained in 7.5 grams, if the dosage is 25 mg?

NOTE: This problem contains two different metric measurements: 7.5 grams and 25 milligrams. To solve the question correctly, the units of measure must be the same. Let's work this problem step by step together:

Step 1 – Set the problem up

It may help to rephrase the problem to yourself. For this problem you might ask, "How many 25 mg doses can I get from 7.5 grams?"

$$\text{Number of doses} = \frac{7.5 \text{ gm}}{25 \text{ mg}}$$

Step 2 – Convert grams to milligrams

Converting 7.5 grams to milligrams is accomplished in order for you to be able to compare like units. If you multiply 7.5 gm by 1000 then you get 7500 mg.

Step 3 – Solving for division

7500 mg divided by 25 mg.

$$\text{Number of doses} = \frac{7500 \text{ mg}}{25 \text{ mg}}$$

$$\text{Number of doses} = 300.$$

Determining the size of each dose

To determine the size of each dose, you divide the total amount of medication by the number of doses to be given to the patient. The following formula is used for this calculation.

$$\text{Size of each dose} = \frac{\text{Total amount}}{\text{Number of doses}}$$

Let's work a sample problem to determine the size of each dose. What dosage should be given if a total of 30 grams of medicine is to be divided into 10 equal doses?

$$\text{Size of each dose} = \frac{30 \text{ g}}{10 \text{ doses}}$$

$$\text{Size of each dose} = \frac{3 \text{ g}}{\text{dose}}$$

As you can see, your patient would receive 3 grams of medication per dose.

Determining the total amount of drug

To determine the quantity of medication to be dispensed (total amount of drug), you multiply the number of doses by the size of each dose.

$$\text{Total amount} = \text{the number of doses} \times \text{the size of each dose.}$$

Example: How much codeine is needed to prepare 20 doses of a 30 mg/dose preparation?

Breaking the question down

Let's take a minute to break this question down into parts while we determine the quantity (total amount) to be dispensed.

1. "How much codeine is needed"? Codeine is your medication, so you're asking how much medication is required. Okay, we know the medication; now, how many times is our patient going to take the codeine?

2. "...is needed to prepare 20 doses." The patient is to receive 20 doses; in other words, your patient is going to take the codeine 20 times. Okay, we know our patient is going to take 20 doses of codeine, but how much medication will the patient receive for each dose?
3. "...of a 30 mg/dose preparation." The third part of the problem tells us that for each dose of medication our patient will receive 30 mg of codeine.

Putting parts together and solving

Okay, let's put all three parts of our problem together and solve.

$$\text{Total amount} = 20 \text{ doses} \times 30 \text{ mg}$$

$$\text{Total amount} = 600 \text{ mg or } 0.6 \text{ g}$$

Calculating the correct dose

Dosage calculations can be based on weight of the patient (in kilograms or pounds), on the age of the patient, or by other methods. Let's take a look at how to calculate the correct dosage using these methods.

Calculating dosage on the basis of weight

Many medications are prescribed based on the patient's weight. This is especially true with pediatric patients. When the pharmacy receives a medication order such as this, a safe dosage can be assessed only when the ordered dose is known along with the patient's weight. When medications are prescribed, there is an acceptable dosage range the patient may receive. The pharmacy's duty is to make sure the prescription's dosage falls within the acceptable range. When we say "*acceptable range*" we mean the patient is not receiving too much medication (overdose), nor receiving too little medication (underdose). The goal is to make sure that the patient is receiving a therapeutic dose of medication to treat his/her condition.

To calculate a dose on the basis of weight, you will generally see the appropriate dosage listed in your approved reference as milligrams per kilogram (mg/Kg) or milligram per pounds (mg/lbs).

NOTE: Review your problem carefully. If you are given the patient's weight in pounds and your reference lists the dosage in kilograms, it will be necessary to convert pounds to kilograms before solving the problem. Your standard conversion is 1 kilogram = 2.2 pounds (1 Kg = 2.2 lbs).

To reinforce your knowledge, plug your own weight in pounds into the formula and solve for kilograms.

$$\frac{1\text{kg}}{2.2\text{lbs}} = \frac{X\text{ kg}}{\text{Your Weight(lbs)}} \rightarrow X\text{ kg} = \frac{\text{Your Weight(lbs)}}{2.2\text{lbs}}$$

Got it? Now let's try a few practice problems.

Example problem 1

A 29-year-old female patient who weighs 62 kg is prescribed 500 mg of acyclovir IV every eight hours. The recommended dose is 5 mg/kg every eight hours.

1. First calculate the *recommended dose* for this patient. Read the recommended dose like this: "The recommend dose is five milligrams of medication for every kilogram of body weight."
 $\text{Dose} = 5 \text{ (dose per unit of weight in mg)} \times 62 \text{ (weight of patient in kg)}$
 $\text{Does} = 310 \text{ mg}$
2. The next step is to find out if the patient is receiving greater than, less than, or equal to the recommended dose.

3. The recommended dose for this patient is 310 mg every eight hours. The prescriber has prescribed a dosage of 500 mg every eight hours. The prescribed dose exceeds the recommended dose, so you need to call the prescriber before the medication is dispensed.

Example problem 2

A 45-year-old male has a prescription that reads, “Amoxicillin 500 mg, *bid* (two times a day), dispense 28 tablets.”

First, check an approved reference: According to Drug Facts and Comparisons, the adult dosage for a nose or throat infection is 500 mg every 12 hours or 250 mg every 8 hours.

The dose is appropriate because the prescribed patient dosage falls within the guidelines of our reference; let’s take a closer look.

Example problem 3

A 65 year old patient who weighs 220 lbs is to receive treatment for an aspergillosis infection. The doctor wishes to use the drug Amphotericin to treat his condition; the recommended adult dosage of Amphotericin is 3 to 4 mg/kg IV daily. Using the recommended dosage guidelines, what is the lowest dose that can be prepared for a patient weighing 220 pounds?

1. First, convert the patient’s weight from lbs to kg. Remember, 1 kg = 2.2 pounds. To solve the following equation, cross multiply ($1 \times 220 = 220$, then divide by 2.2).

$$\frac{1 \text{ kg}}{2.2 \text{ lbs}} = \frac{X \text{ kg}}{220 \text{ (lbs)}} \rightarrow X = \frac{220}{2.2} \text{ kg} \rightarrow X = 100 \text{ kg}$$

2. Therefore, this 220-pound patient weighs 100 kg.

Now you can follow the steps shown previously.

$$\text{Dose} = 3\text{--}4 \text{ (dose per unit of weight in mg)} \times 100 \text{ (weight of patient in kg)}$$

$$\text{Dose} = 300\text{--}400 \text{ mg}$$

Do you think you have the hang of it now? Let’s try one more to make sure.

Example problem 4

There is a 25 Kg child receiving 200 mg of erythromycin every six hours. The recommended dosage range is 30 to 50 mg/Kg per day divided in four doses. In mg/day (milligrams per day), what is the dosage range this child should receive?

1. Do you remember how to determine the mg/kg per day dosage?

$$\text{Dose/day (mg/day)} = 30 \text{ (dose per day in mg per day)} \times 25 \text{ (weight of the patient in kg)}.$$

$$\text{Dose/day} = 750 \text{ mg (minimum dosage range per day)}.$$

$$\text{Dose/day (mg/day)} = 50 \text{ (dose per day in mg per day)} \times 25 \text{ (weight of patient in kg)}.$$

$$\text{Dose/day} = 1,250 \text{ mg (maximum dosage range per day)}.$$

The dosage range for this 25 Kg child is 750 mg to 1,250 mg per day, divided in four doses.

2. This 25 kg child is receiving 200 mg every six hours (4 doses) for a total of 800 mg per day. This 800 mg per day dosage is within the dosage range of 750 mg to 1,250 mg per day.

Now, let’s learn to calculate a dose on the basis of age.

Calculating dosage on the basis of age

The following is an example of information that may be found on the label of an over-the-counter children’s medication.

Pediatric antitussive syrup

Active ingredient: Dextromethorphan hydrobromide - 7.5 mg per mL.

Indications: For relief of coughing due to cold and flu for up to eight hours.

Actions: Antitussive

WARNING: Should not be administered to children for persistent or chronic cough such as occurs with asthma or emphysema or where cough is accompanied by excessive secretions except under physician's advice.

How supplied: Cherry-flavored syrup in plastic bottles of 2 and 4 fl oz. The following table displays the recommended dosage for each age group:

Age	Dosage
Under 2 years	As directed by provider; call the provider if necessary.
2 to under 6 years	7.5 mg every 6 to 8 hours (not to exceed 30 mg daily).
6 to under 12 years	15 mg every 6 to 8 hours (not to exceed 60 mg daily).
12 years and older	10–20 mg every 4 hours or 30 mg every 6 to 8 hours (not to exceed 120 mg daily).

On the basis of the dosage table above, what is the dosage of this pediatric antitussive syrup for a 4-year-old child? You should be able to figure this out fairly easily. The dosage is 7.5 mg every 6 to 8 hours (not to exceed 30 mg daily). If age is the only consideration for a dosage, it is usually a simple process. But what if you have a patient who is 8 years old and weighs 20 kg? What dosage do you give to this child?

Normally, you would automatically say this child should receive a dosage of 15 mg every 6 to 8 hours. Sometimes you may need to contact the prescriber to determine which standard you are to go by to determine the dosage appropriate for a child. Remember, when in doubt, CALL!

You have a very important job in calculating dosages. When performing these calculations, ensure you double-check your calculations to verify that they are correct.

606. Performing intravenous administration rate calculations

There are times when you will be required to calculate the flow rates for IV infusion, to calculate the volume of fluids administered over a period of time, and to control the total volume of fluid administered to a patient during a stated period of time. These calculations can all be achieved by the use of ratio proportions. Let's take a look at these required calculations.

IV administration rate

Prescribers often order IV solutions to run for a stated number of hours. You may have to calculate the number of drops per minute to comply with this order. There is one important note to keep in mind before we begin: Infusions that are administered to a patient by gravity flow are infused through IV sets that are calibrated in drops per milliliter. The rate of infusion is expressed as drops per minute.

Calculating flow rate

To calculate the flow rate using the ratio proportion method, follow these three steps:

1. Determine the number of mL the patient will receive per hour.
2. Determine the number of mL the patient will receive per minute.
3. Determine the number of drops per minute that will equal the number of mL calculated in step 2. The drop rate specified for the IV administration set being used must be considered in this step. The drop (gtt) rate is expressed as a ratio of drops per mL (gtt/mL).

Practice problem

Let's try one problem, just to get some practice.

The prescriber orders 3,000 mL of D5W (dextrose 5% in water) IV over a 24-hour period. If the IV administration set is calibrated to deliver 15 drops per mL, how many drops must be administered to the patient per minute?

Administration set

What is an administration set? The term "administration set" refers to a device that administers fluids to a patient using a combination of tubing, a drip chamber, and a flow regulator connected to a needle that is inserted into the patient's vein. Administration sets deliver fluids simply through gravity or they can be used with IV pumps that can be set for delivery of a specific volume over a specific period of time.

Standard sets are regulated to deliver 10, 15, 20, or a maximum of 60 drops per milliliter of fluid (60 drops per milliliter sets are also known as micro-drip sets). So, to reiterate, if you have a 10 gtt/mL administration set, it would mean that for every 10 drops the administration set delivers, you get 1 mL of solution. Now let's get back to our problem.

Step 1 – Calculate mL/hr

$$\frac{3000 \text{ mL}}{24 \text{ hr}} = \frac{X \text{ mL}}{1 \text{ hr}}$$

The problem above is saying, "If the provider's order is for 3000 mL in 24 hours, then how many milliliters do I need for 1 hour? Remember, these problems are examined with the *if/then* approach.

$$24X = 3,000$$

$$X = 125 \text{ mL/hr or } 125 \text{ mL}/60 \text{ minutes}$$

Step 2 – Calculate mL/min

$$\frac{125 \text{ mL}}{60 \text{ min.}} = \frac{X \text{ mL}}{1 \text{ min.}}$$

The problem above is saying, "If I'm giving 125 mL in 60 minutes, then how many mL do I need for 1 minute?"

$$60X = 125 \rightarrow X = 2 \text{ mL/minute}$$

Step 3. Calculate drops/minute

Calculate drops/minute (gtt/min) using the drop rate per minute of the IV administration set. (**NOTE:** You may have to contact the nursing unit to get the size of the administration set to be used.)

Let's say the IV administration set to be used has a drop rate = 15 drops/mL.

$$\frac{15 \text{ gtt}}{1 \text{ mL}} = \frac{X \text{ (gtt)}}{2 \text{ mL/minute}}$$

Remember, this is the amount we said that we needed from step 2. This last part of the problem may be confusing, so be sure to read it carefully. The problem above is saying, "I have an IV administration set; for every 15 drops of fluid, my patient will receive 1 mL. How many drops (X gtt) are needed if I'm giving 2 mL per 1 minute?"

$$1X = 30 \rightarrow X = 30 \text{ gtt/min.}$$

Let's change the amount of fluid being administered and move on to intravenous administration time.

IV administration time

You can calculate the time required to administer an IV solution when you know three things:

1. The type or size of the IV administration set.
2. The flow rate (mL/hr or mL/min) or drop rate (gtt/mL) of the solution being administered.
3. The volume of the IV solution being administered.

First, we're going to assume you have a gravity-fed IV administration set, meaning there is no IV pump pushing the solution into your patient. You may be thinking this would never happen; well think again. You could end up in a disaster zone or deployed without power for a few hours or days.

Your patient is receiving 1,500 mL of D5W (dextrose 5% in water), which will be given in three separate 500 mL bags. You also have an IV administration set that is calibrated to deliver 15 gtt/mL.

Let's work this problem together following these three steps:

1. Calculate gtt/min.
2. Calculate mL/hr.
3. Calculate hours needed to administer the total volume of solution.

Begin with assumption

We are going to start with the assumption that you *do not know* or *were not given* the flow rate. We have a 1,500 mL volume of the IV solution being administered, and a 15 gtt/mL administration set. If we *do not* have a flow rate, we'll start our problem by calculating the drop rate (gtt/mL).

1. You know that your administration set is calibrated to 15 gtt/mL (15 drops = 1 mL). If you know how many drops fall within the administration set in one minute, you can calculate your flow rate (mL/min).
2. We'll say you counted the falling drops for 30 seconds and counted 22 drops; that means for one minute you would have 44 drops or 44 gtt/min.
3. Now use your gtt/min data and the administration set data to calculate mL/min.

Calculate the number of mL/min

The following is the drop rate of the IV administration set:

$$\frac{X \text{ mL}}{44 \text{ gtt/min}} = \frac{1 \text{ mL}}{15 \text{ gtt}} \rightarrow 15X = 44 \rightarrow X = 3 \text{ mL/min.}$$

NOTE: If you already know the flow rate (in most cases you will be given that information), then you can skip steps 1 and 2.

Calculate the number of mL/hr

Now that we know the drop rate, we can calculate the number of mL/hr. Remember, there are 60 minutes within one hour. By using this information, we can effectively calculate the amount in the following equation:

$$3 \text{ mL/min} \times 60 \text{ min/hr} = 180 \text{ mL/hr}$$

Calculate the number of hours

Now that we know the number of mL/hr, which is 180 mL/hr, we can calculate the number of hours required to administer a particular amount of mL. In this case, let's consider 1500 mL, or the total volume of the solution. In other words, if 180 mL are delivered each hour, how many hours are required to administer 1500 mL? In order to calculate this, let's use the following equation:

$$\frac{180 \text{ mL}}{1 \text{ hr}} = \frac{1500 \text{ mL}}{X \text{ hr}} \rightarrow 180X = 1500 \rightarrow X = 8.3 \text{ hours, or 8 hours and 20 minutes.}$$

If you look carefully, you'll notice the equations to calculate both the numbers of mL/hr and the number of hours to administer a volume of solution are very similar.

IV fluid volume control

There are many times when a patient is restricted to a certain amount of fluid in a stated time. There can be many reasons for this, one of which is diminished kidney functioning. The prescriber's order may read something like this: "Restrict patient IV fluid intake to 1,500 mL/24 hours."

To determine the maximum hourly IV administration flow rate to achieve 1,500 mL in 24 hours, you simply divide 1,500 mL by 24 hours. Your maximum IV administration flow rate is 62.5 mL/hr.

Drug amount calculations

Calculate how much aminophylline 25 mg/mL injection you should add to the 1,000 mL IV bag of D5W, to achieve the 1,500 mg aminophylline dose. You remember this problem; just set up the ratio proportions and solve for X.

$$\frac{25 \text{ mg}}{1 \text{ mL}} = \frac{1500 \text{ mg}}{X \text{ mL}} \rightarrow 25X = 1500 \text{ mg} \rightarrow X = 60 \text{ mL}$$

Add 60 mL of aminophylline (25 mg/mL) injection to the IV bag.

Staying with the same IV aminophylline order, you can determine how much aminophylline the patient is receiving per day.

Determine IV total volume

An order is written to administer 1.5 grams of aminophylline in 1,000 mL of D5W; the flow rate is to run at 50 mL/hr. How much aminophylline is the patient receiving per day? To calculate the amount of aminophylline this patient will receive in a 24-hour period, follow these steps:

Determine the total volume of IV solution the patient is receiving per day.

$$\frac{15 \text{ mL}}{1 \text{ hr}} = \frac{X \text{ mL}}{24 \text{ hr}} = 1200 \text{ mL}$$

Find the medication and IV bag information from your provider's order and place that information next to your total volume per day information; now you can solve.

$$\frac{1500 \text{ mg (1.5 g) of aminophylline}}{1000 \text{ mL of D5W}} = \frac{X \text{ mg}}{1200 \text{ mL}}$$

$$1000X = 1500 \times 1200 \text{ mg} \rightarrow 1000X = 1,800,000 \text{ mg} \rightarrow X = 1800 \text{ mg}$$

The patient will receive 1800 mg (1.8g) of aminophylline in 24 hours.

We're almost done with the IV administration problems. The last IV problem we'll look at combines IV administration and dosing of patients based on their weight.

IV administration and dosing of patients

A child weighs 40 Kg and the dosage rate of aminophylline is 1 mg/Kg/per hour. At what rate should the previously discussed aminophylline IV (1,500 mg in 1,000 mL) be administered to this child?

To calculate this, follow these steps:

1. Determine the hourly dosage of medication for the child.

$$\frac{1 \text{ mg}}{\text{kg/hr}} = \frac{X}{40 \text{ kg}} \rightarrow X = (40 \times 1) \rightarrow X = 40 \text{ mg/hr.}$$

2. Determine the amount of IV solution that contains the 40 mg of aminophylline.

$$\frac{1500 \text{ mg aminophylline}}{1000 \text{ mL of D5W}} = \frac{40 \text{ mg/hr}}{X \text{ mL}} \rightarrow 1500X = (40 \times 1000) \rightarrow X = \frac{40,000}{1500}.$$

$$X = 27 \text{ mL/hr.}$$

The patient's aminophylline IV solution should be administered at a rate of 27 mL/hr to provide the dosage of 40 mg/Kg/per hour.

Calculating dosage for a child

Can you calculate what the total daily dose of aminophylline should be for this child? To calculate the total daily dose, follow these steps:

1. Determine the hourly dose of medication given to the patient (40 mg of aminophylline per hour).
2. To determine the daily dose, multiply your hourly dose by 24 (24 hours in a day). In this case, 40 mg x 24 hours = 960 mg of aminophylline per day.

Piggyback IV infusion calculations

When the prescriber orders medications to be administered piggyback with IV electrolyte fluids, you need to dissolve the medication in a separate IV fluid container or syringe. These medications are normally dissolved in 50 to 100 mL of an IV solution and generally administered over one hour or less through an open IV administration line. You calculate the flow rate for these piggyback IV infusions the same way as you calculated the regular IV solutions.

Although many pharmaceutical products are available commercially, they may not be the proper strength or combination of ingredients that a prescriber desires for a patient. There will be times when you will be asked to prepare a product, and you will have to calculate the dosages. You may also be asked to prepare a preparation for a specific patient, specialty, or prescriber. This can involve an array of calculations. In the next segment, we discuss how to reduce and enlarge formulas, determine the concentration and dilution of preparations, and prepare percentage solutions.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

605. Performing dosage calculations

1. How many doses are contained in 480 mL, if the dosage is 30 mL?
2. What dosage should be given if a total of 30 grams of medicine is to be divided into 10 doses?

3. How much codeine is needed to prepare 12 doses of a 30 mg/dose preparation?
4. How many pounds are equivalent to 1 kilogram?
5. The recommend dose for injectable acyclovir is 5mg/kg every eight hours. What is the total daily dosage needed for a patient who weighs 62 kg?
6. If the recommended daily dose of Amphotericin is 3 to 4 mg/kg, what is the dosage range for a patient weighing 220 lbs?
7. What do you do when there is no recommended dose for a one-year old patient?

606. Performing intravenous administration rate calculations

1. Why is it important to calculate the flow rates for IV infusions?
2. Standard administration sets deliver 10, 15, 20, or 60 drops per milliliter; what is the 60 drop set known as?
3. What is the flow rate in mL/hr if 3 liters is infused over 24 hours?
4. What is the flow rate in mL/minute for the same 3 liters infused over 24 hours?
5. What is the flow rate in gtt/minute if the same 3 liters of solution are now infused over 12 hours using a 15 gtt/mL set?
6. Sometimes you will be given the flow rate by the provider. If 180 mL of an antibiotic solution are to be delivered each hour, how many hours are required to administer 1500 mL?
7. The provider orders 1.5 grams of aminophylline in 1,000 mL of D5W and the flow rate is set to run at 50 mL/hr. How many milligrams of aminophylline will the patient receiving per day?

8. How many mL per hour does the same patient above require if the recommended dose is 40mg/kg?
9. What is the general administration time for an IV piggyback solution?

1-3. Compounding Calculations

The bulk compound preparations made in your pharmacy are from proven formulas that have been tested. According to AFI 44-102, these formulas will come from official compendia, other references, or locally developed formulas. Most likely the official compendia formulas come from either the United States Pharmacopeia-National Formulary (USP-NF) or MICROMEDEX®. These formulas list the amount of each ingredient needed to make a certain amount of the preparation. At times, it is necessary to reduce or enlarge a formula to satisfy the needs of your pharmacy.

This lesson covers the most commonly used calculations that you will need in compounding drug preparations for your patients.

607. Performing reduction and enlargement of compounding formulas

For certain disease states, some providers will develop their own formulas that they consider will work best for their patients. At times you will be asked to prepare these provider-developed formulas or formulas from other official resources. If the formula does not meet the patient's needs, you may have to reduce or enlarge this formula.

Most manufacturing formulas are based on a quantity of 100 g or 1,000 mL, although your local master formula cards may be based on any amount. Since you may need to make a smaller or larger quantity, you need to know how to reduce or enlarge this formula. In order to help you to become comfortable solving these problems, we will approach these calculations using two different formulas, including the ratio proportion formula and the factor method formula. To calculate the desired amount of ingredients, use one of these formulas.

Reducing/enlarging formula 1: ratio proportion

You will recognize the following formula from using it earlier in this unit.

$$\frac{\text{(b) Amount of individual ingredient listed on official formula/recipe card.}}{\text{(c) Quantity of total preparation listed on official formula/recipe card.}} = \frac{\text{(X) Amount of individual ingredient needed for your compounded preparation.}}{\text{(a) Quantity of total preparation desired - how much of the preparation you want.}}$$

$$(c \times X) = (a \times b) \rightarrow cX = ab \rightarrow X = \frac{ab}{c}$$

Reducing/enlarging formula 2: The factor method

Unlike ratio proportion formulas in which your calculations are performed in one self-contained problem, the factor method is broken into three separate steps. This method is also called "the new over old" method by many technicians in our career field.

Step one

For this step, you need two pieces of information.

1. How much preparation do you want to make?

2. Then, on your official formula/recipe card, what is the total quantity of the preparation? In other words; what is your new amount and what is your old amount?

Place these two pieces of information in the following formula.

$$\frac{\text{Quantity of total preparation desired} \\ \text{(how much of the preparation you want to make).}}{\text{Quantity of the total preparation listed} \\ \text{on the official formula/recipe card.}} = \text{The Factor.}$$

NOTE: Make sure the information that you place in this formula are in like units (i.e., mL and mL, gm and gm, etc.).

Step two

Multiply the quantity of each ingredient in the official formula by *The Factor*. The resulting answers will be the amounts you need for each ingredient in your preparation.

Those are your two formulas. In order to determine which formula you're comfortable with, let's solve a few practice problems together.

Practice problem 1

Using the official formula from the Pharmacy Master Formula Card (fig. 1–2), 455 gm of 10% Urea in 0.1% TMC (triamcinolone acetone cream), calculate the amounts of each ingredient in the following formula to prepare 3000 gm.

Figure 1–2. AF Form 2381, Pharmacy Master Formula Card.

To conserve space in this publication, only the calculations for the urea crystals will be shown in each formula. All ingredient calculations will be shown at the end of this practice problem.

Using formula 1: ratio proportion

$$\frac{\begin{array}{l} 45 \text{ gm – urea crystals.} \\ \text{(Amount of individual ingredient listed} \\ \text{on official formula/recipe card.)} \\ 455 \text{ gm 10\% urea in 0.1 TMC.} \\ \text{(Quantity of total preparation listed} \\ \text{on official formula/recipe card.)} \end{array}}{\quad} = \frac{\begin{array}{l} (X) \text{ gm – of urea crystals.} \\ \text{(Amount of individual ingredient needed} \\ \text{for your compounded preparation.)} \\ 3000 \text{ gm 10\% urea in 0.1 TMC.} \\ \text{(Quantity of total preparation desired -} \\ \text{how much of the preparation you want.)} \end{array}}{\quad}$$

$$(455 \times X) = (45 \times 3000) \rightarrow 455X = 135,000 \rightarrow X = \frac{135,000}{455} = 297.$$

$$X = 297 \text{ gm urea crystals.}$$

Using formula 2: The factor method

$$\frac{\begin{array}{l} 3000 \text{ gm 10\% urea in 0.1 TMC.} \\ \text{(Quantity of total preparation desired} \\ \text{how much of the preparation you want to make.)} \\ 455 \text{ gm 10\% urea in 0.1 TMC.} \\ \text{(Quantity of the total preparation listed} \\ \text{on the official formula/recipe card.)} \end{array}}{\quad} = 6.59 \text{ (The Factor).}$$

Multiply (*The Factor*) 6.59 and the amount of urea crystals listed on the official formula:

$$45 \text{ gm} \times 6.59 \rightarrow 297 \text{ gm of Urea crystals.}$$

Multiply the quantity of each ingredient in the official formula by *The Factor*; the resulting answers will be the amounts you need for each ingredient in your preparation.

Ingredients 10% for Urea in 0.1% TMC	Formula Amt	Factor		Ingredient amounts to compound 3000 grams
Urea crystals	45 gm	x	6.59	= 297 gm
TMC 0.1% cream	410 gm	x	6.59	= 2,702 gm
Sterile water	67 ml	x	6.59	= 442 ml
Orange food color	1 drop	x	6.59	= 7 drops
Formula for 455 gm	NOTE: You will only see a factor if you use the factor method.			

Let's try one more practice problem to ensure you understand the concept of reducing and enlarging formulas. To conserve space in this publication, you will no longer see a Pharmacy Master Formula Card, but the problem will be presented in a grid as shown above or in a word problem format.

Practice problem 2

Using the official formula for 1,000 mL of Compound Tincture of Benzoin, calculate the amounts of each ingredient to prepare 3,784 mL (1 gallon) of preparation.

Formula for Compound Tincture of Benzoin 1000mL	Amounts from original formula		Amounts needed to prepare 3,784ml
Benzoin	100 gm		
Aloe	20 gm		
Storax	80 gm		
Tolu Balsam	40 gm		
Ethyl Alcohol....QSAD	1,000 mL		
NOTE: QSAD means to "Add Quantity Sufficient to make total amount."			

Formula for Compound Tincture of Benzoin 1000mL	Amounts from original formula	Factor		Ingredient amounts to compound 3784mL
Benzoin	100 gm	x	3.784	= 378.4 gm
Aloe	20 gm	x	3.784	= 75.7 gm
Storax	80 gm	x	3.784	= 302.7 gm
Tolu Balsam	40 gm	x	3.784	= 151.4 gm
Ethyl Alcohol....QSAD	1,000 mL	-	-	= QSAD 3784 mL
NOTE: You will only see a factor if you use the factor method. If the factor method was used 3.785 (3,785/1,000 mL) is used to calculate each ingredient.				

608. Performing extemporaneous compounding calculations

The concentration of one substance in another substance may be expressed as a percentage or as ratio strength. Since there are no percentage weights on an electronic balance or on a graduate cylinder, you must have the ability to work with pharmaceuticals which have their strengths and concentrations expressed in a variety of ways.

Determining the concentration and dilution of preparations

Many of the prescriptions received in the pharmacy have the amounts of active ingredients expressed as percentage strengths as opposed to a weight or volume that can be measured. The providers know that certain active ingredients, when given in specific percentage strengths, give the desired therapeutic effects. Sometimes the provider does not calculate the amount of each ingredient needed for the prescription. Instead he or she simply indicates the percentage strength desired for each ingredient and expects the pharmacy to calculate the amount of each ingredient based on its percentage strength. Therefore, percentage values on a prescription must be changed to amounts which can be weighed in grams or measured in milliliters.

Concentration expressed in different types of percentages

Recall that the term “percent” means “parts per hundred” and is expressed in the following manner:

$$\frac{\text{Number of Parts}}{100 \text{ Parts}}$$

There are three different ways to express the concentration of a product as a percentage:

1. Weigh-in-weight (w/w).
2. Weight-in-volume (w/v).
3. Volume-in-volume (v/v).

Weight-in-weight

A weight-in-weight percentage means parts of a drug in parts of a mixture by weight. Percentage w/w expresses the number of grams of a drug or active ingredient in 100 grams of a mixture (gm/gm).

1. Example 1: A 5% (w/w) boric acid ointment would contain 5 grams of boric acid in each 100 grams of boric acid ointment.
2. Example 2: A 3% (w/w) hydrocortisone cream would contain 3 grams of hydrocortisone in every 100 grams of hydrocortisone cream.

NOTE: When the type of percent is not stated, it is understood that a dry ingredient in a *dry* preparation is percent (w/w).

Weight-in-volume

A weight-in-volume percentage is parts by weight in parts by volume. Percentage weight-in-volume expresses the number of grams of a drug or active ingredient in 100 milliliters of a mixture.

1. Example 1: A 10% (w/v) potassium chloride (KCL) elixir would contain 10 grams of potassium chloride in every 100 milliliters of KCL elixir.
2. Example 2: A 0.5% (w/v) Phenobarbital elixir would contain 0.5 grams of Phenobarbital in every 100 milliliters of Phenobarbital elixir.

NOTE: When the type of percent is not stated, it is understood that a dry ingredient in a *liquid* is percent (w/v).

Volume-in-volume

A volume-in-volume percentage is parts by volume of the total mixture. Percentage volume-in-volume expresses the number of milliliters of a drug or active ingredient in 100 milliliters of a mixture and is usually used for mixtures of liquids in liquids.

1. Example 1: A 70% (v/v) alcoholic solution would contain 70 milliliters of alcohol in every 100 milliliters of solution.
2. Example 2: A 0.5% (v/v) glacial acetic acid solution would contain 0.5 milliliters of glacial acetic acid in each 100 milliliters of solution.

NOTE: When the type of percent is not stated, it is understood that a liquid in a liquid is percent (v/v).

Further examples

Before you start solving these problems, the following provide a few more examples:

1. 0.9% sodium chloride (w/v) is equal to 0.9 g of sodium chloride in 100 mL of solution.
2. 5% dextrose in water (w/v) is equal to 5 g of dextrose in 100 mL of solution.

Terminology

Before you work the next problem, you need to be familiar with some terminology.

1. Dextrose in water is the same as D5W.
2. 0.9% sodium chloride (NaCl) is the same as normal saline (NS).
3. Saline is NOT the same as NS.
4. Half-normal saline is $\frac{1}{2} \times 0.9\% \text{ NaCl} = 0.45\% \text{ NaCl}$. This may also be referred to as 0.45 NS or $\frac{1}{2}$ NS.

Now you are ready to work a problem to see if you understand the concept of (w/v). You can use the proportional method to solve this problem.

Practice problem

How many grams of dextrose are in 1 liter of 5% D5W?

1. Known ratio: D5W means $\frac{5 \text{ gm dextrose}}{100 \text{ mL solution}}$.
2. Unknown ratio: $\frac{X \text{ gm}}{1 \text{ L}}$.
3. Write the proportional formula: $\frac{X \text{ gm}}{1 \text{ L}} = \frac{5 \text{ gm}}{100 \text{ mL}}$.

Before we can cross-multiply, we need to convert liters to milliliters so that terms across from each other are in the same units. Since $1 \text{ L} = 1,000 \text{ mL} \rightarrow \frac{X \text{ gm}}{1,000 \text{ mL}} = \frac{5 \text{ gm}}{100 \text{ mL}}$, we can now cross multiply:

$$(X \text{ gm} \times 100 \text{ mL}) = (5 \text{ gm} \times 1,000 \text{ mL}) \rightarrow 100 X = 5000 \text{ gm} \rightarrow X = 50 \text{ gm}.$$

There are 50 gm of dextrose in 1 liter of 5% D5W.

Concentration expressed as ratio strength

The concentration of solutions is sometimes expressed as ratio strength. For example, epinephrine is available in three concentrations: 1:200 (verbalized 1 to 200); 1:1,000; and 1:10,000.

A 1:200 concentration of epinephrine means there is 1 g of epinephrine in 200 mL of solution; a concentration of 1:1,000 means there is 1 g of epinephrine in 1,000 mL of solution; and 1:10,000 concentration of epinephrine means there is 1 g of epinephrine in 10,000 mL of solution. Use this definition of ratio strength to solve the following problem.

How many grams of potassium chloride should be used in preparing 500 mL of a 1:2,500 solution?

$$\frac{1 \text{ gm}}{2,500 \text{ mL}} = \frac{X \text{ gm}}{500 \text{ mL}}.$$

$$(1 \text{ gm} \times 500 \text{ mL}) = (X \text{ gm} \times 2,500 \text{ mL}) \rightarrow X = \frac{500 \text{ gm}}{2,500} \rightarrow X = 0.2 \text{ gm}.$$

You would use 0.2 gm of potassium chloride to prepare 500 mL of a 1:2,500 solution.

Percentage preparation method

Percentage preparation is used to obtain formula requirements when you have to determine one of the following:

1. The total amount of active ingredient desired or contained in your preparation when the (percentage or ratio strength) and (total volume or weight) of a preparation is known.
2. The total (volume or weight) (desired or contained) in your preparation when the percentage or ratio strength and amount of active ingredients are known.
3. The percentage or ratio strength of a preparation when the amount of (active ingredient) and (total volume or weight) of preparation are known.

With the information you received on percentages and ratios, you're ready to start solving a few problems using the percentage preparation method. Before we begin the calculations, let me remind you of a few mathematical rules for solving these problems.

Follow these rules before solving formulas:

1. Change all known weights to grams.
2. Change all known volumes to milliliters.
3. Change all known ratios or the percentages represented as a fraction to a numeral percent (i.e., $1:200 = 1/200 = 0.005 = 0.5\%$ and $(\frac{1}{2}\% = 0.5\%)$).

The formula for these calculations is always the same. Each of these equations will consist of four pieces of information:

- Two known pieces of information (variables).
- One constant (will always be the same piece of information and is considered part of your formula).
- Your unknown: the part of the formula you desire to know, represented by (X).

Once we've placed your information in the formula correctly, it will be solved using the standard ratio proportion calculation method. Look at the formula set-up for these problems, and then we'll start some practice problems.

$$\frac{\text{Total amount of active ingredient in milliliters or grams.}}{\text{Quantity of total preparation in milliliters or grams.}} = \frac{\text{Strength of preparation listed as a percent.}}{\text{The constant - This part of the formula you will always have (100%).}}$$

Practice problem 1

How many milliliters of a 5% (w/v) boric acid solution can be made from 20 grams of boric acid?

First, let's break down the problem:

1. Active ingredient - 20 grams of boric acid.
2. Quantity of total preparation - Unknown; this is your X (X mL).
3. Strength of the preparation in a percent- 5%.
4. The constant - Always listed as 100%.

Now, set your problem up using the example provided:

$$\frac{20 \text{ gm}}{X \text{ mL}} = \frac{5\%}{\text{The constant } \{ 100\% \}}$$

Now, solve for (X) like any ratio proportion problem:

$$(20 \text{ gm} \times 100\%) = (X \text{ mL} \times 5\%) \rightarrow 5X = 2000 \text{ mL} \rightarrow X = 400 \text{ mL}$$

Practice problem 2

How many grams of ephedrine sulfate are needed to make 120 mL of a 2% (w/v) ephedrine sulfate solution?

$$\frac{X \text{ gm}}{120 \text{ mL}} = \frac{2\%}{\text{The constant } (100\%)}$$

Now, solve for (X) like any ratio proportion problem:

$$(X \text{ gm} \times 100\%) = (120 \text{ mL} \times 2\%) \rightarrow 100X = 240 \text{ gm} \rightarrow X = 2.4 \text{ gm}.$$

Practice problem 3

How many grams of zinc oxide are needed to make 120 grams of 20% zinc oxide paste?

First, let's break down the problem. This is a problem where you have two weights (w/w). Can you identify the active ingredient?

1. Active ingredient – the amount of zinc oxide is unknown; this is your X (X gm of zinc oxide).
2. Quantity of total preparation – 120 grams of zinc oxide paste.
3. Strength of the preparation in a percent – 20%.
4. The constant – always listed as 100%.

$$\frac{X \text{ gm}}{120 \text{ gm}} = \frac{20\%}{\text{The constant } (100\%)}$$

Now, solve for (X) like any ratio proportion problem:

$$(X \text{ gm} \times 100\%) = (120 \text{ gm} \times 20\%) \rightarrow 100X = 2400 \text{ gm} \rightarrow X = 24 \text{ gm}.$$

Practice problem 4

If 5 gm of a chemical is dissolved in enough water to make one liter of preparation, what is the percentage strength of the solution?

First, let's break down the problem. (Hint: Remember the rules).

1. Active ingredient - 5 gm of chemical.
2. Quantity of total preparation - 1 liter of preparation (change to 1000 mL).
3. Strength of the preparation in a percent - the amount of the chemical is unknown (this is your X in percent).
4. The constant - Always listed as 100%.

$$\frac{5 \text{ gm}}{120 \text{ mL}} = \frac{X\%}{\text{The constant } (100\%)}$$

Now, solve for (X) like any ratio proportion problem:

$$(5 \text{ gm} \times 100\%) = (1000 \text{ mL} \times X\%) \rightarrow 500 = 1000X\% \rightarrow X = 0.5\%$$

Dilutions made from stock solutions

Stock solutions are bulk solutions of known concentration frequently prepared for convenience in dispensing. They are frequently concentrated solutions from which more dilute solutions can be quickly prepared, although dilute solutions are also compounded. The concentration of one substance in another substance may be expressed as a percentage or a ratio strength. The following formulas were developed to assist you with these problems; however, in order for these formulas to work, the following must be true:

- Volumes and weights must be expressed in the same units.
- Concentrations must be expressed in the same units.

The formula for concentration and dilution problems is:

$$\text{Amount}_1 \times \text{Percent}_1 = \text{Amount}_2 \times \text{Percent}_2$$

Another way to look at this formula is:

$$\text{Volume}_1 \times \text{Concentration}_1 = \text{Volume}_2 \times \text{Concentration}_2$$

Or, as:

$$V_1 \times C_1 = V_2 \times C_2, \text{ where}$$

- V_1 = the volume of the stock preparation.
- C_1 = the concentration of the stock preparation expressed as a decimal, percent, or ratio strength.
- V_2 = the volume of the desired preparation.
- C_2 = the concentration of the desired preparation expressed as a decimal or percent, or ratio strength.

NOTE: If the definitions above are still a little fuzzy, think of these problems in this manner: You have three pieces of information, and you need the fourth. So plug in your three pieces of known information, and solve for the fourth. Let's try a few practice problems.

Practice problem 1

How many milliliters of a 2% stock solution of potassium permanganate (KMnO_4) would be needed to compound 120 mL of 0.02% potassium permanganate solution? Let's consider this problem in four steps.

1. Write the formula (remember, V = volume and C = concentration):

$$V_1 \times C_1 = V_2 \times C_2$$

2. Substitute the values:

$$(X \text{ mL} \times 2\%) = (120 \text{ mL} \times 0.02\%)$$

3. Check units. Units of concentration are both percent. The unknown value (X) will have the same units as the volume on the other side of the equal sign (milliliters, in this case).
4. Solve for x :

$$2X = (120 \times 0.02) \rightarrow 2X = 2.4 \rightarrow X = 1.2 \text{ mL}$$

NOTE: To compound the order: obtain 1.2 milliliters of the 2% stock solution of potassium permanganate, place it in a graduate cylinder, and QSAD (add quantity sufficient to make total amount) to 120 mL with distilled water.

Practice problem 2

How many milliliters of 10% povidone-iodine (Betadine) solution would be needed to make 4 liters of a 1:2000 Betadine solution? Let's consider the following four steps:

1. Write the formula:

$$V_1 \times C_1 = V_2 \times C_2$$

2. Substitute the values.

$$(X \text{ mL} \times 10\%) = (4 \text{ L} \times 1:2000)$$

3. Check units: change 4 liters to milliliters. The units of volume will be the same on both sides of the equal sign (milliliters, in this case).

$$(X \text{ mL} \times 10\%) = (4000 \text{ mL} \times 1:2000)$$

Then change the ratio 1:2000 to a percent.

$$(1:2000) = (1/2000) = (2000\overline{)1}) = 0.0005 = 0.05\%$$

$$(X \text{ mL} \times 10\%) = (4000 \text{ mL} \times 0.05\%)$$

4. Solve for X:

$$10X = (4000 \times 0.05) \rightarrow 10X = 200 \rightarrow X = 20 \text{ mL}$$

Let's do one more; this time we'll make this problem have two parts.

Practice problem 3

You need to prepare 1,000 mL of a 1% Neomycin solution for a bladder irrigation. You only have a 10% Neomycin stock solution available in the pharmacy.

Part 1: How many milliliters of the stock solution do you need to make this preparation?

Part 2: How many milliliters of sterile water do you need to add (QSAD) to complete the product?

1. Write the formula:

$$V_1 \times C_1 = V_2 \times C_2$$

2. Substitute the values:

$$(X \text{ mL} \times 10\%) = (1000 \text{ mL} \times 1\%)$$

3. Check units: The units are already the same on both sides of the equal sign, so go to the next step.

4. Solve for X:

$$10X = 1000 \rightarrow X = 100 \text{ mL}$$

Part 1: How many milliliters of the stock solution do you need to make this preparation? *Use 100 mL of 10% Neomycin stock solution.*

Part 2: How many milliliters of sterile water do you need to add (QSAD) to complete the product? *Add 900 mL of sterile water to your 100 mL of 10% Neomycin stock solution to complete this product.*

Concentration and dilution using the measurement of weight

The same premise of calculation we used with volumes of liquid can also be applied to bulk creams and ointment bases. Let's try another practice problem using weight instead of volume. The rules we used with volume still apply; we are just substituting weights for volumes.

- Weights must be expressed in the same units.
- Concentrations must be expressed in the same units.

The following is the formula for concentration and dilution problems:

$$\text{Amount}_1 \times \text{Percent}_1 = \text{Amount}_2 \times \text{Percent}_2$$

The following is another way to look at this formula:

$$\text{Weight}_1 \times \text{Concentration}_1 = \text{Weight}_2 \times \text{Concentration}_2$$

By using abbreviations, this can be expressed as $W_1 \times C_1 = W_2 \times C_2$, where the following apply:

- W_1 = the weight of the stock preparation.
- C_1 = the concentration of the stock preparation expressed as a decimal, percent, or ratio strength.
- W_2 = the weight of the desired preparation.
- C_2 = the concentration of the desired preparation expressed as a decimal or percent, or ratio strength.

NOTE: Think of these problems in this manner—you have three pieces of information, and you need to solve for the fourth. So plug in your three pieces of known information, and solve for the fourth.

Consider the following as a practice problem. How many grams of 14% zinc oxide ointment can be made from one pound of 20% zinc oxide ointment?

1. Write the formula: (remember, W = Weight and C = Concentration).

$$W_1 \times C_1 = W_2 \times C_2.$$

2. Substitute the values.

$$(X \text{ gm} \times 14\%) = (1 \text{ lb} \times 20\%)$$

3. Check the units. Units of concentration are both percent. The unknown value (X) should have the same units of weight on both sides of the equal sign. But if you notice, they are not the same. The lbs must change to grams because the answer is to be in grams. If you recall, 454 grams = 1 lb.

$$(X \text{ gm} \times 14\%) = (454 \text{ gm} \times 20\%)$$

4. Solve for X :

$$(14X = 9080 \text{ gm} \rightarrow X = 648.57 \text{ gm (which can be rounded to 648.6 gm)})$$

Calculations using the alligation method

Alligation is a method used to solve problems that involve mixing two products of different strengths to form a product having a desired intermediate strength. The alligation is used to calculate the following:

- The amount of diluent that must be added to a given amount of higher strength preparation to make a desired lower strength.
- The amount of active ingredient which must be added to a given amount of lower strength preparation to make a higher strength.
- The amount of higher and lower strength preparations that must be combined to make a desired amount of an intermediate strength.

It is often more practical to dilute a known strength preparation than it would be to compound an entire preparation. Compounding may involve weighing, measuring, heating, and extensive mixing of all the ingredients to achieve the finished product. Sometimes a simple calculation using alligations allows us to calculate the amount of diluent to be added to an already prepared higher strength preparation to form the strength desired. The job would then be simplified by the combining of the two ingredients.

Sometimes it is necessary to increase the strength of a preparation by adding an active ingredient. If a provider is treating a patient with 1% coal tar ointment and he decides to increase the strength to 2%, it can be accomplished by adding an unknown amount of coal tar (100%). Because this problem involves the mixing of a higher and a lower strength to form an intermediate strength, the unknown amount may be found by using the alligation method.

1. Draw a “tic-tac-toe” board (three horizontal boxes × three vertical boxes). We’ll refer to this “tic-tac-toe” board as a matrix from this point forward.
2. Label the columns across the top of the matrix (from left to right): Have, Want, and Proportional Parts.
3. Enter the percentage strength of the stronger preparation in the upper-left box (A).
4. Enter the percent strength of the weaker preparation to be mixed in the lower-left box (B).
5. Enter the desired percent strength of the preparation in the center box (C).
6. Let x and y equal the unknown parts of the preparation to be mixed to obtain the desired mixture.
7. Enter x in the upper-right box.
8. Enter y in the lower-right box.
9. Add an extra column to the right of your matrix, and place a label above that column: Amount.

This all sounds confusing until you picture it. Your alligation matrix should look like this:

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
(A) Percent (%) of Stronger Preparation	<i>Blank</i>	x	

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
<i>Blank</i>	(C) Percent (%) of Desired Preparation		
(B) Percent (%) of Weaker Preparation	<i>Blank</i>	<i>y</i>	

It is not unusual for technicians to have difficulty with alligation problems. This is understandable due to the complexity of the problems. So we are going to work through the calculations that can be accomplished with the matrix step-by-step. Each problem presented will become more complex, but as we step through each problem, you will become more confident in your ability to use and solve alligation problems.

For this first alligation problem, we will solve for proportional parts only. An example of proportional parts would be the mixing of fruit punch. Your recipe could read: use one part ginger-ale and two parts fruit juice. Depending on the amount of punch you need, you could mix a small amount of punch: 1 quart (1 part) of ginger-ale and 2 quarts (2 parts) of fruit juice; or you could mix a larger amount: 1 gallon (1 part) of ginger-ale and 2 gallons (2 parts) of fruit juice. Now let's try some practice problems.

Practice problem 1

In what proportions should 95% alcohol and 50% alcohol be mixed to make 70% alcohol?

First let's break down the problem:

- What do I have? Answer - 95% alcohol and 50% alcohol.
- What do I want? Answer - 70% alcohol.

Procedures to solve the problem:

1. Subtract C from A to solve for *y*.
2. Subtract B from C to solve for *x*.

NOTE: You should never have negative numbers as an answer for these calculations. So if you end up with a negative number, you've most likely set up your problem wrong.

Another way to look at steps 1 and 2 is by asking yourself, "What's the difference between the numbers?" (i.e., the difference between 95 and 70 is 25, and the difference between 50 and 70 is 20.)

So, $x = 20$, and $y = 25$. This would mean that to attain 70% alcohol you would mix 20 parts of 95% alcohol and 25 parts of 50% alcohol together; the resulting mixture would be a 70% alcohol solution. Now work one more step to complete this problem. Look at the matrix above; picture the 20 and 25 as a fraction ($\frac{20}{25}$) that can be reduced to its simplest form, $\frac{4}{5}$, which is interpreted as 4 parts to 5 parts, or a total of 9 parts. The final answer to the problem would be 4 parts of 95% alcohol and 5 parts of 50% alcohol would obtain a 70% alcohol mixture.

Sometimes, alligations are expanded to include calculations that determine the volume amount of each component you have. Once you determine the volume amount of each component, you can combine them to obtain the precise amount and strength of the desired solution.

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
A 95%	Blank	x 20	
Blank	C 70%		
B 50%	Blank	y 25	

Using the previous example, we'll expand the next practice problem to include a desired volume amount of our 70% alcohol.

Total number of parts

Starting where we left off with practice problem 1:

You took your 20 and 25 parts and reduced them to their simplest form of 4 parts of 95% alcohol and 5 parts of 50% alcohol to obtain a 70% alcohol solution (for a total of 9 parts).

NOTE: The 9 parts are obtained by simply adding the 4 parts and 5 parts together and recording your answer in the center box; hence, you have 9 parts of 70% alcohol. The matrix below reflects these updates.

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
A 95%	Blank	x 4	
Blank	C 70%	↓ Add 4 parts and 5 parts = 9 Parts ↑	
B 50%	Blank	y 5	

Practice problem 2

Determine how many milliliters of 95% alcohol and 50% alcohol is required to make 200 milliliters of 70% alcohol.

First, let's break down the problem:

- What do I have? Answer - 4 parts of 95% alcohol and 5 parts of 50% alcohol that equal 9 parts of 70% alcohol.
- What do I want? Answer - 200 milliliters of 70% alcohol.
- Stop here and look at the matrix below.

When solving these problems you could block out the section you're not working with a piece of paper. This is shown by shading the sections of the matrix that are not part of the calculation we're working for that step (i.e., the non-shaded areas of the matrix are the active sections for this part of the problem).

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
A 95%	Blank	x 4	Z
Blank	C 70%	Add 4 parts and 5 parts = 9 Parts	G 200 mL
B 50%	Blank	y ◀ 5	W

Read the practice problem once more to yourself. You should recognize that this problem will have two separate answers.

1. How many milliliters of 95% alcohol do I need for this solution? (Matrix box Z).
2. How many milliliters of 50% alcohol do I need for this solution? (Matrix box W).

NOTE: The total of these two amounts (matrix boxes Z and W) will equal our desired amount of solution (matrix box G). Algebraically, it would look like this: ($Z + W = G$).

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
A 95%	Blank	x 4	Z
Blank	C 70%	Add 4 parts and 5 parts = 9 Parts	G 200 mL
B 50%	Blank	y ◀ 5	W

At this point your matrix should look like the one above. The next two calculations are simple ratio proportion problems.

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
A 95%	Blank	x 4	Z 88.9 mL
Blank	C 70%	T 9 Parts	G 200 mL
B 50%	Blank	y 5	W



Okay, we've reached the last two calculations of our alligation problem. The non-shaded areas in the preceding matrix and the following matrix are ratio proportion calculations, just like the ones you've solved throughout this unit. In the preceding matrix, we're solving to see how many milliliters of 95% alcohol we need to prepare our 70% alcohol:

$$(9 \times Z) = (4 \times 200) \rightarrow 9Z = 800 \rightarrow Z = 88.9 \text{ mL of 95\% alcohol}$$

Alligation Matrix			
<u>Have</u>	<u>Want</u>	<u>Proportional Parts</u>	<u>Amount</u>
A 95%	Blank	x 4	Z 88.9 mL
Blank	C 70%	T 9 Parts	G 200 mL
B 50%	Blank	y 5	W 111.1 mL



In the preceding matrix, we're solving to see how many milliliters of 50% alcohol we need to prepare our 70% alcohol:

$$(9 \times W) = (5 \times 200) \rightarrow 9W = 1000 \rightarrow W = 111.1 \text{ mL of 50\% alcohol}$$

Now that you have your final calculations, you can see that you need 88.9 mL of 95% alcohol and 111.1 mL of 50% alcohol. The two alcohols will be mixed together to prepare our desired 200 mL of 70% alcohol.

NOTE: If you add 88.9 mL (matrix box Z) and 111.1 mL (matrix box W), the sum is the desired volume of 200 mL (matrix box G). This is a good way to double-check your calculations.

Preventing calculation errors

We have discussed a variety of calculations that you will use to perform your duties as a pharmacy technician. Before we end this discussion, let's look at a few preventative measures you can take to prevent an error in calculation, thus preventing a medication error.

- Always place a “leading” zero before a decimal expression less than one. *Example:* .25mg may be read as 25 mg. The correct way is to write 0.25 mg.
- Never place a decimal point and a “trailing” zero after a whole number. The decimal may not be seen and result in a tenfold overdose. *Example:* 5.0 mg may be read as 50 mg. The correct way is to write 5 mg.
- Avoid using decimals whenever whole numbers can be used as alternatives. *Example:* 0.5 g should be expressed as 500 mg.
- Whenever possible, use the metric system rather than grains.

Developing a working knowledge of pharmaceutical calculations is crucial for success in your career as a pharmacy technician. Patients' safety depends on your accuracy each time you calculate a dose or make a pharmaceutical preparation. Another important aspect of your job, especially when making those pharmaceutical preparations, is pharmaceutical chemistry. In the next unit, we will cover basic concepts of chemistry and properties of pharmaceuticals. But first, answer the following questions to see if you have developed that working knowledge of pharmaceutical calculations.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

607. Performing reduction and enlargement of compounding formulas

1. What quantity or amounts are most manufacturing formulas are based upon?
2. What are the two ways used to reduce or enlarge a pharmaceutical formula?
3. How many grams of urea crystals are needed to 3,000 grams of 10% urea in 0.1%?
4. If you use the factor formula provided within this lesson to make 1,000 mL of Benzoin Tincture, and you are given 100 gm of Benzoin, 20 gm of Aloe, 80 gm of Storax, and 40 gm of Tolu Balsam, how many grams of each of these ingredients are needed to make 1 gallon?

608. Performing extemporaneous compounding calculations

1. What does a “percentage weight in volume” express?
2. What is the w/v of 0.5 grams of Phenobarbital in 100 mL?

3. How many grams are there in 100 mL of 5% dextrose in water?
4. How is the concentration of a solution expressed?
5. How are volumes expressed in percentage preparation formulas?
6. How many milliliters of a 5% (w/v) boric acid solution can be made from 20 grams of boric acid?
7. If 5 gm of a chemical is dissolved in enough water to make one liter of preparation, what is the percentage strength of the solution?
8. Define "stock solutions."
9. How many milliliters of a 2% stock solution of potassium permanganate (KMnO_4) would be needed to compound 120mL of 0.02% potassium permanganate solution?
10. How many milliliters of 10% povidone-iodine (Betadine) solution would be needed to make 4 liters of a 1:2000 Betadine solution?
11. How many grams of 14% zinc oxide ointment can be made from one pound of 20% zinc oxide ointment?
12. What is an allegation?
13. On an allegation matrix, where do you enter the desired percent strength of a preparation?
14. In what proportions should 95% alcohol and 50% alcohol be mixed to make 70% alcohol?
15. How many milliliters of 95% alcohol and 50% alcohol are required to make 200 milliliters of 70% alcohol?

16. What depends on your accuracy each time you calculate a dose or make a pharmaceutical preparation?

Answers to Self-Test Questions

601

1. The numerator.
2. An improper fraction.
3. By dividing the numerator by the denominator.
4. A proper fraction that has been reduced to its lowest terms.
5. $1/3$.
6. They both have fractions.
7. It does not change.
8. Ten.
9. It is multiplied by 10.
10. A 10-fold dosing error.
11. Leading.
12. Whole.
13. 13.07.
14. By dividing the numerator by the denominator.
15. 2.75.
16. $3\frac{1}{2}$.
17. Meter for length, gram for weight, and liter for volume.
18. 1,000.
19. Multiply by 1,000 or move the decimal point three places to the right.

602

1. Per or out of 100.
2. Write the number that precedes the % sign over 100; then simplify the resulting fraction.
3. $1/4$.
4. 75%.
5. Multiply the decimal value by 100 or move your decimal point two places right and add the percent symbol.

603

1. The amount of medication that a patient must take at one time to produce the optimum therapeutic effect.
2. Three.
3. Avoirdupois system.
4. Apothecary system.
5. 15.432.
6. Fluid ounce, 29.57 mL.
7. Thirty mL.

604

1. I = 1, V = 5, X = 10, L = 50, C = 100, D = 500, and M = 1,000.
2. XLV.

3. Nineteen.
4. That the numeral is multiplied by 1,000.

605

1. Sixteen doses.
2. Three grams.
3. 360 mg.
4. 2.2.
5. 930 mg.
6. 300–400 mg.
7. Call the provider.

606

1. To control the total volume of fluid administered to a patient during a stated period of time.
2. Micro-drip.
3. 125 mL/hr.
4. Two mL/min.
5. 62 gtt/min.
6. 8 hours and 20 minutes.
7. 1,800 mg.
8. 27 mL/hr.
9. One hour or less.

607

1. A quantity of 100 g or 1,000 mL.
2. Ratio proportion or factor method.
3. 297 gm.
4. Benzoin–378.4gm, Aloe–75.7 gm, Storax–302.7 gm, Tolu Balsam–151.4 gm.

608

1. The number of grams of a drug or active ingredient in 100 mL of a mixture.
2. 0.5%.
3. Five grams.
4. By ratio strength.
5. In milliliters.
6. 400 mL.
7. 0.5%.
8. Bulk solutions of known concentration frequently prepared for convenience in dispensing; they are frequently concentrated solutions from which more dilute solutions can be quickly prepared.
9. 1.2 mL.
10. 20 mL.
11. 648.6 gm.
12. A method used to solve problems that involve mixing two products of different strengths to form a product having a desired intermediate strength.
13. Center box.
14. 4:5.
15. 88.9 mL of 95% and 111.1 mL of 50%.
16. Patients' safety.

Do the unit review exercises before going to the next unit.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter. When you have completed all unit review exercises, transfer your answers to the Field Scoring Answer Sheet.

Do not return your answer sheet to Air Force Career Development Academy (AFCDA).

1. (601) What type of fraction has a numerator that is *smaller than* the denominator and an overall value less than one?
 - a. Proper.
 - b. Improper.
 - c. Complex.
 - d. Multicomplex.
2. (601) What type of fraction has a numerator that is *greater than* the denominator and an overall value greater than one?
 - a. Proper.
 - b. Improper.
 - c. Complex.
 - d. Multicomplex.
3. (601) What is $\frac{6}{8}$ reduced to its lowest terms?
 - a. $\frac{2}{4}$.
 - b. $\frac{3}{4}$.
 - c. $\frac{4}{6}$.
 - d. $\frac{5}{6}$.
4. (601) What is 0.525 divided by 0.67?
 - a. 0.7836.
 - b. 0.8753.
 - c. 1.276.
 - d. 1.672.
5. (601) Fractions are converted to decimal numbers by
 - a. dividing the denominator by the numerator.
 - b. dividing the numerator by the denominator.
 - c. multiplying the numerator and the denominator.
 - d. subtracting the denominator from the numerator.
6. (601) The standard metric measure for volume is the
 - a. milliliter.
 - b. centiliter.
 - c. meter.
 - d. liter.
7. (601) How many milligrams are in 1 gram?
 - a. 10.
 - b. 100.
 - c. 1,000.
 - d. 10,000.

8. (602) What is 40 percent converted to a fraction?
- a. $\frac{1}{4}$.
 - b. $\frac{2}{4}$.
 - c. $\frac{2}{5}$.
 - d. $\frac{4}{5}$.
9. (603) How many pints are there in 1 gallon?
- a. 2.
 - b. 4.
 - c. 6.
 - d. 8.
10. (603) How many tablespoonfuls are in 1 fluid ounce?
- a. 1.
 - b. 2.
 - c. 3.
 - d. 4.
11. (603) How many milliliters (mL) are in 1 pint?
- a. 454 mL.
 - b. 480 mL.
 - c. 960 mL.
 - d. 3840 mL.
12. (604) Convert Roman numeral III to an Arabic number.
- a. 3.
 - b. 10.
 - c. 30.
 - d. 100.
13. (604) Convert Roman numeral XCIV to an Arabic number.
- a. 94.
 - b. 96.
 - c. 114.
 - d. 116.
14. (604) What does a bar placed over a numeral mean?
- a. Divide by 100.
 - b. Divide by 1000.
 - c. Multiply by 100.
 - d. Multiply by 1000.
15. (605) What dosage in milligrams (mg) should be given if a total of 3 grams (g) are to be divided into 5 equal doses?
- a. 0.6 mg.
 - b. 6 mg.
 - c. 60 mg.
 - d. 600 mg.

16. (605) The recommended dose of cefamandole nafate for a pediatric patient is 50 milligrams/kilograms (mg/kg) per day. How many milligrams must be given daily to a 60-pound child?
- 1364 mg.
 - 1100 mg.
 - 910 mg.
 - 746 mg.
17. (605) The recommended dosage range is 30 to 50 milligrams/kilograms (mg/kg) a day divided in four doses. What is the dosage range for a 25 Kg child receiving 200 mg of erythromycin every six hours?
- 30–50 mg per day.
 - 50–750 mg per day.
 - 750–1250 mg per day.
 - 1250–3750 mg per day.
18. (606) An IV piggyback of lincomycin containing 1 gram (g) of drug in 100 milliliters (mL) is to be infused over 1 hour. The IV set is calibrated to deliver 15 drops per/mL (gtt/mL). How many drops/minute should be administered?
- 31.
 - 25.
 - 15.
 - 6.
19. (606) An intravenous (IV) infusion containing 750 milliliters (mL) is to be administered at a drop rate of 40 drops per minute (gtt/min). If the IV set is calibrated to deliver 20 gtt/mL, how long will it take to administer the entire infusion?
- 18 hours and 45 minutes.
 - 12 hours and 30 minutes.
 - 10 hours and 15 minutes.
 - 6 hours and 15 minutes.
20. (607) If 48 milliliters (mL) of Nystatin suspension are required to make 1000 mL of aphthous ulcer mix, how many milliliters of Nystatin suspension are required to make 250 mL of aphthous ulcer mix?
- 10.
 - 12.
 - 11.
 - 15.
21. (608) Calculate the number of grams (g) of dextrose in a 500 milliliter (mL) bag of 5% dextrose in water.
- 10 g.
 - 12 g.
 - 20 g.
 - 25 g.
22. (608) How many milliliters (mL) of 8% solution can be made if 1 liter of 30% solution is mixed with water?
- 2750.
 - 3000.
 - 3750.
 - 4000.

23. (608) Given a 95% and a 50% alcohol solution, how many milliliters (mL) of the 50% alcohol solution are required to make 750 mL of a 70% alcohol solution?
- a. 333.
 - b. 417.
 - c. 500.
 - d. 557.

Please read the unit menu for unit 2 and continue ➔

Student Notes

Unit 2. Pharmaceutical Chemistry

2–1. Concepts of Pharmaceutical Chemistry	2–1
609. Basic chemistry.....	2–1
610. Chemical bonding and reactions.....	2–4
2–2. Applying Chemistry in Pharmaceutical Compounds.....	2–8
611. Solutions and chemical solubility	2–8
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ADVANCES IN MEDICINE have brought about the need for the pharmacy technician to have an expanded knowledge of drugs and their actions. In this section, we will give a basic overview of chemistry in order to provide you with some insight into the use and actions of drugs. While it is impossible to cover the entire subject in detail, it is important to review the fundamental aspects of atomic structure and the forces involved in the formation of different structural types of compounds.

In the second section of this unit, we will discuss the applications of basic chemistry to pharmaceutical compounds. It's important to not only have a knowledge of chemistry, but also how it applies to solutions and balancing acids and bases.

2–1. Concepts of Pharmaceutical Chemistry

You are surrounded by objects you normally take for granted. Two such objects include the air you breathe and the water you drink—both chemical compounds. If you take the time to analyze each object for its chemical composition, you will find that chemistry can answer many questions. It explains why substances dissolve, why water freezes, and why antiseptics kill germs.

The science of chemistry contains many terms you'll need to do your job. We briefly discuss these basic chemistry terms (i.e., elements, matter, atoms) through definitions that will help you make sense of aspects discussed later. In addition, we will also consider the bonding and reactions that chemicals have with each other.

609. Basic chemistry

Let's begin with some very basic facts to lay the foundation for our discussion on the concepts of chemistry. Although you are not expected to become chemists, you should have a basic understanding of the makeup of the pharmaceuticals.

Matter

Matter is an endless array of materials you come in contact with each day. It can be defined as anything that has mass and takes up space. Matter exists in the three physical states of solid, liquid, and gas. A *solid* has the characteristic of definite shape; however, it does not necessarily have to fill or take the shape of its container. A *liquid* has the characteristic of having particles move freely while still retaining a definite volume. These particles are held together by strong chemical forces, but are not held as tightly as a solid. Liquids, while maintaining a definite volume, have indefinite shape; they take the shape of their container. A *gas* does not have a definite shape or volume. The particles in a gas have enough "energy" or activity to overcome the chemical attractive forces that hold solids and liquids together. A gas continuously presses in all directions upon the walls of the vessel in which it is contained; thereby completely filling its container.

The two basic properties that matter possesses are *physical* and *chemical*. Such characteristics as smell, color, shape, freezing and boiling point, and solubility are considered physical properties of matter. Chemical properties are those characteristics associated with changes in the composition of the substance; the behavior of a substance when it chemically reacts with other substances.

These two types of properties, physical and chemical, also describe the types of changes that can occur in matter. Physical changes would consist of changes in size, shape, or state of matter without any change in composition. For example, the changing of ice into water and water into steam are physical changes from one state to another; however, no new substance is formed.

In a chemical change, substances are formed that are totally different in properties and composition from the original substance. As an example, when copper wire is placed in a burner flame, a change in appearance occurs. While the color change represents a physical change, the product formed when copper combines (chemically) with oxygen during the heating process is copper oxide, a new substance.

In addition to the two types of properties (physical and chemical), matter is also classified into one of three different groups: elements, compounds, and mixtures.

Elements

An element is a substance that cannot be broken down into other substances. Some of the elements that are part of your everyday life include oxygen, iron, and gold. Several elements are essential to life functions. The following table shows the elements making-up the human body.

Element	Atomic Symbol	% of Human Make-up by Weight	Body Functions
Oxygen	O	65	Part of water and most organic molecules. Also molecular oxygen.
Carbon	C	18	The backbone of all organic molecules.
Hydrogen	H	10	Part of all organic molecules and of water.
Nitrogen	N	3	Component of proteins and nucleic acids.
Calcium	Ca	2	Constituent of bone. Also essential for the action of nerves and muscles.
Phosphorus	P	1	Part of cell membranes and of energy storage molecules. Also a constituent of bone.
Potassium	K	0.3	Important in nerve action.
Sulfur	S	0.2	Structural component of most proteins.
Sodium	Na	0.1	The primary ion in body fluids. Also important for nerve action.
Chlorine	Cl	0.1	Component of digestive acid. Also a major ion in body fluids.
Magnesium	Mg	Trace	Important for the action of certain enzymes and for muscle contraction.
Iron	Fe	Trace	A constituent of hemoglobin, the oxygen-carrying molecule.

Compounds

A compound is a substance composed of two or more elements chemically combined in a definite proportion. There are millions of known compounds including water, ammonia, and table salt. They can be broken down into their constituent elements only by chemical change and not by physical means. For example, using electricity, you can separate water into the elements hydrogen and oxygen. A compound has properties separate and distinct from its constituent elements. Water, a liquid at room temperature, has chemical and physical properties different from either of its constituents, hydrogen or oxygen, which are both flammable gases.

Mixtures

A mixture is a combination of two or more substances that retain their individual properties. They are held together by physical rather than chemical means and include soil, most rocks, and milk. Mixtures that are uniform throughout are *homogenous* and those that are not uniform (one part of the mixture has a composition that is different from another part) are *heterogeneous*. We will discuss mixtures in greater detail when we talk about non-sterile manufacturing and compounding in unit 3.

Atomic structure

The atomic structure is the story of how materials are made from atoms. There are only about 100 elements in the universe and whether these atoms form trees, animals, water, or the air you breathe depends upon how they are put together. Atomic structure not only determines the appearance of materials, but also their properties. When a lump of coal becomes a diamond or a common cold becomes a deadly virus, we begin to realize how important it is to understand the structure of materials.

Protons, neutrons, and electrons

Matter is composed of minute particles called *atoms*. Atoms are the smallest particles possessing the properties of an element that can enter into a chemical combination. They are made of protons, neutrons, and electrons, which are called *subatomic particles*.

1. *Protons* are particles with a positive charge.
2. *Electrons* are particles with a negative charge.
3. *Neutrons* are particles with no charge.

Together, the proton and neutron make up the nucleus of most atoms; while electrons orbit the nucleus at different distances referred to as *shells*.

Electrons farthest from the nucleus (outer shell), often termed *valence electrons*, are important to the bonding capabilities of an atom and the formation of bonds between elements. Atoms will lose, gain, or share electrons to achieve this goal. If an atom gains electrons, it becomes more negatively charged. If an atom loses electrons, it becomes more positively charged. Any atom having a charge, either positive or negative, is called an *ion*; more specifically, a negatively charged atom is called an *anion* and a positively charged atom is called a *cation*.

The capacity of an element to combine with another element is called *valence*. The electrons in the outer shell and the protons in the nucleus determine which elements combine in what proportions. The valence number is the number of electrons involved in the combination process.

Quarks

For years, protons and neutrons were thought to be the fundamental particles. However, protons and neutrons are now known to be triplets of more basic particles called *quarks*. There are three quarks in every proton and three in every neutron. Quarks themselves possess various masses and have charges that are either one-third or two-thirds of a single positive or negative charge. They combine in twos or threes to form other particles, making it feasible to combine them in ways that produce a positive, negative, or neutral charge.

Isotopes

Isotopes are atoms of the same element containing the same number of protons but different number of neutrons. Elements usually occur in nature as mixtures of isotopes. All isotopes of a given element have essentially the same chemical characteristics. Some isotopes with excess neutrons are unstable and tend to break down or decay into a more stable isotope (usually of a different element). Such isotopes are termed radioisotopes, since they emit high-energy radiation when they decay.

Molecules

Molecules are formed when two or more atoms combine chemically. For example, if two atoms of oxygen combine, a molecule of oxygen is formed. Different kinds of atoms can combine to form a *chemical compound*. Water is a chemical compound in which each molecule consists of two atoms of hydrogen combined with one atom of oxygen (H_2O).

610. Chemical bonding and reactions

Primarily the number and arrangement of electrons in the outermost energy level (electron shell) determines the chemical properties of an element.

- The few elements where the outermost shell is filled are called *noble gases*. These elements are chemically inert, meaning that they will not readily combine with other elements.
- The electrons in the outmost energy level of an atom are referred to as *valence electrons*. The valence electrons are chiefly responsible for the chemical activity of an atom.

When the outer shell of an atom contains fewer than eight electrons, the atom tends to lose, gain, or share electrons to achieve an outer shell of eight.

Major types of chemical bonding

The elements in a compound are always present in a certain proportion. This reflects the fact that atoms are attached to each other by chemical bonds in a precise way to form a compound. A *chemical bond* is the attractive force that holds two atoms together. Each bond represents a certain amount of potential chemical energy. The atoms of each element form a specific number of bonds with the atoms of other elements; a number dictated by the number of valence electrons.

There are two principal types of chemical bonds that actually “cement” atoms into compounds—ionic and covalent. Let’s discuss ionic bonds first.

Ionic bonding

This is a chemical bond that can occur due to the opposing electrical charges of atoms attempting to gain the desired electrons in the outer shells. Ionic compounds formed through this bonding normally have high melting points (above 200 degrees Celsius [$^{\circ}\text{C}$]) and are soluble in water.

An excellent example of an ionic bond occurs in the compound you frequently use—sodium chloride (NaCl) or salt. It has an 801°C melting point and dissolves easily in water. Sodium ions possess a positive (+) charge that means they have more protons than electrons, and the chloride ions are negatively (–) charged (more electrons than protons). Using some of the knowledge you’ve gained in the last section, sodium is therefore a *cation* and chloride is an *anion*. These two ions have opposite charges; as a result, they act like magnets where opposites attract to form a compound formula.

Ionic compounds are collections of ions held together by oppositely charged cations and anions. When an ionic compound is dissolved, a breakdown in this orderly arrangement occurs. The attractive forces between the ions and the solvent are greater than the inter-ionic forces within the compound by itself.

In general, ionic compounds are insoluble in all liquids, except water. This suggests an electrical attraction between the ions and water molecules is responsible for dissolving the ionic compounds. Using NaCl , you can see how this dissolution process works.

When a crystal of NaCl is placed in H_2O , certain water molecules’ partially positive (+) charged hydrogen atoms attract negative (–) charged chloride ions on the surface of the sodium chloride crystal. Other water molecules will place the partially negatively charged oxygen atom near the positive charge of sodium ions on the crystal surface. This process is called *hydration* because it reduces the attraction between the charged ions within the crystal. The result of this attraction is a gradual breaking away of ions in the crystal that is exposed to the water molecules and the hydration

process continues. Thus, the crystal is literally picked apart and the ions are dispersed as the compound dissolves.

There are other compounds that separate differently from ionic compounds because they are formed differently—by covalent bonding, which just happens to be our next topic.

Covalent bonding

Covalent compounds do not consist of ions and, therefore, do not have the electrical activity of ionic compounds. Covalent bonding binds atoms in small groups called molecules. The atoms within each molecule are very strongly attracted while the force of attraction from outside molecules is generally small.

Covalent bonding is the sharing of an electron pair between two atoms, each atom supplying one electron to the bond. An atom may furnish *both* electrons to form the bond, and this is called a coordinate covalent bond. Either way, two electrons are involved. So, a covalent bond is the result of a sharing of an electron pair between two atoms to form the bond. Figures 2-1 and 2-2 show examples of ionic and covalent bonding.

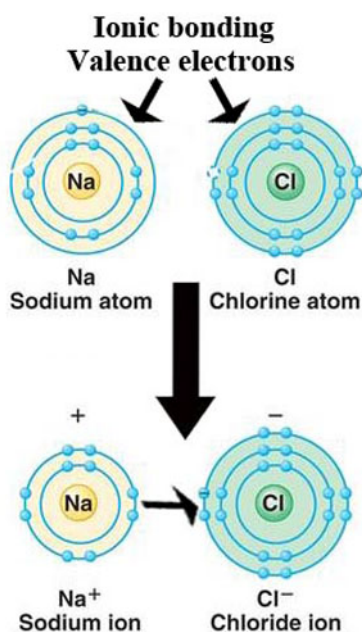


Figure 2-1. Ionic bonding.

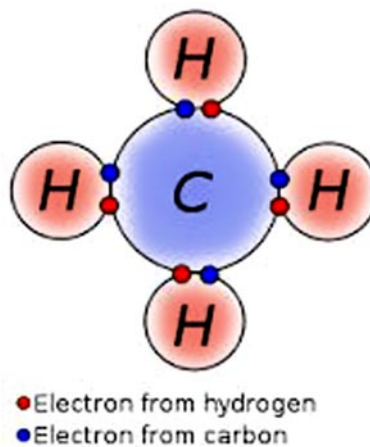


Figure 2-2. Covalent bonding.

So why is all of this important? It is noteworthy that about 98 percent of all drugs used today come from various combinations of the elements of carbon, nitrogen, sulfur, oxygen and/or hydrogen bonded with covalent (organic) bonds.

Chemical reactions

Chemical reactions happen all around us; this includes when we light a match, start a car, or eat dinner. A chemical reaction is the pathway in which two substances bond together and this plays an important role in the way drugs work.

Types of reactions

A chemical reaction is when one or more substances react with each other to form new compounds. These reactions are classified by type. Let's take a look at some of the most common types of reactions.

Combination

Combination is the direct joining of two or more simple substances, either elements or simple compounds. These substances form a more complex compound. For example, when copper and oxygen combine, copper oxide is formed.

Decomposition

Decomposition is the breakdown of a compound into simpler elements or compounds. Water is decomposed during electrolysis, resulting in the separation of water into its constituent elements, hydrogen and oxygen.

Replacement

Replacement is the substitution of one element for another in a compound. The reaction occurs in car batteries as the element iron and the compound sulfuric react to form iron sulfate and hydrogen. The iron replaces the hydrogen that was bonded to the sulfate.

Double replacement is the process in which two compounds react to form two new compounds as they exchange parts. An example of double replacement is when silver nitrate and sodium chloride react to form silver chloride.

Oxidation-reduction reactions

Oxidation is a process in which electrons are lost, while reduction is a process in which electrons are gained. For the most part, oxidation describes the way an element or compound reacts with oxygen. Oxygen is highly electronegative; that is, it takes electrons from other elements to fill its electron sub-shell. Thus when pure iron is exposed to moist air, it oxidizes, forming rust. The iron atoms lose electrons to the oxygen in the air. The oxygen gains these electrons, thereby filling its outer shell. This process is called an oxidation-reduction reaction or a *redox* reaction.

Corrosion

The single most destructive chemical reaction is corrosion. It is caused by chemical processes such as oxidation or through the action of a chemical agent. For example, despite the strong electro negativity of oxygen, iron will not rust in dry air. Corrosion is caused by the presence of oxygen and water.

Catalysts

Catalysts are substances that control rates of chemical reaction. Initially, catalysts were thought to change the rates of reaction but not to interact in the reaction. It is now known that some catalysts do interact with some reactants. Examples of catalysts in biochemistry are the enzymes that aid in the breakdown of large food molecules, such as proteins, into smaller molecules of amino acids.

Now that you have a basic foundation of chemistry, the next section will convey how it relates to pharmaceutical products.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

609. Basic chemistry

1. What are the three physical states of matter?

2. Name the two types of properties matter possesses.
3. What is a substance that cannot be broken down into other substances?
4. What type of electrons are important to the bonding capabilities of atoms and the formation of bonds between elements?
5. Define valence.
6. What are atoms of the same element that contain the same number of protons but different number of neutrons?

610. Chemical bonding and reactions

1. Name the two principal types of chemical bonds.
2. What type of compound is insoluble in all liquids except water?
3. What type of bonding is the result of a sharing of an electron pair between two atoms to form the bond?
4. What type of chemical reaction is the direct joining of two or more simple substances to form a more complex compound?
5. What are substances that control rates of chemical reactions?

2-2. Applying Chemistry in Pharmaceutical Compounds

So far, our discussion of chemistry has been at a microscopic level, covering processes and theories that are not visible. We now move on to processes that are extremely visible or that can be measured visually.

If the medications we dispense are not adequately soluble in the delivery vehicles we choose, such as solutions or elixirs, it makes it difficult for the patients' bodies to properly absorb the medications needed to treat targeted diseases. Equally important to pharmaceutical preparations is the proper balance between acidity and alkalinity. Without this proper balance, the human body will have difficulty absorbing the preparations properly. This section will discuss these two important aspects of pharmacological chemistry.

611. Solutions and chemical solubility

To a pharmacy technician like yourself, solubility is quite possibly the most important aspect of chemistry. This concept called solubility has applications in the preparation of ointments, suspensions, and IV fluids. To understand factors of solubility, you must first understand what a solution actually is.

The term solution immediately brings to mind a liquid; however, solutions also occur in gaseous and solid states. Air is an example of a gaseous solution; on the other hand, 14K gold, which is a mixture of gold, silver, and copper, is an excellent example of a solid solution. In this segment, we'll limit our discussion of solutions to liquids at room temperature.

A solution is a chemically and physically homogenous (uniform) mixture of two or more substances. When a solid or gas is mixed into a liquid to produce a solution, the solid or gas is called the solute and the liquid is called the solvent. If two liquids are mixed to form a solution, the liquid with the greatest volume is normally called the solvent and the lesser amount of liquid, the solute.

When discussing solutions, we consider the dispersion of one substance in other substance(s). Depending on the size of the dispersed particles, they are classified as true solutions, suspensions, or colloidal solutions.

When sugar is dissolved in water, it forms a *true solution*. Officially, this type of solution is one in which particles of true molecular dimensions are universally dispersed. For our purposes, let's say a "true" solution is a mixture of substances in which the solute is not visible, does not separate under normal conditions, and the end solution is transparent to light. The component particles are so small that even filtration does not remove them.

If the particles in a solution settle by the force of gravity, as sand particles in water do, then the solution is called a *suspension*.

Finally, if the particle size of the solute is too large to fit the definition for a true solution, yet the particles do not settle under the force of gravity, the resulting solution is termed a *colloid*. Milk of magnesia is an excellent example of a *colloidal solution*.

When a solute is brought in contact with a solvent, molecules of the solute are dispersed with molecules of the solvent to form a solution. The extent to which the solute dissolves is referred to as its solubility. Some materials dissolve in certain solvents while others do not. To fully understand this process of solubility, we must briefly consider the factors which influence solubility and the various types of solutions.

Factors affecting solubility

The following factors influence the degree of solubility of substances:

- Polarity of solute and solvent.
- Solute surface area.

- Stirring.
- Temperature.

Polarity of solutes and solvents

Water is considered a universal solvent and termed a *polar compound*. Parts of a water molecule have either a positive or negative charge (attraction). Because of these slightly polar charges, water dissolves most inorganic compounds, which are also polar. Simply put, polar solvents dissolve polar solutes.

Organic compounds (those containing carbon) are mostly non-polar solutes. An exception to this would be alcohols, which are generally water-soluble.

Solute surface area

A solute in the form of large crystals takes longer to dissolve than the same substance in a finely powdered form. This is because in a powder much more of the surface area comes in contact with the solvent.

Stirring

Stirring allows the solute surface to come in contact with the solvent more frequently.

Temperature

Increasing the temperature of a solvent increases the rate of solution.

Types of solutions

There are many types of different solutions you will be working with during your pharmacy career. Not all medications are compatible with these different types of solutions. Therefore, you must understand the difference between dilute, concentrated, saturated, supersaturated, and molar solutions.

Dilute solution

In a dilute solution, the amount of solute is small compared to the amount of solvent.

Concentrated solution

In a concentrated solution, the amount of solute is larger compared to the amount of solvent.

Saturated solution

A saturated solution is one in which no additional amount of solute can be dissolved by the solvent without external forces, such as heat or stirring. For every part of solute that dissolves after a solution is saturated, an equal amount crystallizes out of the solution.

Supersaturated solution

Because most solids dissolve with increased temperature of the solvent, more solute can be put into solution when heat is applied. The result of this formulation is a supersaturated solution.

Molar solution

A mole is equal to the gram molecular weight (GMW) of a given substance.

For some pharmacy preparations, it is desirable to make solutions in such a way that the amount of solute (in terms of its molecular weight) can be calculated from the amount of solution. Thus, a molar solution is made by weighing out 1-gram molecular weight of solute and dissolving it in water to a final volume of 1 liter (1,000 mL).

Now that you understand basic solubility concepts, we can better discuss the process of dissolution of covalent (molecular) compounds and dissolution of ionic compounds.

Dissolution of covalent compounds

Molecular, non-polar compounds or those containing carbon (organic) compounds generally do not dissolve in water or other polar solvents. The reason for this lack of solubility stems from the lack of bonding between polar and non-polar compounds. Organic compounds consist of molecules strongly bonded together individually. They are strongly bound or attracted to one another due to the near absence of electrical activity outside of the molecule. Thus, if a solvent which equals or closely approximates this attractive force, the molecular compound is attracted to it and dissolves. Polar solvents, such as water, have a strong electrical charge and therefore have little or no effect on noncharged compounds.

Dissolution of ionic compounds

We know that when an ionic compound is dissolved, the attractive forces between ions in the solute and those in the solvent are greater than the inter-ionic forces within the solute itself. We also know that, in general, ionic compounds are insoluble in all liquids, except water. This suggests that an electrical attraction between the charged (polar) ions and the polar water molecules is responsible for dissolving ionic compounds through the process of hydration.

612. Balance of acids and bases

Before we finish this section on chemistry, we must take a look at acids and bases and consider how they apply to the function of the body. *Homeostasis* is the state of equilibrium of the internal environment of the body. Survival depends on the body maintaining, or quickly restoring, the acid-base balance of its fluids. Maintaining an acid-base balance means keeping the concentration of hydrogen ions in body fluids relatively constant. This is of vital importance because if the hydrogen ion concentration veers away from the normal status, cellular chemical reactions cannot take place and survival is threatened.

Definitions of acids and bases

Before we get into a discussion of the homeostasis of the body, let's define acids and bases and look at the scale used to measure acidity or alkalinity.

Acids

There are three modern definitions of an acid.

1. An acid can be a solution of a compound that contains hydrogen ions as the only positive ion.
2. An acid can be a substance that acts as a proton donor.
3. An acid is a molecular substance that releases positive hydrogen ions in an aqueous solution.

There are many types of acids. For example, acetic or ethanoic acid is vinegar, while ascorbic acid is vitamin C. Acid is also responsible for the sour taste of wine that has aged by exposure to the air. Oxygen in the air reacts with the ethanol in the wine to form the acid.

Bases

A base can also be defined in three ways:

1. A base is a substance that reacts with an acid to produce only water and a salt. When the base reacts with an acid, the process is called neutralization.
2. A base is a substance that acts as a proton acceptor, rather than as a donor.
3. A base is the hydroxide of a metal (i.e., a metal combined with the hydroxide ion).

A soluble base is called an *alkali*. Strong alkalis include sodium and potassium hydroxides, which are good solvents for oil and grease, but they can burn the skin.

pH value measurement

The measure of pH indicates the scaled measurement of acidity or alkalinity of a substance and describes the concentration of free hydrogen ions in a solution. Because an acid is by definition a solution in which there are hydrogen ions, an acidic solution has a high concentration of free ions. However, pH is not a count of hydrogen ions but rather a measure of gram equivalent, or mass in grams per liter of solution. The concentration of hydrogen ions in a liter of solution ranges from 1 gram equivalent to 10 to 14 gram equivalents. Rather than use the actual number, the pH scale uses the negative exponent of the concentration. For example, if a solution's concentration is 10^{-7} , then its pH is expressed as 7.

The pH scale was devised to represent pH as shown in figure 2-3. The scale ranges from 0 to 14, with a 0 to 6.9 indicating more acidic solutions. Measurements of 7.1 to 14 indicate more alkaline solutions. The number 7.0 (pure water) represents a neutral solution, neither acidic nor alkaline. The "p" of pH is from the Danish word *potenz*, which means "strength"; and the "H" is the symbol for hydrogen. Thus, pH means the strength of the hydrogen ions.

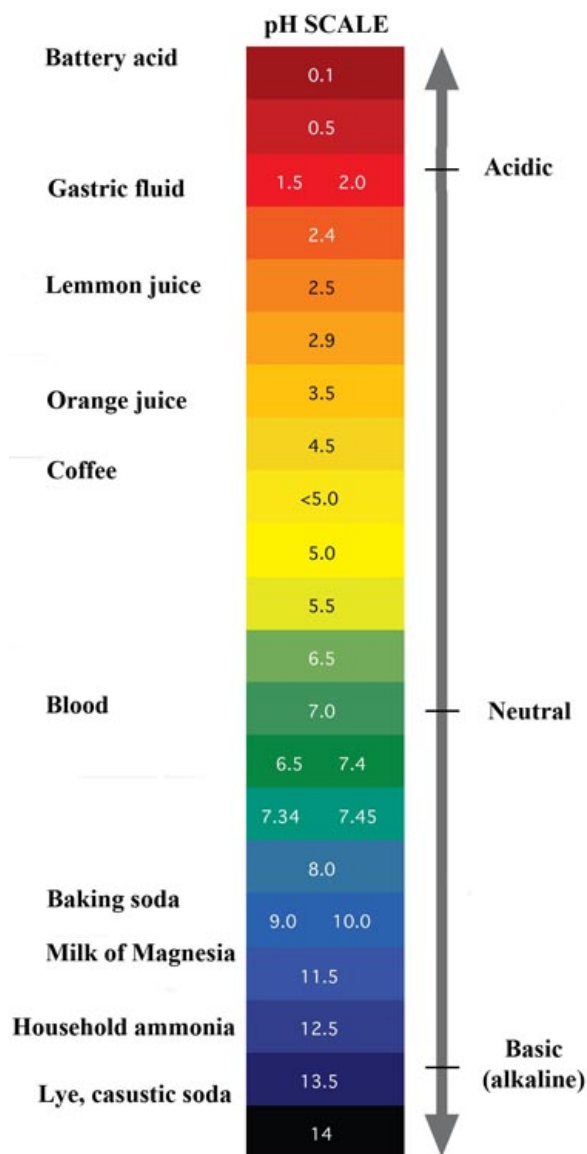


Figure 2-3. pH scale.

Mechanisms that control body fluid pH

The body has three mechanisms for regulating the pH of its fluids: the buffer mechanism, the respiratory mechanism, and the urinary mechanism. Together they constitute the complex pH homeostatic mechanism; that is, the body functions that keep blood slightly alkaline with a pH that stays remarkably constant. Its usual limits are very narrow, about 7.35 to 7.45.

Buffer mechanism

Buffers are chemical substances that prevent a sharp change in pH of a fluid when an acid or base is added to it. Strong acids and bases, if added to blood, would “dissociate” almost completely and release large quantities of hydrogen (H^+) or hydroxide (OH^-) ions. The result would be drastic changes in blood pH. Survival itself depends on protecting the body from such drastic pH changes.

More acids than bases are usually added to body fluids. This is because catabolism, a process that goes on continually in every cell of the body, produces acids that enter blood as they flow through tissue capillaries. Almost immediately, one of the salts present in the blood (a buffer) reacts with these strong acids to change them into weaker acids. The weaker acids decrease blood pH only slightly, whereas the stronger acids formed by catabolism would have decreased it greatly if they were not buffered.

Respiratory mechanism

Respiration plays a vital part in controlling pH. With every expiration, carbon dioxide (CO_2) and H_2O leave the body in the expired air. CO_2 remains in the arterial blood leaving the lung capillaries, so less of it is available for combining with water to form carbonic acid (H_2CO_3). Hence the arterial blood contains less H_2CO_3 and fewer hydrogen ions and has a higher pH (7.45) than does venous blood (pH 7.35).

How can a change in respiration change blood pH? Suppose you were to pinch your nose and hold your breath for a full minute. Obviously, no CO_2 would leave your body by way of expired air during that time and the blood's CO_2 content would increase. This would increase the amount of H_2CO_3 and the hydrogen-ion concentration of blood, which in turn would decrease blood pH. Here then are two useful facts to consider. Anything that causes a decrease in respirations will in time produce *acidosis*. Anything that causes an excessive increase in respirations will in time produce *alkalosis*.

Urinary mechanism

Kidneys are vital organs that help maintain a normal internal body environment. In addition to regulating the production of urine, kidneys also help control blood pressure and blood pH. The kidneys are the body's last and best defense against wide variations in blood pH. If they fail, the body cannot achieve homeostasis.

The importance of pH values in pharmaceuticals

There may be several occasions when you are asked to prepare a pharmaceutical product for one of your patients. We will discuss procedures for making these products in the next unit; however, before we move on, let's look at why pH levels in pharmaceutical products are important.

The physiological pH of tears is approximately 7.4. From a comfort and safety standpoint, this would be the optimal pH for ophthalmic formulations. When a formulation is administered to the eye, it stimulates the flow of tears. Tear fluid is capable of quickly diluting and buffering small volumes of formulations; therefore, a fairly wide range of formulation pHs can be used. Ophthalmic solutions generally are buffered in a pH range from 4.5 to 11.5. But the useful range to prevent corneal damage is 6.5 to 8.5.

Similar to tears, blood plasma has a pH of 7.4. In other words, it is slightly alkaline. Parenteral solutions, if they are not administered to alter the acidity or alkalinity of the blood, must have a close to neutral pH value.

This concludes the pharmaceutical chemistry unit. Although it may seem too in-depth for your daily activities as a pharmacy technician, knowledge of these chemistry basics is essential to other studies of pharmacy and pharmacology. The ways in which chemicals bond, interact, react, and dissolve play an important role in determining how much of a particular drug actually enters the bloodstream, how long it stays there, and how long it takes before it is excreted. In addition, you need this knowledge to better understand some techniques involved in compounding and manufacturing pharmaceutical preparations, which will be discussed in our next unit.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

611. Solutions and chemical solubility

1. What is the term for a solid or gas that is mixed into a liquid to produce a solution?
2. Name the three classifications of solutions.
3. What are the four factors that can affect the solubility of substances?
4. What affect does increasing the temperature of a solvent have on the rate of solution?
5. How can more solvent be put into a solution, thus creating a supersaturated solution?

612. Balance of acids and bases

1. What is a molecular substance that releases positive hydrogen ions in an aqueous solution?
2. What is the pH range for acid and alkaline solutions?
3. What three mechanisms does the body use to regulate the pH of its fluids?
4. What is a buffer?
5. What can produce acidosis in the human body?

6. What is the body's last and best defense against wide variations in blood pH?
7. In order to prevent corneal damage, what should the pH range for ophthalmic solutions be?

Answers to Self-Test Questions

609

1. Solid, liquid, and gas.
2. Physical and chemical.
3. Element.
4. Valence electrons.
5. The capacity of an element to combine with another element.
6. Isotopes.

610

1. Ionic and covalent.
2. Ionic compounds.
3. Covalent.
4. Combination.
5. Catalysts.

611

1. Solute.
2. True solutions, suspensions, and colloidal solutions.
3. The polarity of the solute and solvent, the solute surface area, stirring, and temperature.
4. It increases it.
5. By applying heat.

612

1. An acid.
2. 0 to 6.9 and 7.1 to 14, respectively.
3. Buffer, respiratory, and urinary.
4. A chemical substance that prevents a sharp change in pH of a fluid when an acid or base is added.
5. Anything that causes a decrease in respirations.
6. The kidneys.
7. 6.5 to 8.5.

Do the unit review exercises before going to the next unit.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter.

Do not return your answer sheet to AFCDA.

24. (609) What property of matter is characterized by shape, color, and boiling point?
- Physical.
 - Chemical.
 - Therapeutic.
 - Physiological.
25. (609) A substance that *cannot* be broken down into other substances is a/an
- element.
 - mixture.
 - molecule.
 - compound.
26. (609) The capacity of an element to combine with another element is called
- shell.
 - quark.
 - energy.
 - valence.
27. (609) What are atoms of the same element that contain the same number of protons, but have a different number of neutrons?
- Quarks.
 - Isotopes.
 - Elements.
 - Electrons.
28. (610) What type of bonding is the sharing of an electron pair between two atoms, each atom supplying one electron to the bond?
- Polar.
 - Ionic.
 - Covalent.
 - Hydrogen.
29. (610) What substances control *rates* of chemical reaction?
- Catalysts.
 - Isotopes.
 - Cations.
 - Anions.
30. (611) When a solid or gas is mixed into a liquid to produce a solution, the solid or gas is called the
- solute.
 - particle.
 - solution.
 - suspension.

31. (611) Which polar compound is considered a universal solvent?
- a. Water.
 - b. Alcohol.
 - c. Acetone.
 - d. Normal saline.
32. (611) Which type of solution is formed when no additional amount of solute can be dissolved by the solvent without external forces?
- a. Molar.
 - b. Dilute.
 - c. Saturated.
 - d. Concentrated.
33. (612) A substance that reacts with an acid to produce only water and a salt is a/an
- a. ion.
 - b. base.
 - c. buffer.
 - d. isotope.
34. (612) What is/are the body's *last and best defense* against wide variations in blood pH?
- a. Lungs.
 - b. Buffers.
 - c. Kidneys.
 - d. Circulatory system.
35. (612) What is the useful pH range for ophthalmic solutions to prevent corneal damage?
- a. 3.5 to 6.
 - b. 4.5 to 10.
 - c. 6.5 to 8.5.
 - d. 8.5 to 12.5.

Please read the unit menu for unit 3 and continue ➔

Unit 3. Sterile Pharmaceutical Compounding

3–1. Sterile Product Operations and Requirements.....	3–1
613. Principles of intravenous admixtures.....	3–1
614. Principles of aseptic technique	3–9
615. Sources of contamination	3–10
616. Requirements for maintaining an aseptic environment.....	3–12
3–2. Unique Compounding Requirements and Considerations	3–19
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THIS UNIT DISCUSSES THE IMPLEMENTATION of the *USP–NF* Chapter 797 Pharmaceutical Compounding – Sterile Preparations, located within the 2015 edition of *USP Compounding Compendium*. You’ll learn about the quality control procedures you should take prior to and during the sterile compounding process and aseptic technique guidelines. We will also cover how to determine and minimize sources of contamination while maintaining the clean room environment to meet sterile compounding requirements.

Additionally, you will learn about reporting adverse events along with stability of sterile compounded products. We will then describe cytotoxic and hazardous biological agents and how to safely store, compound, and transport them. A discussion of pharmacy references will close out the unit and this volume.

3–1. Sterile Product Operations and Requirements

The administration of drugs to a patient by injection, under or through one or more layers of the skin, is classified as parenteral route. Since this route bypasses the highly efficient protective barriers of the body, an exceptional level of purity of the dosage form must be achieved. Your technical school training gave you a fundamental understanding of sterile product preparation; now it’s time to fill in the finer details.

613. Principles of intravenous admixtures

There are many policies and directives regarding how to safely prepare these products. Your goal is to make parenteral products that are as clean as possible to prevent infections from being transmitted to patients whose immune systems have already been compromised. To establish clear standards for sterile products, *USP 797* was created in 2004.

The purpose of *USP 797* is to ensure patients are not harmed by compounded sterile products (CSP) and to ensure the safety of each CSP produced by any facility. *USP 797* enacted guidelines to ensure those standards are met. It must be understood that these guidelines are no longer recommendations; all facilities must be in compliance with these rules and regulations.

Regardless of how a medication is administered, it cannot be distributed throughout the body until it reaches the blood. A drug administered orally must be absorbed across the wall of the intestine to reach the blood circulation. Often, much of the drug administered by this route does not cross this barrier efficiently, so the amount of the drug reaching the bloodstream may be somewhat less than the amount administered. Parenteral administration bypasses the intestinal barrier to absorption. Therefore, they provide an increased availability of the medication in the bloodstream for distribution.

In an emergency situation, parenteral routes are preferred for their rapid drug onset, but they can be just as useful for their slow and smooth onset of actions. Parenterals come in many sterile dosage

forms and can be administered by several routes. However, before we cover these topics, let's discuss the advantages and disadvantages of parenteral administration.

Advantages

When compared to other dosage forms, injections possess distinct advantages. If immediate physiological action of a drug is needed, it can usually be provided by an intravenous injection of an aqueous solution. The therapeutic response of a drug is more readily controlled by parenteral administration since the irregularities of intestinal absorption are circumvented. Drugs can be administered parenterally when they cannot be given orally because of an unconscious or uncooperative patient or because of lack of absorption in the intestinal tract.

Disadvantages

Among the disadvantages are the risks of irritation or infection of the injected area, the real or psychological pain factor, and the difficulty of correcting an error, should one be made. In fact, in this last situation, correction of the error may be impossible. Once a drug is injected, especially intravenously, it begins producing all of its effects, including those that are undesirable. These effects are actually magnified when given parenterally because of the immediate distribution in the bloodstream. In most cases, unless a direct pharmacological antagonist is immediately available, the effects are irreversible.

Injectable sterile dosage forms

Injectable sterile dosage forms can be classified into the following six general categories:

1. Solutions ready for injection.
2. Dry, soluble products ready to be combined with a solvent prior to use.
3. Suspensions ready for injection.
4. Dry, insoluble products ready to be combined with a vehicle prior to use.
5. Emulsions.
6. Liquid concentrates ready for dilution prior to administration.

Routes of administration

Route of administration is a way to introduce a drug into the body. The main routes of administration are oral, transmucosal, topical, inhalation, and parenteral. Parenteral refers to any drug injected into the bloodstream, muscle, or skin.

These injectable drugs may be administered by one or more parenteral routes to include intraosseous (into the bone), intrathecal (into arachnoid membrane of the brain or spinal cord), epidural (into the spine), or intraperitoneal (into the abdomen). However, the following are the most common parenteral routes:

- Subcutaneous (Sub-Q).
- Intramuscular (IM).
- IV.

The subcutaneous route

Subcutaneous injections of a small quantity of fluid are given through the layers of the skin and into the underlying tissue. The term subcutaneous means "under the skin." Acceptable abbreviations include SQ, SC, and Sub-Q. Common injection sites are the outer surface of the upper arm and the front or outer surface of the thigh. Generally, the onset of drug action is more rapid than the oral route but slower than the intramuscular or intravenous routes. To reiterate, the subcutaneous route generally has a quicker onset of action when compared to oral medications, but is also known for its slow and steady release of some medications injected as suspensions. Drugs that can be injected subcutaneously are generally limited to those that are very soluble, but can also include many

suspensions, and are potent enough to be effective in small volumes. Drugs that are irritating to the tissues cannot be used subcutaneously because they can cause inflammation and abscess. Subcutaneous medication volumes generally begin at fractions of a milliliter and rarely exceed 2 milliliters.

The intramuscular route

Intramuscular injections are made through the skin and subcutaneous tissue and into the underlying muscle mass. The term intramuscular means “within the muscle” and is abbreviated IM. Drugs may be administered intramuscularly as either a suspension or a solution. When a drug is injected as a solution, absorption and onset of action are prompt as when compared to a suspension. When a drug is given IM as a suspension, the onset of action is not as rapid, but the duration is prolonged. Aqueous drug solutions are absorbed into the blood circulation more rapidly by the IM route than by the subcutaneous route.

Intramuscular injections are usually given in the gluteal muscle of the buttock or in the deltoid muscle, the large muscle that covers the shoulder joint and the upper part of the arm. The gluteal muscle is usually preferred if the drug is irritating or the volume of the fluid to be administered is relatively large. The amount of fluid given intramuscularly will depend on site of injection and whether the patient is a pediatric or an adult. The volume can range from 0.5 to 5 mL maximum. When given properly in the recommended site, the intramuscular injection is less painful and less irritating than the subcutaneous injection. Because of the depth of the IM injection, there is a danger of directly injecting into a vein instead of a muscle. If the needle or drug damages a nerve, it can cause severe pain and even permanent paralysis.

The intravenous route

Intravenous administration is made directly into a vein; it is a very predictable route of administration. The dose can be more precisely calculated because the drug bypasses all potential barriers of absorption. This route is rapidly effective, but it is also the most dangerous one. Once the drug is placed into the vein, it cannot be recalled, and its action cannot be slowed easily.

Drugs that are too irritating to be given by one of the other parenteral routes may possibly be given intravenously, provided the rate of administration is slow. The inner lining of the vein is relatively insensitive to pain and the drug is rapidly diluted by a large volume of blood. Administering the drug in a diluted form also helps to reduce irritation. Only drugs in aqueous (or water based) solutions should be introduced by IV; suspensions of drugs or drugs in oil generally are not administered by IV, although there are some exceptions.

There are several methods of administering drugs via the IV route, including the following types:

- IV push.
- IV drip.
- IV piggyback.
- IV total parenteral nutrition (TPN).

IV push

This technique involves injecting a relatively small volume of solution (rarely exceeding 50 mL) into the vein using a needle and syringe. This type of injection, sometimes referred to as a *bolus*, may be administered directly into the vein or through an injection port of an IV administration set (fig. 3-1) of a running IV solution. An IV push is often used when the drug must be introduced quickly into the bloodstream or when a very rapid effect is desired.



Figure 3-1. IV administration set and plastic IV bag.

IV drip

The IV drip technique is also known as an *intravenous infusion*. It is used to administer small or large volumes of IV solutions over long time periods and to carefully regulate the quantity of drug administered. A plastic bag or bottle and an IV set are required.

The IV drip method is one where you will use all that dosage calculation knowledge you learned previously. The drip rates of this type of IV administration are adjusted so that a specific volume of fluid can be administered over a given period of time. The IV drip may be used to supply the patient with fluid and nutrients as well as medications. The rates are often in drops per minute, which yield a certain number of milliliters per minute and thus, milliliters per hour.

IV piggyback

A piggyback is an intermittent IV drip of a secondary IV solution which is delivered through an injection site of an established primary IV solution's administration set. In other words, the patient receiving a piggyback already has a primary IV solution running into his or her body through an established primary IV administration set or IV line. Health care providers can use this established primary IV administration set to "piggyback" a secondary solution.

Piggybacks are accomplished by connecting a separate IV administration set to the piggybacked IV solution and then connecting the piggyback administration set to the primary IV solution's administration set through an injection port.

Antibiotics are the most common IV additive used as a piggyback. It is common to administer these drugs either every four to six hours or every eight, twelve, and twenty-four hours. This technique can easily be started and stopped for each dose administered. For these reasons, this technique is often referred to as *intermittent IV therapy*.

A relatively new development in piggyback infusions involves the use of syringes instead of piggyback containers as a means of administering the drug. Syringe systems use a syringe pump, which expels the contents of the syringe over a specific time period.

TPN

Total parenteral nutrition solutions, also known as *hyperalimentation*, is the IV administration of nutrients needed to sustain life. These nutrients include carbohydrates, protein, fats, water, electrolytes, vitamins, and trace elements.

TPN therapy is usually initiated for patients who cannot receive their nutritional needs from any other source for an extended period of time. These include patients who cannot eat, will not eat, should not eat, or cannot eat enough.

- Patients who cannot eat include those who have had head and neck surgery, are comatose, are either awaiting surgery or have just had surgery.
- Those patients who will not eat include those with chronic diseases, psychological disorders, and geriatric patients.
- Patients who should not eat include those with esophageal obstruction or inflammatory bowel disease.
- Those who cannot eat enough (because their food doesn't provide either enough nutrients or sustenance due to their diseases or conditions) include patients with cancer, burns, or trauma.

Components of parenteral nutrition solutions

Components of parenteral nutrition solutions are often broken down into what are termed *base components* and *additives*. Base components are usually mixed first and make up much of the volume of the TPN. They are composed of dextrose (carbohydrates) and amino acids (protein) and may also include fat and water. Additives are usually added to the base component and include life-sustaining nutrients, electrolytes, vitamins, and trace elements. They may also include drugs such as heparin, hydrogen (H₂) antagonists, and insulin.

NOTE: Only *regular insulin* should be used for IV administration and can either be added to a TPN or administered separately.

Carbohydrates

Carbohydrates are usually administered in the form of dextrose because of its low cost and easy availability. Commercially available concentrations vary between five and 70 percent. Usually a 50 or 70 percent solution is used in TPN preparation; the final dextrose concentration in the TPN is usually around 25 percent for solutions administered via a central vein. The dextrose concentration is significantly less for infusions intended for peripheral administration.

Protein

Protein is required for tissue synthesis and repair, transport of body nutrients and waste, and maintenance of the immune function. Protein is usually given as a commercially available product of amino acids. Numerous synthetic crystalline amino acid formulations are available. A number of special formulations are also available for pediatric patients and patients who have kidney disease, liver disease, or high stress.

Fats

Fats (or lipids) are usually administered as fat emulsions. Fat emulsions are administered to prevent essential fatty acid deficiency and as a source of calories. They are commercially available as 10 percent or 20 percent emulsion and are iso-osmolar. They can be given through a peripheral IV line or central line. Alternatively, fats can be added to the TPN solution. In this case the fat emulsion is considered a third-base component along with dextrose and amino acids, and the TPN is called a 3-in-1 solution or a total nutrient admixture. The 3-in-1 technique offers several nutritional advantages but has certain mixing, stability, and compounding disadvantages. Therefore, some facilities prefer not to prepare TPNs in this manner.

Water

Water is in all preparations and is usually derived from the components used in the preparation. Sterile water for injection may be added to obtain the desired final concentration or volume. The purpose of adding water is to offset normal bodily losses and prevent dehydration. Separate IV fluids may be given in addition to the TPN solution used for fluid replacement.

Electrolytes

Electrolytes are needed to meet daily metabolic needs and correct deficiencies. The electrolytes usually include sodium, potassium, chloride, acetate, phosphate, magnesium, and calcium. Electrolytes are usually administered (and calculated) by using a specific salt of the product. For example, sodium is frequently given as sodium chloride. Potassium can be given as potassium chloride, potassium acetate, or potassium phosphate. The patient's clinical condition and laboratory values usually determine the amount and form of electrolytes.

Vitamins

Vitamins are usually administered in a standard formulation of fat- and water-soluble vitamins. Commercial formulations include vitamins A, D, C, E, B1, B2, B6 and B12, folic acid, pantothenic acid, biotin, and niacin. Vitamin K (phytonadione) is usually given separately as a subcutaneous injection. However, it can be administered via IV or IM if the SQ route is not feasible.

Trace elements

Trace elements are required for proper enzymatic reactions and for use as energy sources in the body. Typical elements administered are copper, zinc, chromium, manganese, selenium, and iron. Commercial products are available that include combinations of trace elements and allow administration of a few milliliters to meet the daily requirements.

The automated compounders are used inside the laminar flow hood and must be cleaned daily according to the manufacturer's instructions. These systems require routine maintenance and calibration to ensure accurate compounding. To minimize the potential for errors, the compounders should be observed during operation. Quality control procedures may be implemented to verify final contents of the product. These systems are occasionally used for compounding other solutions. Great care should be taken to avoid compounding errors.

Mixing 3-in-1 solutions

There are two proper methods for mixing 3-in-1 solutions. The mixing orders are fats, amino acids, then dextrose (FAD) or dextrose, amino acids, then fats (DAF).

FAD method

When using the FAD method, it is vital you add the amino acids *before adding the dextrose*. Adding dextrose before the amino acids will cause fat emulsion disruption, thus compromising the product. Adding the amino acids before adding the dextrose buffers and protects the fat.

DAF method

When using the DAF method, it is important you add the amino acids *before adding the fats*, which will protect the fat emulsion from being disrupted.

TPN orders

Procedures for ordering and dispensing TPN solutions vary and are specific to each institution. Many institutions use a standardized TPN ordering form to make the orders straightforward and consistent, yet patient-specific. Often a specific cutoff time for order changes or new orders is used to maximize efficiency and minimize waste. This allows for multiple bags to be prepared since setting up to make just one TPN can be wasteful.

TPN solutions are ordered specifically to meet a patient's metabolic and nutritional needs. These solutions are usually administered by means of a pump to maximize safety. There are two types of TPNs – central and peripheral. Central TPNs are more concentrated and generally contain fat emulsion and are administered into the subclavian vein (central vein), which is located under the patient's clavicle. The subclavian vein is bigger so it can handle more concentrated solutions. Peripheral TPNs, although less preferred, are less concentrated and can be administered through a

peripheral vein (such as the arm). An order for a central 2-in-1 TPN solution might look like the example in the following table:

Solution	Dosage
Dextrose	250 g
Amino acids	42.5 g
Sodium chloride	60 *mEq
Potassium chloride	40 mEq
Potassium phosphate	20 mEq
Calcium gluconate	1 g
Magnesium sulfate	1 g
Trace elements	2 mL
**MVI-12	10 mL
Total volume	1,000 mL
--Infuse at 100 mL per hour. --Also, give vitamin K 10 mg every week SQ, 10 percent fat emulsion 500 mL 3 times per week. *mEq = milliequivalent. **MVI = multi-vitamin.	

The following table provides an example of an order for a 3-in-1 central TPN solution:

Solution	Dosage
Dextrose	250 g
Amino acids	85 g
Fat emulsion	50 g
Sodium chloride	80 mEq
Potassium chloride	60 mEq
Potassium phosphate	60 mEq
Trace elements	2 mL
MVI-12	10 mL
Total volume	2,000 m
--Infuse over 24 hours. --Give vitamin K 10 mg SQ every week.	

A system of checks and balances must be built into each step of the TPN ordering, preparation, and administration process. Calculations should be verified and double-checked; solutions and their ingredients should be checked and double-checked, regardless of the system used. The accuracy provided by the automated compounders cannot totally substitute for all checks and balances in ensuring the quality of the product. Equipment will differ, but figure 3-2 shows a typical TPN automated machine.

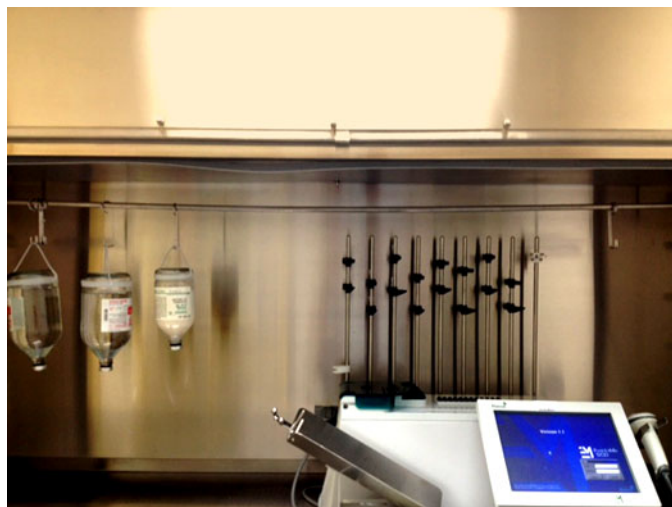


Figure 3–2. TPN set-up.

Large and small volume parenterals

Large volume parenteral (LVP) solutions are typically packaged as bags or bottles containing large volumes of IV solutions. Common uses of LVP solutions without additives include the following:

- Correction of electrolyte and fluid balance disturbances.
- Nutrition.
- Vehicles for administering other drugs.

LVP solutions are packaged in containers holding 250 mL or more and can be packaged in one of the three types of containers: glass bottle with an air vent tube; glass bottle without an air vent tube; plastic bags, or non-PVC (polyvinyl chloride) bags.

Small-volume parenteral (SVP) solutions are usually less than 250 mL and are packaged according to intended use. SVPs are typically packed as ampules, vials, small IV bags, and pre-filled syringes.

Types of IV containers

We discuss three basic types of IV containers: glass with an air tube, glass without an air tube, and flexible plastic.

For solution to flow out of a glass container, air must be able to enter the container at the same time. This is achieved through a vented administration set or through an air tube. A vented set must be used when a container does not have an air tube. The vented set must contain an air filter, which prevents contaminants from entering the bottle. Flexible plastic containers do not require venting, as either gravity or a programmable IV pump allows the fluid to flow into the vein. The sides of the container collapse, preventing a vacuum from occurring that would stop the flow.

Plastic IV containers offer many advantages, such as being lightweight and unbreakable. However, flexible plastic containers composed of PVC plastic may sometimes interact with medications. Certain medications have a tendency to adsorb or “stick” to PVC, making less of the drug available to the patient. Polyolefin and nonplasticizer vinyl IV containers are available that provide benefits of flexible plastic without the drawbacks of PVC.

Premixed solutions

Many drugs and doses are available in premixed form. If premixed products are not stable for long periods of time at room temperature, they are often frozen by the manufacturer, sold frozen, and then thawed by the pharmacy shortly (hours or days) before being administered. Adding drugs to these

solutions is generally not recommended, and most containers do not have an injection port. These solutions are administered and handled by the nurse in the same manner as other piggyback setups.

Labeling

Once an IV admixture or other sterile product is compounded, it should be properly labeled with the following information:

- Patient name, identification number, and room number (if inpatient).
- Bottle or bag sequence number, when necessary.
- Name and amount of drug(s) added.
- Name and volume of admixture solution.
- Approximate final total volume of the admixture, when necessary.
- Prescribed administration rate.
- Date and time of scheduled administration.
- Date and time of preparation.
- Beyond use date.
- Initials of person who prepares and of person who checks the IV admixture.
- Auxiliary labeling, if required, containing supplemental instructions and precautions.

The following label is an example:

Robert Dorsett	ID # 2424242424	Rm # 202E
Bag # 4		Hang at 1800 /10 October 15
Amikacin		1 g
In 0.9% Sodium Chloride		100 mL
Infuse every 12 hours		
Infuse over 60 minutes		
Use before 1600 /11 Oct 15		Prepared by: <i>AG</i> 0600–10 Oct
Keep refrigerated		Checked by: <i>ms</i>

Perform a final inspection of the admixture for cores and particulates. The pharmacist should check all drug and IV solution containers used in preparing the admixture to verify the technician added the proper amount of the correct drug to the correct IV solution.

As we move away from traditional hospitals to more ambulatory facilities, the likelihood of compounding sterile products in our facilities is decreased. However, you need to be prepared to compound sterile products during emergency situations at any deployed location.

614. Principles of aseptic technique

Products used to compound parenteral solutions must be clean and sterile; however, it is the personnel compounding the products who are ultimately responsible for preparing a safe product.

Because most, if not all, supplies and products used in the production of sterile preparations are commercially prepared, sterility testing is usually not a component of an IV admixture program. It's much safer for the government to purchase products commercially prepared and then have us use those products for our specific IV compounding needs. Having said this, *USP 797* directs pharmacy departments to perform sterility testing to check the competency of personnel compounding admixtures. These sterility tests check the individual's ability to make a clean product, or measures proper aseptic technique.

Asepsis is the absence of bacteria, viruses, or other disease-causing microorganisms. Aseptic technique is the term frequently used to describe the method for handling sterile parenteral dosage forms. Aseptic technique requires that personnel who prepare IV solutions handle these products in clean environments without introducing microorganisms into the product. A sterile parenteral dosage form is free from living microorganisms, particulate matter, or pyrogens. The Air Force can build the best clean room in which we prepare our sterile products and buy the finest equipment to maintain an aseptic environment, but it would be money down the drain if personnel compounding our sterile products weren't trained properly.

Personnel must be properly trained in sterile compounding through hands-on training and follow-up evaluations. Day-to-day operations include visual inspection of the finished product and a review of all orders and each ingredient that goes into the final product. During training and follow-up evaluations, personnel should be observed putting on the protective equipment properly, and they must perform aseptic technique procedures perfectly.

Didactic (classroom) instruction includes theory and practice in sterile compounding. In addition, personnel who compound sterile products must be re-evaluated to prove competency for low- and medium- risk level compounding annually and high-risk compounding semiannually. These evaluations must include a written test as well as a practical to determine if they are maintaining proper aseptic technique.

615. Sources of contamination

Contamination is defined as the introduction of disease, germ, or infectious material into a normally sterile object. But when it comes to compounding sterile products, that definition expands to—dust, skin flakes, makeup, and respiratory gasses—which can be further defined as particulate matter. Our goal, of course, is to not contaminate our patients while preparing their sterile products. To accomplish this goal, we must work in a state of asepsis. These harmful microorganisms, especially bacteria, are everywhere in large numbers. For example, biologists estimate that as many as 30 billion bacteria are found in a single cubic gram of soil. It is extremely easy to introduce bacteria or other contaminants onto a sterile object or device or into a sterile solution. Contamination during the process of sterile products compounding occurs by three primary means: touch, air, and water.

1. Touch—Bacteria lives on our skin, in our hair, and under our nails. Proper scrubbing to reduce the numbers of bacteria on the hands prior to handling sterile products is very important.
2. Air—Microorganisms are commonly found in the air, in dust particles, and in moisture droplets. It is important to prepare sterile products in a special area in which the number of possible contaminants are maintained at a low level.
3. Water—Tap water is not free of microorganisms, and moisture droplets in the air, especially after a sneeze, often contain harmful microbes. It is important not to contaminate sterile products by exposure to droplets of tap water or other sources of contaminated moisture.

Touch contamination

Thorough hand washing is the first essential step in aseptic technique. Any suitable antimicrobial cleanser such as chlorhexidine gluconate or povidone-iodine may be used. Since it is not possible to completely sterilize the skin, sterile gloves must be used during IV preparation. However, gloves may give a false sense of security. Keep in mind that gloved hands can become contaminated as easily as ungloved hands. Touch contamination can happen quickly and easily if personnel are not careful when preparing parenterals. For example, the plunger of a syringe that comes in contact with a person's contaminated glove or other object should not be reused, because the potential exists for the plunger to come in contact with the inner barrel of the syringe, leaving contaminants or other particulate matter behind. If you are using gloves that aren't sterile, you must wash your glove-covered hands before you begin compounding. Also, you must re-sterilize your gloves approximately every 30 minutes with a 70 percent alcohol solution during compounding operations. You must also

rewash your hands and/or gloves when returning from outside the compounding area or whenever there is any possibility you have contaminated your hands. Finally, when you are done compounding, don't forget to wash your hands again. Remember, gloves don't always keep your hands perfectly protected from contaminants.

Contamination from lesions, cuts, or illness

If you are ill or have lesions or cuts on your hands you should not prepare a sterile product. You could pass a bacterial or viral contaminant on to a patient through the product you prepared. Remember, sick people are in a weakened state and are more susceptible to infections and disease. You must make sure the products you make do not cause the patient harm.

Special clothing

USP 797 mandates that anyone who prepares parenterals wear personnel protective equipment (PPE) in order to decrease the chance of product contamination. Personnel must follow a specific dressing protocol when preparing to work in the clean room. You must put on PPE in the order as shown in the following table:

Donning PPE in the Following Order	
1.	Shoe covers.
2.	Head/facial hair cover.
3.	Facial mask/eye shield.
4.	Gown. NOTE: Follow proper hand washing procedures before donning gown.)
5.	Gloves. NOTE: Prior to donning gloves, you should use a waterless alcohol-based surgical hand scrub and allow hands to dry. If gloves touch any non-sterile surface after donning, you can disinfect them with 70% isopropyl alcohol (IPA).

The regulation also states that hanging a gown in the ante room inside out allows personnel to wear it multiple times. The gown is the *only* protective gear that may be used again. Once you've removed your gloves, whether you're wearing one or two pairs, you *must* rewash your hands. Gloves don't completely protect your hands from all contamination.

Makeup, artificial nails, nail polish, and jewelry are prohibited in the clean room because they can cause contamination of a sterile product. Powdered makeup can release dust particles in the air (masks won't always contain the spread of flaking), and jewelry and artificial nails are breeding grounds for bacteria (these items may puncture gloves and spread infection). Nail polish flakes produce airborne particles which can destroy the sterility of the product that you worked so hard to prepare.

Finally, it's important to consider some other, slightly less obvious items that can also cause dust particles that could compromise your CSPs. Lab coats and fuzzy sweaters must not be worn in the clean room. Finally, eating, drinking, and gum-chewing aren't allowed in the clean room, either.

Contamination of equipment and supplies

Just because products are used in the preparation of sterile compounds doesn't mean they can't contaminate your sterile preparation, so let's address the importance of using and cleaning the correct items. Use sterile supplies, sterile needles and syringes, and sterile water or saline for solution. Always clean all injection ports with an antimicrobial agent prior to use. There can be contamination during the preparation of any type of parenteral solution. The risk to patients is bacterium or sepsis from contaminated fluids. *Klebsiella*, a gram-negative organism, is a common contaminant. Also

candida, or yeast, is seen in patients having long-term TPN products. The high glucose concentrations in TPNs are an excellent medium for candida to grow. Interventions to decrease the risks include the careful examination of all shipments for signs of rough handling, breakage, and evidence of watermarks. Return defective items to the manufacturer. Avoid temperature extremes in storage areas (e.g., storage areas near boiler rooms), and always handle packages carefully.

Use the appropriate storage for the product, and indicate the beyond-use date clearly on the products that you make. Indicating the beyond-use date is especially important when using multiple-dose vials or containers.

USP 797 defines a multiple-dose container as one that contains more than a single dose that is used on multiple occasions. Multiple-dose containers have a beyond-use date of 28 days after being opened or used for the first time (e.g., punctured by a needle). If the manufacturer states something different than the 28 days, then that specification should be followed.

616. Requirements for maintaining an aseptic environment

Room air typically contains thousands of suspended particles per cubic foot, most of which are too small to be seen with the naked eye. Reducing the number of particles in the air improves the environment in which sterile products are prepared. *USP 797* uses International Organization for Standardization (ISO) class environment standards to measure the number and size of particles in our IV preparation areas. ISO class environments range from 3 to 8, with ISO class 3 being the environment with the lowest number of particles in the air, and thus, being considered the “cleanest.”

Sterile compounding area

Sterile parenteral products should be prepared in a separate room in the pharmacy. This area is usually referred to as a *clean room*. The clean room includes the direct compounding area (where the sterile products are made) and the *buffer area* (where supplies such as IV bags and administrations sets are kept). Laminar airflow hoods will be located in the direct compounding area of the clean room since this is where parenterals will be made. *USP 797* mandates that these clean rooms follow ISO class environment standards. The direct compounding area requires an ISO class 5 environment, while the buffer area must maintain an ISO class 7 air quality.

NOTE: An ISO class 5 environment contains no more than 100 particles per cubic foot that are 0.5 micron or larger in size. *USP 797* refers to these ISO class 5 environments as “critical areas.” This environment is attained by using laminar airflow hoods. Keeping airborne particles to an absolute minimum is one of the most important ways to maintain sterility of CSPs. Your clean room should be cleaned daily and segregated from normal pharmacy operations, nonessential equipment, and other materials that produce particles. For example, the introduction of cardboard into a clean room should be avoided. Traffic flow into the clean area should be minimized. Floors should be disinfected often and trash should be removed frequently and regularly. Other, more sophisticated aspects of clean room design include special filtration or treatment systems for incoming air, ultraviolet irradiation, air-lock entry portals, sticky mats to remove particles from shoes, and positive air pressure to reduce contaminant entry.

Clean rooms are often adjoined by an anteroom that is used for non-aseptic activities related to the clean room operation such as order processing, gowning, stock-handling, and disinfecting supplies so they may be taken into the clean room. Anterooms must be connected to the clean room. The air quality for the anteroom can maintain a 7 or 8 ISO class.

Another requirement spelled out by *USP 797* is that refrigerators, computers, and printers must not be installed in the clean room. These items are too difficult to keep clean and any missed dust particles can cause a compounded product to become non-sterile. Sinks and floor drains must not be installed in the clean room, either, as normal tap water contains millions of bacteria that could contaminate CSPs, and drains are difficult to clean. Traffic flow into the clean room must be restricted and non-sterile activities (such as opening supply boxes) should never be performed in the clean room.

Adhering to these requirements will nearly eliminate dust particles that might potentially contaminate CSPs.

USP 797 also requires a strict cleaning schedule be followed in the ISO class 5 environments, which are preparation areas inside your laminar air flow hoods, biological safety cabinets (BSC), and barrier isolators. ISO class 5 areas must be cleaned at the beginning of each shift. Spills and debris must be removed as they occur during compounding and if environmental quality issues arise. Once the area is cleaned, an acceptable disinfectant, such as 70% IPA is applied and allowed to sit long enough for its antimicrobial properties to work.

Counters and floors within an ISO class 8 environment, at a minimum, must be cleaned daily, while walls, ceilings, and shelves must be cleaned monthly. Any debris or dust must be removed as soon as possible. Mopping floors can be done by custodians with approved cleaners and disinfecting agents, and any mops, brooms, or sponges must be non-shedding. These cleaning items must be dedicated for use only in the clean room. Mops may be used in the clean room and then in the anteroom, but they must be used in that order. Sponges are used only once, but if cleaning tools are used multiple times, they must be rinsed thoroughly, disinfected, and stored in a clean environment between uses. Any trash removed from these areas must be placed in appropriate plastic bags and the air must be disturbed as little as possible to minimize airborne particles.

Proper protocol must be followed when disinfecting surfaces in the anteroom with an appropriate disinfectant, such as 70% IPA. All supplies must be swabbed or wiped down once they are removed from the boxes in which they came. Bottles, bags, vials, and syringes need to be wiped down by using 70% IPA. Larger items must be wiped down with 4 × 4 gauze pads and a solution of 70% IPA. It is important to note that before disinfected surfaces are used for compounding, you must wait at least 30 seconds to allow the disinfectant properties to act on them.

Clean room specifications

The size of the clean room varies according to space limitations and the individual institution's bed size, which dictates the number of products to be prepared. The number of people preparing parenteral products and the equipment necessary also determine the amount of space needed. Several recommendations about the clean room used to prepare parenteral products are provided within the following list.

- Tiled, washable floor covered with a coat of vinyl or epoxy sealant to provide a continuous surface.
- Plastic covered clean room grade tiles for the ceiling.
- High-efficiency particulate air (HEPA) filters installed in ceiling fans for proper ventilation.
- Horizontal or vertical laminar airflow hoods and/or barrier isolator units.
- Preparation equipment, such as needles, syringes, alcohol prep pads, gloves, masks, gowns, receptacles for disposables, small- and large-volume parenterals for use as diluents and vehicle solutions, must be disinfected before being taken into the clean room.
- Good lighting.
- Adequate counter space.
- Restricted area or minimized traffic flow.
- Prohibition of smoking, beverages, food, and unauthorized personnel.

Determine compounded sterile product risk levels

Any place where CSPs are prepared must meet *USP 797* requirements. This includes clinics, hospitals, and main and/or satellite pharmacies. In addition, everyone who prepares compounds must meet training requirements. The first thing pharmacies must do is to determine risk levels of products compounded within the pharmacy and then determine how their current compounding practices

comply with *USP 797*. Your risk levels are defined by the likelihood of contamination affecting a CSP prepared at your installation. Sterile compounding is divided into low, medium and high categories of risk level.

Low-risk compounding

Remember, CSPs are prepared in a clean room with an ISO class 5 environment, adjacent to an anteroom using only sterile ingredients, products, components, and devices. Prepared in this environment is considered low-risk compounding as it involves the transfer, measuring, and mixing manipulations using not more than three commercially manufactured packages of sterile products and not more than two entries into any one sterile container or package (e.g., bag, vial) of sterile product or administration container/device to prepare the CSP. For example, reconstitution of single-dose vials of antibiotics or other SVP, or preparation of hydration solutions.

Medium-risk compounding

Again, CSPs are prepared in an ISO class 5 environment. However, when prepared under the following conditions, the products increase to a medium risk of contamination.

- Using multiple individual or small doses of sterile products to prepare a CSP administered either to multiple patients or to one patient on multiple occasions.
- The compounding process includes complex aseptic manipulations other than the single-volume transfer. For example: compounding total parenteral nutrition fluids using manual or automated devices during which there are multiple injections, detachments, and attachments of nutrient source products to the device or machine to deliver all nutritional components to a final sterile container.
- The compounding process takes longer than normal duration.

High-risk compounding

High-risk compounding occurs when non-sterile ingredients are mixed and weighed in environments worse than ISO class 5 for more than one hour. If personnel who are compounding these agents are improperly protected (e.g., no gown or gloves), or commercially manufactured sterile products and their components are exposed to less than ISO class 5 environments, this is also considered high-risk compounding and there must be a final sterilization process. Sterilization procedures for high-risk level compounding are pretty complex, but they include a filtration procedure that must be accomplished in the ISO class 5 environment. High risk compounding examples include CSPs compounded from bulk, non-sterile components or measuring sterile ingredients in a non-sterile container without sterilizing it. Working with radioactive materials for nuclear compounding is also considered high-risk compounding.

Perform gap analysis

After your compounding risk has been assessed, you need to perform a gap analysis; *USP 797* lays out guidance for compliance. When each line of guidance from *USP 797* is compared with your facility's current practices, the differences (or gaps) are the areas which are not in compliance with the regulation. A few areas your facility may find gaps are in its environmental quality, preparation process, and personnel training.

These gap areas must then be prioritized by fiscal and human resource costs and an action plan must be put into place. The immediate goal of risk-level assessment and gap analysis is to identify and eliminate any unsafe compounding practice that may lead to the contamination of the final CSP.

A written action plan is also used as documentation to prove to accreditation agencies, such as The Joint Commission, that your facility is either compliant with *USP 797* or that it is working on coming into compliance. The details of your action plan should include a focus on day-to-day operations such as training, media-fill testing records, personal protective gear use, sanitation procedures, and

microbial environment monitoring. Having the gap analysis and action plans in place will show that your facility is taking the appropriate steps to secure the cleanest compounding methods possible.

Clean room sampling and testing

Environmental controls must be maintained in order to ensure that the clean room environment remains clean. In order for this to be accomplished, *USP 797* requires that air quality be sampled by electronic means at least every six months. Operational and at rest are the two types of air sampling that must occur. Operational testing means that normal clean room activities should be occurring during testing, while no clean room activities should be occurring during at rest testing. Primarily, environmental control procedures such as airflow volume, air pressure differentials, and containment or filter leaks should be tested. This specialized testing is usually performed by your local biomedical equipment repair technician section.

While the next few paragraphs will not go too deeply into the equipment and procedures of air sampling, you should still be aware that the ISO report is very detailed. The following items should be included within the report:

- The organization that conducts the test.
- What type of equipment is used and the calibration certificate.
- The ISO reference.
- Test and sample locations.
- Any deviation from the ISO test method.
- Test results.
- Data analysis.
- Particle concentration levels.

The standard for testing the air is found in ISO 14644-1, located in the *USP 797*.

Laminar airflow hoods

You must strictly adhere to good aseptic technique when preparing parenteral products. Laminar airflow hoods are very effective at providing a clean area. However, the use of poor aseptic technique can easily cancel out the benefits of laminar airflow devices.

Laminar airflow hoods provide filtered air that flows through the hood in straight parallel lines. The air is filtered through a HEPA filter that removes 99.97 percent of all particles larger than 0.3 μm (microns) in size. Essentially, this filter is able to remove all microbial contaminants and particulate matter. The air flows at a sufficient velocity to keep a work area free from contamination.

Horizontal flow (fig. 3-3) and vertical flow (fig. 3-5) are the two common types of laminar airflow hoods. In a horizontal hood, the HEPA filter is located at the back of the hood and air flows to the front as shown on figure 3-4. In a vertical hood, airflow passes through a HEPA filter at the top and is drawn out at the bottom through grates as shown on figure 3-6. Vertical laminar airflow hoods provide protection to the operator as the airflow is contained within the hood. This type of hood is used to prepare hazardous products, such as chemotherapy agents.



Figure 3-3. Horizontal flow hood.

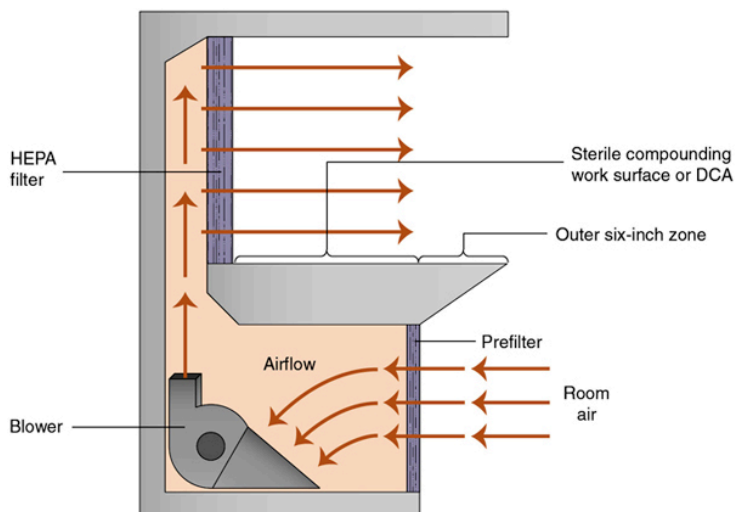


Figure 3-4. Horizontal hood air flow.
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Figure 3-5. Vertical flow hood.

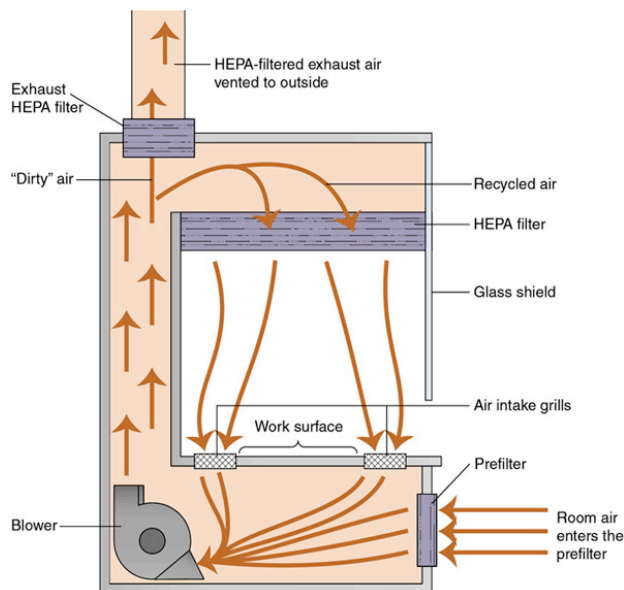


Figure 3-6. Vertical hood air flow.
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Good aseptic technique is essential to maximize the benefits of a laminar airflow hood. However; it is important to remember that laminar airflow can be easily disrupted. Such disruptions increase the risk of contamination. Sneezing, coughing, and even talking directly into a laminar airflow hood can disrupt the airflow sufficiently to contaminate the work area. Breezes from sudden hand movements within the hood can disrupt the airflow.

If the laminar airflow hood has been turned off, it must be allowed to run for 30 minutes before starting manipulations. There is a specific way to clean the laminar airflow hoods, and these procedures must be strictly adhered to in order for the CSP to remain sterile. Remember, the goal is to keep airborne particles to an absolute minimum. When preparing to clean the hoods, you must use gauze that doesn't produce *any* lint. You must swab the interior bottom work surfaces with sterile water and allow surfaces to air dry. After this is accomplished, use 70% IPA on the surfaces, going

from side to side and then back to front. Once more, this solution must be allowed to air dry. Finally, take only what you need to compound your products, and keep in mind that you want to limit the amount of times you enter and exit the clean room. Make sure you remove any carts that you take into the room, but the best approach is to try not to use them in the first place. You must clean the flow hoods before you begin to compound, once you are finished compounding, and if any spills happen while you are compounding.

Gather all the materials you need for each product. Place them in the hood in a manner that does not obstruct the clean airflow. Check solutions and additives for expiration dates and freedom from particulate matter. Squeeze plastic solution containers to check for leaks.

Perform your work in the center of the hood. There must be no obstruction between the HEPA filter and the product being prepared. In a horizontal hood, do your work at least six inches inside the hood. The airflow at the outer six inches of the hood is subject to many disturbances and may be contaminated. With a vertical hood, lower the viewing screen to its proper position to contain the airflow within the hood.

All laminar airflow hoods must also be routinely inspected for proper functions and contamination. Often, medical logistics has contracts with vendors for testing hoods. Routine hood maintenance (e.g., filter replacement) is usually arranged through the hospital maintenance or plant inspection department.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

613. Principles of intravenous admixtures

1. What are the six general categories of injectable sterile dosage forms?
2. What are the three most common routes of parenteral administration?
3. What drugs can be injected subcutaneously?
4. In what muscles are intramuscular injections usually given?
5. What route of administration is the most dangerous?
6. What method of intravenous administration of drugs involves injecting a relatively small volume of solution (rarely exceeding 50 mL) into the vein using a needle and syringe?
7. What type of IV administration delivers a secondary IV solution through an injection site of an established primary IV solution's administration set?

8. What is a total parenteral nutrition solution?
9. What are the base components of a TPN?
10. Why are fat emulsions administered to patients?
11. What is the proper order of mixing when making a 3-in-1 TPN solution?
12. What type of system needs to be in place to make sure that the quality of the TPN is assured?

614. Principles of aseptic technique

1. Who is ultimately responsible for distributing a safe product?
2. According to *USP 797*, what does sterility testing check?
3. Define aseptic technique.

615. Sources of contamination

1. What are the three primary sources of contamination during sterile compounding?
2. What is the first essential step in aseptic technique?
3. If you have lesions or cuts on your hands and you prepare a sterile product, what could you pass to the patient?
4. What is the only piece of personal protective equipment that can be used multiple times?

616. Requirements for maintaining an aseptic environment

1. In what type of environment should sterile products be compounded?

2. What types of equipment must not be installed in the clean room?
3. How often should the walls, ceilings, and shelves be cleaned in an ISO Class 8 clean room?
4. Into what three categories does *USP 797* divide sterile compounding?
5. What is a gap analysis?
6. How often should the air be sampled in a clean room environment?
7. What are the types of laminar airflow hoods used for sterile compounding?
8. If a laminar airflow hood has been turned off, how many minutes must it run before starting manipulations?

3-2. Unique Compounding Requirements and Considerations

The IV technician is a vital part of a parenteral admixture program. The unique role that a technician plays varies from base to base, as do the compounds he or she may be required to prepare. The degree to which parenteral admixture services are provided also varies considerably among different facilities, but this does not negate your responsibility to be prepared to compound a wide range of admixtures. In order to do your part in maintaining patient safety, you must know the procedures for reporting any adverse events, know about compatibility and stability, know how to handle biological compounds, and know how to use reference books.

617. Adverse events reporting

USP 797 requires any facility dispensing CSPs to have a mechanism in place that encourages personnel to participate in adverse event reporting and product defects programs sponsored by the Food and Drug Administration (FDA). It must also establish guidelines for patients (and any other interested persons) to ask questions and report concerns regarding the CSPs that they have received.

As part of this mechanism, facilities must have standard operating procedures manuals which contain specific instructions for receiving, acknowledging, and dating receipts. In addition, they must have specific procedures in place for recording, filing, and evaluating reports of adverse events and the quality of preparation of the CSP that was associated with the claim. Any complaints of adverse events involving CSPs must be investigated by compounding supervisors immediately and thoroughly, and actions must be taken to correct and prevent future occurrences.

Quality assurance programs

One of the most important things that your facility needs to have in place, as a provider of CSPs, is a formal Quality Assurance (QA) plan. The emphasis of a QA program is placed on maintaining and improving the quality of systems. It is also important that provisions for patient care are included in the QA program. The program also not only includes plans to correct any identified problems, but it also notes any follow-up actions and if their implementations were effective in correcting the problems.

The QA program must include objective, measurable indicators for monitoring activities that are identified as high-risk, high-volume, or problem-prone. These indicators will be reassessed annually.

An integrated QA plan will be formalized in writing and contain the following:

- Consideration of all aspects of compounding and dispensing, including but not limited to, environmental testing and validation results, and any aspects noted in *USP 797*.
- Specific procedures for reporting and evaluating results.
- Identification of follow-up actions when action limits or thresholds are exceeded.
- Delineation of individuals who are responsible for each part of the QA program.

In essence, a QA program states that your facility is following established procedures. A QA program is the written proof that you are following those procedures outlined by *USP 797* in regards to personnel training, maintenance of equipment, and testing of aseptic environment.

Patient monitoring

Part of your responsibilities in dispensing sterile products are monitoring your patient for any effects, either appropriate or adverse. *USP 797* mandates facilities dispensing CSPs to have programs in place that monitor the quality of practices and products dispensed. The patient monitoring program, guided by your state's healthcare practitioner licensure board and/or accepted standards of practice, also shows that your facility has a mechanism in place for handling patient complaints related to adverse events.

618. Compatibilities and stability principles

Adequate reference materials are an essential component of an IV admixture program. The *Handbook on Injectable Drugs, 18th Edition*, is published by the American Society of Health-System Pharmacists (ASHP), is one of the most widely used references for researching incompatibility and stability information. Well referenced compatibility and stability charts, often supplied by manufacturers, are also useful in an IV preparation area. The last lesson of this volume will look at reference materials more in depth.

An intravenous admixture is incompatible when the prescribed drugs cannot be combined safely and satisfactorily. This incompatibility may be between two drugs or between a drug and an intravenous solution. The incidence of incompatibilities is relatively low when compared to the number of intravenous admixtures prepared, but the possibility of an unexpected or undesirable combination always exists. If an incompatibility occurs and goes undetected, the patient may not receive the full therapeutic effect of the medication. A more serious consequence is that an incompatibility may lead to the formation of toxic products having an adverse effect on the patient. Incompatibilities are classified as physical, chemical or therapeutic.

Physical incompatibilities

A physical incompatibility occurs when two drugs are combined in a solution to produce a change in the appearance of that solution. This visual change may be recognized as a change in color, evolution of a gas, development of a haze or formation of a precipitate. Physical incompatibility is the easiest type to detect because it may be visually observed.

Chemical incompatibilities

A chemical incompatibility occurs when two drugs react to cause the chemical degradation of one or both drugs. This type of incompatibility may be a non-visual incompatibility that can be detected only by analytical methods or by discerning a physical change in the solution. For example, when acyclovir is mixed with dobutamine, a discoloration will develop within 25 minutes and a cloudiness and brown color will develop within about two hours. This is due to the oxidation of the dobutamine.

Therapeutic incompatibilities

A therapeutic incompatibility occurs when two drugs are administered together to produce a response that differs in nature or intensity from that which was intended. Therapeutic incompatibilities generally occur at the site of the drug action—for example, the bacterial cell wall.

Factors affecting incompatibilities

The following table provides a list of many of the factors affecting the incompatibility of intravenous admixture drugs which should be thoroughly researched before compounding begins.

Factors Affecting Incompatibilities	
Factor	Description
pH of the admixture	This is the most common cause of incompatibilities in an IV admixture. The resulting pH is usually unsatisfactory for one of the ingredients.
Complexation	A chemical complex is formed that reduces the antibacterial activity of one of the ingredients (e.g., tetracycline and calcium-containing preparations).
Light	Exposure of some drugs to light may cause destruction or reduce their potency.
Amount of dilution	Concentration of a drug or its degree of dilution in solution may be a factor in its compatibility with other drugs.
Time	Many drugs degrade over time when placed in an intravenous solution. Many incompatibilities are not caused instantaneously but are time-related. Some drugs, initially stable, form a precipitate after a period of a few hours.
Parenteral solution	Drugs are usually more stable in one solution than in another; each drug varies.
Temperature	The degradation of a drug in solution may be regarded as a chemical reaction. Heat increases the rate of most chemical reactions. Thus, one would expect a more stable solution at a refrigerated temperature than at room temperature. It is not uncommon for refrigerated solutions to remain stable 8 to 10 times longer than the non-refrigerated stability period.
Buffer capacity of the additive or the solution	The buffer capacity of a solution is the ability of that solution to resist a change in pH when either an acidic or basic (alkaline) substance is added to it.
Order of mixing	The order of adding drugs to the solution may be a factor in causing an incompatibility. For example, if two drugs are not well-diluted before they come into contact in the solutions, they may react chemically. When making hyperalimentation solutions, incompatible electrolytes (such as calcium and magnesium with phosphate) are commonly prescribed. By adding the electrolytes last and mixing well after each addition, the electrolytes are well diluted when they come into contact with each other, and the chance of precipitation is minimized.

In addition, many pharmacies prepare institution-specific charts that facilitate the order entry and preparation processes by listing pre-calculated doses, concentrations, and administration rates. These charts may include the following information:

- Amount and type of diluent to add to a lyophilized or powdered medication and the resulting concentration.

- The recommended final diluent (e.g., 5 percent dextrose in water, 0.9 percent sodium chloride, 0.45 percent sodium chloride, etc.) and the concentration to be used for optimal stability for each particular medication.
- Lists of specific medications showing the volume of a drug required to prepare commonly used dosages.
- Expiration dates for compounded medications, frozen products that are thawed, and medications prepackaged in syringes.
- Standardized diluents and concentrations used in the institution.

If the pharmacy is on a computerized patient profile system, most of this information can be added directly to the drug profile. When orders are entered, this information helps properly identify the solution and final quantity. The following tables show examples of standardized charts for preparing IV admixtures that contain the preceding information.

Drug	Size	Diluent	Amount to add	Approximate final diluted concentration	Expiration date (days)
Ceftriaxone	250 mg	Bacteriostatic water	0.9 mL	250 mg/mL	10 r
	500 mg		1.8 mL	250 mg/mL	10 r
	1 g		3.6 mL	250 mg/mL	10 r
	2 g		7.2 mL	250 mg/mL	10 r
Cefotaxime	500 mg	Bacteriostatic water	10 mL	50 mg/mL	7 r
	1 g		10 mL	95 mg/mL	7 r
	2 g		10 mL	180 mg/L	7 r
NOTE: r = refrigerated.					

Methylprednisolone Concentrations for Syringes				
40 mg/mL	30 mg=0.75 mL	20 mg=0.5 mL	10 mg=0.25 mL	48 hr r
125 mg/mL	100 mg=1.6 mL	80 mg=1.3 mL	60 mg=0.96 mL	48 hr r
NOTE: r = refrigerated.				

Gentamicin Concentrations for Syringes or SVPs			
40 mg/mL vial	10 mg=0.25 mL	50 mg=1.25 mL	90 mg=2.25 mL
	15 mg=0.375 mL	55 mg=1.375 mL	95 mg=2.375 mL
	20 mg=0.5 mL	60 mg=1.5 mL	100 mg=2.5 mL
	25 mg=0.625 mL	65 mg=1.625 mL	105 mg=2.625 mL
	30 mg=0.75 mL	70 mg=1.75 mL	110 mg=2.75 mL
	35 mg=0.875 mL	75 mg=1.875 mL	115 mg=2.875 mL
	45 mg=1.125 mL	85 mg=2.125 mL	125 mg=3.125 mL

Once parenteral medication charts have been obtained or prepared, someone should be responsible for maintaining and updating them. Charts and reminders found in a pharmacy parenteral area usually signify a well-organized practice with the fewest possible errors.

The nursing unit is another important area where standardized charts should be kept. These include charts for determining IV infusion rates. Examples of medications that may require rate charts are aminophylline infusions of 1 g in 250 mL, 500 mL or 1,000 mL of diluent, as well as standard dilutions for IV cardiac medications. Many hospitals establish standard dilutions and compile charts to determine infusion rates for different dosages. Such charts help standardize dosages throughout the hospital, decreasing chances of medication errors.

Expiration dates

Expiration dating for parenteral products is established through rigorous stability testing by the pharmaceutical manufacturer. Analytical and qualitative methods are used to test products stored under different environmental conditions, such as varying temperature and lighting conditions. Pharmaceutical scientists or independent investigators may also perform these tests on compounded parenteral products to obtain stability information about a drug once it has been added to an IV solution (e.g., 5 percent dextrose in water, 0.9 percent sodium chloride) or mixed with another drug.

The stability of the active ingredient in parenteral products may be affected by the container in which it is placed, by environmental conditions such as light and temperature, by the diluent used to administer the product and by other drugs that may be mixed with the product. Keep in mind that glass does not deteriorate under handling and storage conditions encountered in institutional practice. Glass is also considered environmentally safe. However, don't confuse stability with sterility. Although a compounded parenteral product may be stable for several days to weeks, it may not remain sterile that long. The pharmacy's parenteral policies and procedures should specify expiration dating for parenteral products on the basis of published stability and sterility data.

Beyond-use dates

USP 797 also discusses "beyond-use" dating. It is important to note that beyond-use dating is different than expiration dating. Expiration dating is assigned to each individual medication by the manufacturer. The beyond-use date identifies the time by which the preparation (once each individual medication is compounded together) must be used before it is at risk for chemical degradation or contamination; this is assigned by the pharmacy.

Personnel who compound CSPs may consult the manufacturer of all products being used so they can get advice regarding beyond-use dating. Personnel must assign beyond-use dates based on the chemical and physical stability parameters outlined by the manufacturers. Beyond-use dating can also be assigned by obtaining information from the most current drug literature and/or direct testing. If neither the literature nor direct testing justifies a beyond-use date, then the date must be assigned according to the Stability Criteria and Beyond-Use Dating in *USP-NF, Chapter 795, Pharmaceutical Compounding – Nonsterile Preparations*.

Pharmacists may consult the literature and documentation regarding stability, compatibility, and degradation information of each medication in order to assign appropriate beyond-use dates. Storage conditions, the container in which the CSP will be packaged, and the duration of treatment must also be considered before finally assigning the beyond-use date.

Manufacturers assign expiration dates based on stability, compatibility, storage conditions, and temperature conditions of the individual medications they produce. These same considerations must be taken into account for the final CSP before assigning its beyond-use date. Stability information of the original drugs must be carefully interpreted and applied to the composition of the final CSP – how it will be stored, how it will be used, and the amount of each drug used in the preparation.

If the beyond-use date is assigned by using more than just publication information, such as tables, charts, etc., the date that is predicted is called a theoretical beyond-use date. Theoretical beyond-use dating is based on several assumptions, some of which can cause a minor inaccuracy or a complete error when assigning the final date. The degree of error or inaccuracy would be caused by the degree of difference between the characteristics of the final product (composition, concentration of

individual ingredients, volume of product, and final container used) and the characteristics of the products from which stability information is obtained. A theoretical beyond-use date must never be assigned to a dating period of over 30 days.

The most accurate way to assign beyond-use dates is by obtaining the literature containing the results of assays that have been conducted on each individual drug that has gone into the final CSP. You might be asking, “What are assays?” According to the International Society for Complexity, Information, and Design Encyclopedia of Science and Philosophy, assays are analytical procedures that test the properties, composition, and/or strength of drugs (and a variety of other substances) by chemical means. Having the results of these tests will ensure that the most accurate beyond-use date will be assigned to your final product.

Before closing this section, you must be aware of beyond-use dating and multiple-dose containers. When multiple-dose containers used in sterile compounding are accessed appropriately (i.e., the stoppers are inspected for physical integrity, disinfected with an IPA wipe, and penetrated with a sterile needle), then the beyond-use date after the initial access is 28 days; if the manufacturer specifies otherwise (either for more or less than the 28 days), then those specifications must be followed.

Pharmacies must have policies and procedures in place that are consistent regarding beyond-use dating. It must be understood that the properties of drugs, when compounded, will very likely change. Thus, the stability of those drugs won’t be the same as they would be in their original compositions. In essence, whenever personnel are assigning beyond-use dates to CSPs, they must use the most appropriate and current information available to assign the safest beyond-use date possible.

Stability of CSPs must be cross-checked with pharmaceutical references or by performing sterility tests (according to *USP 71*, Sterility Testing). If CSPs aren’t tested according to *USP 71*, then they must not be used past their beyond-use date. If sterility tests are performed on CSPs, then they may be used past their beyond-use date in accordance with the *USP 71* guidelines for low-, medium-, and high-risk level compounding. The following table is from *USP 797*, and reproduced from *USP 71*.

Risk Level	Room Temp	Refrigeration	Freezer ($\leq -20^{\circ}\text{C}$)
Low	48 hours	14 days	45 days
Medium	30 hours	7 days	45 days
High	24 hours	3 days	45 days

In addition to maintaining sterility and stability of CSPs, it is preferable for CSPs to not contain pyrogens, although it is acceptable for CSPs to have a low amount of them. It must be kept in mind that the longer a CSP is stored, the more possible it is that sterility will not be maintained and pyrogen formations will occur.

In addition to the limits outlined in the previous table, *USP 797* details additional guidelines for “other” beyond-use dating products. *USP 795* provides guidance for the following:

- Solids and non-aqueous liquids prepared from commercially available dosage forms - no later than the earliest expiration date of the commercial products used, or six months, whichever is earlier.
- Water-containing oral formulations (prepared from ingredients in solid form) – up to 14 days when stored in a refrigerator.
- All other formulations – up to 30 days or the intended duration of therapy, whichever is earlier.

Impact of proper handling on stability

CSPs need to be handled carefully, especially in maintaining the stability of the medication during transport. If a medication gets shaken during transport or is exposed to intense heating or lighting

conditions, its stability could be compromised. It is important that transport be as smooth as possible, and that those personnel who transport such products know the limitations of the medication.

Impact of proper storage on stability

USP 797 clearly describes the storage requirements for units outside the pharmacy. It states that CSPs must be stored so that unauthorized hospital personnel, visitors, and patients don't have access to them. It is imperative that your facility have written policies showing that non-pharmacy areas are in compliance with proper storage for CSPs. Monthly inspections must also prove that food and drugs are stored separately from each other, multiple-dose vials are being used properly, single-use vials aren't being used as multiple-dose vials, and storage conditions (e.g., temperature controls) are being properly maintained. Remember, any of these conditions that are improperly maintained can cause a breakdown in the product's stability.

Determining stability prior to re-dispensing

It is possible for some unused (unopened) CSPs to be returned to the pharmacy for re-dispensing, but this can occur only under certain conditions. Your local pharmacist should be the one to decide if re-dispensing of CSPs is allowed but only after following certain protocols. Sterility, stability, and purity of the products based on storage requirements (refrigeration and/or exposure to light), visual inspection (no tampering or preparation for use), and beyond-use dating procedures (only if assigning a new date would not compromise the stability and sterility of the ingredients) must be determined to be within acceptable limits before re-dispensing can occur.

619. Requirements for compounding cytotoxic and biological agents

Cytotoxic and biological agents can be hazardous to those who touch or inhale them. Because these hazardous drugs initially involved drugs used in treating cancer, the terms "antineoplastic" and "chemotherapeutic" were used to describe them. Antineoplastics, as defined by Taber's *Cyclopedic Medical Dictionary*, is an agent that prevents the growth of malignant cells. The term "cytotoxic," or cell killer was used later. However, not all antineoplastics are cytotoxic and not all cytotoxics are used to treat cancer.

The term "cytotoxic" is used to refer to any agent that may be genotoxic, oncogenic, mutagenic, teratogenic, or hazardous in any way. Exposure to antineoplastics, as well as immunosuppressants, antiviral agents, and biological response modifiers, may pose some of these risks (some effects and risks are more documented than others in the literature).

The term "biological agent" is also called immunotherapy; this type of treatment stimulates or restores the ability of the immune system to fight the cancer. There are several substances that boost, direct or restore normal immune defenses and include interferon, interleukins, vaccines, and monoclonal antibodies.

All of the agents require special handling procedures to minimize the potential for accidental exposure. Contact with these drugs can cause immediate problems, such as dermatitis, dizziness, nausea, headaches, and other medical problems. Studies also suggest that repeated exposure to small amounts of some of these drugs may cause organ or chromosome damage, impaired fertility, and even cancer.

Preparation of these agents requires special procedures for labeling, storage, and transport; protective clothing; use of biological safety cabinets; and special handling of spills and waste. Additional information is available from the ASHP in the form of a technical assistance bulletin on handling cytotoxic and hazardous drugs.

Labeling, storage, and transport

Take steps to prevent accidental exposure to hazardous drugs the moment the drugs enter the facility. Identify all hazardous drugs using distinctive labels that indicate special handling is required. Attach the labels to drug packages and their storage shelves, bins, and areas. All the areas where hazardous

drugs are stored should be marked clearly as containing hazardous drugs. Access to these areas should be limited to authorized personnel who have been trained in handling hazardous drugs. *USP 797* recommends these drugs be stored in a negative pressure room; a negative pressure room is one that has a lower pressure than adjacent locations. The flow of air in a negative pressure room is into the room itself; therefore, it must have adequate exhaust ventilation. Additionally, personnel who handle these agents should wear chemotherapy gloves every time they come into contact with them.

Storage and transport equipment should be designed to minimize breakage. For example, shelves should have front barriers, and carts should have rims. Hazardous drugs should be kept at eye level or lower and stored in bins. Refrigerated hazardous drugs should be stored separately in individual bins.

It is important when transporting these agents that care is taken to ensure that no spillage, leakage, or exposure to personnel occurs. For example, pneumatic tube systems cause mechanical stress to containers and should not be used for transporting hazardous drugs. All hazardous drug containers must be securely capped or sealed. Use Luer lock syringes and connectors, syringe caps, and capping container ports along with using sealed plastic bags and impact-resistant containers with cautionary labels to minimize the potential for breakage, leakage, spill, and exposure. Additionally, IV sets should be primed with compatible IV solution and attach to chemotherapy bag prior to dispensing to the ward. These procedures can certainly help to minimize, if not eliminate, accidents. Finally, personnel who transport these medications must be properly trained to handle such incidents should they occur (obtain a spill kit that contains personal protective equipment and clean-up materials). All hazardous spills need to be reported and documented.

Protective apparel

There is no substitute for good technique, but protective apparel is another fundamental element in protecting personnel who handle or prepare hazardous drugs. Various protective garments can help to shield personnel from exposure. *USP 797* requires that personnel who prepare hazardous compounds must wear the appropriate personal protective equipment when handling any part of these products. You must follow the guidelines for appropriate dressing as outlined above in the “Sources of contamination, special clothing” section of this unit. Any part of the protective wear that becomes contaminated must be changed immediately.

Eyewear and respirators

Protective eyewear and a NIOSH-certified respirator, or surgical mask, are also mandatory when handling these agents. NIOSH is The National Institute for Occupational Safety and Health, a department of the Centers for Disease Control and Prevention. Wearing the appropriate respirator is critical for personnel safety; regular surgical masks won’t protect against airborne particles that might be caused during compounding and should not be worn when making these products.

Gowns

It is important that the gown be a solid-front cover, low-permeability, and made of lint-free fabric. They must have long sleeves and tight-fitting elastic or knit cuffs. They should not be worn outside the work area and should be changed immediately if contaminated. It should be noted that gowns worn during the preparation of hazardous agents *must not* be worn again, unlike those used when preparing non-hazardous CSPs.

Gloves

Gloves are essential protection for all hazardous drug procedures. Wash hands thoroughly before you put the gloves on and after removing them. Use disposable, powder-free latex gloves of good quality or gloves made of nitrile, neoprene, or polyurethane rubber. Never use PVC or powdered gloves. Be aware that surgical latex gloves are preferred because of their fit, elasticity, and tactile sensation. If only powdered gloves are available, wash the powder off before beginning to work.

Depending on the procedure, one or two pairs of gloves may be required. If two pairs are needed, tuck one pair under the cuffs of the gown and place the second pair over the cuff. If an outer glove becomes contaminated, change it immediately. Change both the inner and outer immediately if the outer glove becomes torn, punctured, or heavily contaminated. If only one pair is worn, pull the gloves over the gown's cuff so that the skin is not exposed. The safest policy to follow regarding glove use is to wear two pairs of gloves.

In case of emergency

Every work area in which hazardous drugs are prepared should have an eyewash fountain or sink and appropriate first aid equipment. If skin or eye contact occurs, follow established first aid procedures, obtain medical attention without delay, and document the incident.

Biological safety cabinets

Two of the most important pieces of equipment for handling hazardous drugs safely are the BSC and compounding aseptic isolator (or isolation chamber). A BSC is a type of vertical laminar flow hood (described earlier in this unit) that is designed to protect workers from exposure as well as to help maintain sterility during preparation of products. BSCs must meet standards set by the National Sanitation Foundation or the National Institutes of Health.

When sterile hazardous drugs are being compounded, a Class II or III BSC or an isolator intended for aseptic preparation and containment is required. The front air barrier that the BSC II creates between the handler and the work zone protects the handler from contamination by hazardous drug dusts and aerosols that are generated. Room air is pulled into the front intake grill and filtered through a HEPA filter. The air then passes vertically (downward) through the work zone. The air that passes through the work zone goes through front intake and rear exhaust grilles, passes through a HEPA filter, and is re-circulated through the work zone or exhausted to the outside. Placing objects on or near the front intake or rear exhaust grilles may obstruct the airflow and reduce the effectiveness of the cabinet. The two types of Class II BSCs are (1) Type A BSC and (2) Type B BSC.

Type A BSC

Type A BSCs pump about 30 percent of the air back into the room after it passes through a HEPA filter. Airflow from the exhaust filters should never be blocked.

NOTE: These types of flow hoods have lost favor in the pharmaceutical community due to NIOSH's recommendation that all hazardous drug compounding be performed in BSCs that are 100 percent vented to the outside.

Type B BSC

Type B BSCs send air from the work zone through a HEPA filter and then to the outside of the building through an auxiliary exhaust system. Type B BSCs offer greater protection, because filtered air is sent outside the building and because they have a faster inward flow of air.

The Class III BSC is a type of barrier isolator unit that is gas-tight and maintained under negative air pressure. This type of barrier isolator is used to work with highly infectious, carcinogenic, or hazardous materials. All operations are conducted through rubber gloves attached to entry portals.

Do not use horizontal laminar flow hoods to prepare hazardous drugs. They blow contaminants directly at the preparer. If a horizontal laminar flow hood must be used, turn it off.

The Centers for Disease Control (CDC) investigators suggest that BSCs should be operated continuously, 24 hours per day and should be inspected and certified by qualified personnel annually. Follow the manufacturer's recommendations for proper operation and maintenance, particularly concerning replacement of HEPA filters.

Cleaning and disinfecting BSCs

Work surface plus back and side walls should be cleaned with water or a cleaner recommended by the cabinet manufacturer. Do not use aerosol cleaners; they could damage the HEPA filters and cabinet and could allow contaminants to escape.

Before performing sterile manipulations, the work surface should be disinfected with 70% IPA or another suitable disinfectant and allow the surface to dry. Alcohol is a disinfectant and may remove some substances in the hood that water does not dissolve, but alcohol is not a good cleaner. However, excessive amounts of alcohol should not be used, because vapors may build up in the BSC. Since the gauze and gloves used to clean the BSC are contaminated, use sealable containers to dispose of them along with other hazardous waste.

Extensive decontamination should be performed, preferably on a weekly basis and immediately after a large spill. While cleaning and disinfecting the hood everyone should wear a gown, latex gloves, a respirator, a hair cover, and eye protection. Keep the blower on and clean from the top, where contamination is least, to the bottom, where contamination is greatest. Use heavy toweling or gauze with cleaner and distilled deionized water. Remove the cover over the HEPA filter and clean inside the BSC. Lift the work tray and prop it against the back wall to clean underneath. Scrub the drain spillage trough thoroughly. If you tear your gloves, change them immediately. The cleaner and the water containers as well as all the protective apparel and cleaning materials must be handled and discarded as contaminated waste.

Training for preparers of hazardous agents

Before someone handles a cytotoxic or other hazardous drug, he or she must demonstrate proper manipulative technique and properly use protective equipment and materials. Institutional quality assurance programs should require at least annual reevaluation and documentation of hazardous drug-handling skills and knowledge. We will expand on these issues briefly before discussing how to compound these agents.

Just as for compounding nonhazardous sterile preparations, it is imperative that personnel who handle hazardous agents be adequately trained so that personal, coworker, and patient safety is maintained. Didactic (classroom) training must include overviews of the following types of hazardous drugs:

- Mutagenic.
- Teratogenic.
- Carcinogenic properties.

As new hazardous drugs are introduced to the pharmacy, they must be added to ongoing training programs already in place. Other training issues must be addressed to ensure that personnel can safely compound these agents:

- Safe aseptic practices.
- Negative pressure techniques in the use of BSCs.
- Proper use of closed-system vial-transfer devices (CSTD).
- Containment, clean-up, and disposal guidelines for breaks and spills.

Positive and negative air pressurization

A few other *USP 797* issues need to be addressed before a discussion of compounding hazardous agents can take place. The BSC must meet ISO class 5 standards and be contained within a room that meets ISO class 7, negative air pressure standards. In addition, this room must have an anteroom that meets ISO class 7 or better standards, with a positive air pressure so that it can push any airborne substances back into the room containing the BSC (positive pressure pushes air flow out of a room, while negative pressure pulls air into a room).

Sampling work surfaces

To be certain that aseptic and disinfecting procedures are being followed, surface wipe samples of counters that come into contact with any component of hazardous materials should be performed. A benchmark reading should be accomplished, and then another reading should be done once every six months to be sure that no hazardous materials are found. If there is any contamination on work surfaces, on the floor under the work area, or in patient administration areas, then issues such as retraining, improving cleaning procedures, and improving engineering controls must be addressed.

Compounding procedures for hazardous agents

Now that we have discussed where cytotoxic and hazardous agents should be compounded and how to test to be sure the rules are being followed, we can discuss how to actually compound these agents.

Before preparing sterile hazardous drugs in a BSC, wash your hands and put on a gown and two pairs of latex gloves. Disinfect the work surface with alcohol. Place yourself so the front shield protects your eyes and face. Some institutions place a plastic-backed liner on the work surface. Though this liner may introduce particles into the work zone, it will absorb any small spills.

Assemble sufficient materials for the entire preparation process so you will not have to leave and reenter the work zone. Place only items necessary to the preparation process in the work zone. Make sure these objects do not block the downward flow of air. For example, do not hang IV bags or bottles above sterile objects. Handle sterile objects well inside the BSC so they are not contaminated by unfiltered air at the front air barrier. Air quality is lowest at the sides of the work zone, so work at least three inches away from each side wall.

When possible, attach IV sets to containers and prime them before adding the drug. Use syringes and IV sets with locking fittings; they are less likely to separate than friction fittings. Needles are secured to these Luer-Lok fittings with a quarter turn.

When you are working with drugs in vials, pressure can build up inside the vial and cause the drug to spray out around the needle. Maintain a slight negative pressure inside the vial to prevent this. Too much negative pressure, however, can cause leakage from the needle when it is withdrawn from the vial. Another way of preventing pressure buildup is to use a chemotherapy dispensing pin. This disposable device is attached at one end to the Luer-Lok fitting of the syringe, and a pin on the opposite end is inserted into the drug vial. The device also has a venting unit that allows for constant pressure equalization, thereby eliminating any buildup.

If you are reconstituting a drug in a vial, use a syringe that is large enough so the plunger will not separate from the barrel when filled with solution. After drawing up the diluent into a syringe, insert the needle into the vial top and draw the plunger back to create a slight negative pressure inside the vial and draw air into the syringe. Inject small amounts of diluent slowly and draw equal volumes of air out of the vial. Keep the needle in the vial and swirl the contents carefully until they dissolve completely. With the vial inverted, gradually withdraw the proper amount of drug solution while exchanging equal volumes of air for drug solution. Excess drug should remain in the vial. With the vial in the upright position, draw a small amount of air from the vial into the needle and hub. Then withdraw the needle from the vial.

If there is a need to transfer a hazardous drug to an IV bag, be careful not to puncture the bag. Wipe the IV port, container and set with moist gauze and put a warning label on the IV bag. Place the IV in a sealable bag so any leakage will be contained.

When withdrawing cytotoxic or hazardous drugs from an ampule, gently tap the contents down from the neck and top portion. Spray or wipe the ampule neck with alcohol. Attach a 5-micron filter needle or filter straw to a syringe that is large enough to hold the ampule's contents. Draw the fluid through the filter needle and clear it from the needle and hub. Exchange the filter needle for a regular needle of similar gauge and length. Eject any air and excess drug into a sterile vial, leaving the desired volume in the syringe. You may then transfer the drug to an IV bag or bottle. If the dose is to be

dispensed in the syringe, draw back the plunger to clear fluid from the needle and hub. Replace the needle with a locking cap. Wipe the syringe with moistened gauze and label it appropriately.

Good technique does not end with drug preparation. There are special requirements for waste disposal and cleanup. Put any glass fragments and needles in a puncture-and-leak-resistant container. Do not clip the needles before disposal. Place all other materials in sealable plastic bags along with the outer pair of gloves. Seal all waste containers before removing them from the BSCs, and dispose of them in designated, labeled containers. Finally, remove and dispose of the gown, and, lastly, remove the inner pair of gloves. When removing the gloves, be careful not to touch the fingertips of the gloves to the skin or the inside of the gloves. Wash your hands.

Hazardous waste requirements and procedures

When working with hazardous chemicals, it is important that you know how to properly dispose of waste and handle any accidents that occur. You will not have time to read your operating instructions when accidents occur, so before working with these chemicals familiarize yourself with the proper procedures.

Disposal

There should be institutional policies and procedures for identifying, containing, collecting, segregating and disposing of hazardous waste. Hazardous waste must be stored in leak-resistant containers until it is disposed of in accordance with government and institution policy. All hazardous waste must be separated from other trash and should be handled only by those designated and trained for this purpose. Regular trash should not be placed in hazardous waste containers. Handle the outside of hazardous waste containers only with uncontaminated gloves. Do not ask housekeeping personnel to dispose of hazardous waste if they have not been trained.

Spills

Anyone handling hazardous drugs must be oriented and prepared to handle spills. Spills, as well as routine drug preparation and administration, generate contaminated waste.

In the event of a hazardous drug spill, a *spill kit* should be used, and the cleanup should follow established procedures. Spill kits should be assembled containing all the materials needed to clean up hazardous drug spills and protect healthcare workers and patients. They should be kept readily accessible in any area where hazardous drugs are handled, including the pharmacy and patient care areas. Spill kits should contain protective gear such as eye protection, a respirator, utility and latex gloves, a disposable gown or coveralls, and shoe covers. They should also contain the equipment needed to clean up the spill. These include a disposable scoop and a puncture and leak-resistant plastic container for disposing of glass fragments; absorbent spill pads; gauze and disposable toweling; absorbent powder; and sealable, thick plastic waste disposal bags.

Put up a warning sign to alert other people in the area to the hazard. Put on all of the protective equipment, including latex gloves covered by utility gloves. Put broken glass in the puncture- and leak-resistant plastic container. Absorb liquids with disposable towels or spill pads. Remove powders with dampened towels or gauze. Rinse the contaminated surface with water, wash it with detergent, and then rinse it again. Start at the outside of the spill and work toward the center. Place all the contaminated materials in sealable plastic disposal bags.

There should also be institutional policies and procedures for handling spills in carpeted areas. Some facilities direct personnel to clean the spill with absorbent powder and a “hazardous drug only” vacuum cleaner. Other facilities direct their personnel to soak up the spill with absorbent powder and towels only.

If a large spill occurs in a BSC, certain additional steps must be taken. Obtain the spill kit described above. Use utility gloves when handling any broken glass. Thoroughly clean the drain spillage trough, and decontaminate the BSC if necessary. Seal all contaminated materials in hazardous waste

containers while the materials are still inside the BSC. Transfer these containers to leak-resistant containers. Document the circumstances and the handling of the spill.

Exposure

Any body part exposed to a hazardous chemical should be cleaned immediately. If the substance comes in contact with the skin, wash the skin thoroughly with soap and water and seek appropriate medical attention. If the substance comes in contact with the eyes, flush the affected eye or eyes with large amounts of water or use an eye flush kit, and then seek appropriate medical attention.

620. Reference library

As a pharmacy technician, you will be confronted with numerous pharmacy related questions from physicians, nurses, other health care professionals (including other pharmacy technicians) and patients. Sometimes it's necessary to find answers before entering medication orders into the computer, preparing an IV admixture, and filling or dispensing outpatient prescriptions. Of course, you can't possibly be expected to know everything. Whether you're working in outpatient or inpatient pharmacy, you need to know how to utilize available professional pharmacy resources.

Reference library requirements

The information provided in professional references is essential for day-to-day operations. It provides answers to routine questions on medications or invaluable assistance in handling emergency situations. However, it is imperative that you recognize your limitations, and don't attempt to provide an answer to a question that is asked outside your authority or beyond your personal limits. Don't be afraid to say, "I don't know." The clinical consequences could be grave if you provide incorrect information or exceed the limits of your position. Your pharmacy should have some method of identifying which types of questions you are allowed to handle and which types should be handled by a pharmacist or other senior pharmacy personnel.

Pharmacy reference material

When you are asked questions that are appropriate for you to respond to, the references available to you will be a great asset and you must know how to use them.

Pharmacy reference material is utilized in three basic ways:

1. Education.
2. Research.
3. Current awareness (from previous education, research, or information from other pharmacy personnel).

Of course there's not enough room here to talk about all the books of an institutional pharmacy. Hundreds of references are available that might have some use in the practice of pharmacy, and hundreds of new ones are published each year. With so many references available it would be wise to be selective in regard to new acquisitions. A good way to learn about a new reference is to read the review sections of periodicals such as the *American Journal of Hospital Pharmacy* and the *American Journal of Pharmaceutical Education*. Procedures for ordering reference materials will differ from military treatment facility (MTF) to MTF.

Let's take a look at references that most pharmacies have available to see how they may be helpful to you when you're on the job.

Joint Commission requirements

As discussed in volume 2, The Joint Commission (TJC) is one of the agencies that surveys and accredits MTFs. The primary purpose of TJC is to assess the quality of care provided. One of TJC's requirements covers knowledge-based information resource standards.

TJC states that knowledge-based information resources should be readily available, current, authoritative, and that hospital practitioners and staff should have access to knowledge-based information to do the following:

- Acquire and maintain the knowledge and skills needed to maintain and improve competence.
- Assist with clinical/service and management decision making.
- Provide appropriate information and education to patients and families.
- Support performance improvement and patient safety activities.
- Support the institution's educational and research needs.

TJC standards also state that knowledge-based information resources can be made available to clinical/service staff through electronic means, after-hours access to an in-house collection, or other methods.

Following the standards listed above TJC surveyors should not expect smaller MTFs to have a full-scale drug information center, because the references required for your facility are dependent on the type of services provided at your MTF and the extent of each pharmacy's needs and responsibilities. Nevertheless, they do expect the pharmacy to have current references, the capability to provide information on drugs to the professional staff, and access to an outside source of drug information. Thus, they may ask you to provide a list of references maintained in the pharmacy.

Pharmacy references

Our reference media may also be classified according to the form in which they are published or produced; TJC's list of examples include current texts, periodicals, indexes, abstracts, reports, documents, databases, directories, discussion lists, successful practices, equipment and maintenance user manuals, standards, protocols, practice guidelines, clinical trials, and other resources. Other resources may include the following:

- Videotapes.
- Audiotapes.
- Package inserts.
- Pamphlets and booklets.
- Advertising and other promotional materials.

In this lesson, you will read about only the three basic types—periodicals, online services, and textbooks.

Periodicals

The types of periodicals used in the pharmacy include peer-reviewed journals; abstracting and indexing journals; current affairs publications; newsletters; and Air Force publications, including those that are local, or from major commands (MAJCOM), and USAF levels. There are also some periodicals that are a mixture of two or more of the previously listed types. The following paragraphs provide a sample listing of periodicals commonly referenced in our pharmacies.

The American Journal of Pharmaceutical Education

The American Journal of Pharmaceutical Education is the official publication of the American Association of Colleges of Pharmacy. The Journal is directed to all those with interest in professional, graduate, and postgraduate pharmaceutical education. Its purpose is to document and advance pharmaceutical education in the United States and internationally. The journal features original research articles, editorials, reports on the state of pharmaceutical education, descriptions of teaching innovations, and book reviews.

U.S. Pharmacist

U.S. Pharmacist is a monthly journal dedicated to providing the nation's pharmacists with up-to-date, authoritative, peer-reviewed clinical articles relevant to contemporary pharmacy practice in a variety of settings, including community pharmacy, hospitals, managed care systems, ambulatory care clinics, home care organizations, long-term care facilities, industry, and academia. The publication is also useful to pharmacy technicians, students, other health professionals, and individuals interested in health management.

American Journal of Hospital Pharmacy

The *American Journal of Hospital Pharmacy* is the official publication of the American Society of Hospital Pharmacists, and is a journal that provides a continuing source of professional material regarding pharmacy practices. It contains articles on current drug therapy and innovative procedures.

Hospital Pharmacy

The *Hospital Pharmacy* publication is an independent peer-reviewed journal. It is practitioner focused and dedicated to the promotion of best practices and medication safety. It is published monthly with the exception of a combined July and August issue.

Online services

This area of reference material has grown at a rapid pace, and many printed publications are now available online. An advantage of using online resources instead of paper-based medical references is the quick access to specific information. These types of references are accessible from any computer through intermediary on-line database vendors. Also, many of these databases can be loaded directly onto any Smartphone or other electronic devices many practitioners now use for reference when treating patients. There are several major on-line database vendors in the US, and each of them carries a number of literature databases that may be useful to both the pharmacy and medical staff in providing accurate, timely drug information.

MICROMEDEX

MICROMEDEX Solutions® is primarily a drug information system. This product contains full-text databases on chemical, pharmaceutical, and related biological substances used in clinical patient care. The databases cover subjects such as pharmaceutical information relating to diseases, toxicology, lab, and drug information. *MICROMEDEX Solutions*® also includes drug reviews, guidelines, clinical reviews, and information from package inserts and drug texts to help determine drug dosing, side effects, and interactions.

Lexicomp

Lexicomp Online™ provides drug information that helps healthcare professionals make safe and faster decisions with easy-to-use clinical information and advanced technology. *Lexicomp Online*™ provides the necessary tools to help improve patient safety, ensure compliance, and elevate the quality of care patients receive. The pharmacology content of *Lexicomp Online*™ is useful for patients of all ages and positively impacts treatment outcomes.

The US Food and Drug Administration center for drug evaluation and research

The Center for Drug Evaluation and Research (CDER) is America's consumer watchdog for medicine. The CDER is tasked with making sure all drugs in the United States are safe and effective. It is part of one of the nation's oldest consumer protection agencies—the FDA, which is an agency of the federal government's Department of Health and Human Services.

Orange Book

The FDA Website also contains the *Orange Book* – the FDA Approved Drug Products with Therapeutic Equivalence Evaluations guide. The *Orange Book* identifies drug products approved on the basis of safety and effectiveness by the FDA under the Federal Food, Drug, and Cosmetic Act. An

electronic *Orange Book* query enables searching of the approved drug list by active ingredient, proprietary name, applicant holder, or applicant number. This will allow you to check medications for therapeutic equivalency. This term indicates that a medication can be substituted with the full expectation by the patient and physician that the medication will have the same clinical effect and safety profile as the innovator drug. The evaluations have been prepared by CDER to serve as public information and advice to state health agencies, prescribers, and pharmacists to promote public education in the area of drug product selection and to foster containment of health care costs.

Reference textbooks

Again, there's not enough room here to talk about all the books of an institutional pharmacy. Hundreds of books are available that might have some use in the practice of pharmacy. With so many books available it would be wise to be selective in regards to new acquisitions. Reading the book review sections of periodicals such as the *American Journal of Hospital Pharmacy* and the *American Journal of Pharmaceutical Education* really is a great help in selecting new books. Keep in mind procedures for ordering reference materials will differ from MTF to MTF.

United States Pharmacopoeia-Dispensing Information

The *USP Drug Information (USP DI®)* drug reference guides provide clinically relevant information about the use of medicines and other healthcare products in three volumes: Volume I, *Drug Information for the Health Care Professional*; Volume II, *Advice for the Patient*; Volume III, *Approved Drug Products and Legal Requirements*. Let's take a look at what types of information are included in each volume.

Volume I, Drug Information for the Health Care Professional

This volume includes information for the prescriber, dispenser, or administrator concerning medicines in categories on the following:

- *USP DI®* Volume I: *Drug Information for the Health Care Professional* contains fully reviewed, industry-respected drug information to support prescribing and dispensing decisions.
- Provides information on labeled and off-label uses of generic and brand name drugs dispensed in the US and Canada.
- Contains in-depth monographs that cover dosing, indications, interactions, pharmacology/pharmacokinetics, side/adverse effects, and patient counseling guidelines.

Volume II, Advice for the Patient

This volume provides easy-to-understand, in-depth material to help educate patients about medications and their proper uses.

USP DI® Volume II: *Advice for the Patient® - Drug Information in Lay Language* provides patient information written at a 12th-grade literacy level; documents provide greater detail than most patient education leaflets and include brand names, descriptions, proper use, precautions, and side effects. Instructions for how to handle missed doses are included, as are guidelines for when to seek medical assistance or supervision.

Volume III, Approved Drug Products and Legal Requirements

Volume III reproduces information on therapeutic equivalence and helps you quickly identify a drug's chemical properties related to drug product selection (Food and Drug Administration's *Orange Book*):

- Gives *USP* legal requirements that affect dispensing.
- Provides guidance on safe, legal handling and dispensing of drugs and compounding chemicals.
- Provides color pill charts to quickly identify medications.

- Offers data on quality, packaging, storage, and labeling requirements.
- The publisher states that, “*USP DI*®, Volume III, is the single most comprehensive source for guidelines and laws governing the safe handling and distribution of drugs.”

Trissel’s Handbook on Injectable Drugs and King’s Guide to Parenteral Admixtures

Two references, *Trissel’s Handbook on Injectable Drugs* and *King’s Guide to Parenteral Admixtures*, contain information valuable to pharmacy technicians and pharmacists who are involved with compounding sterile products. They contain information on such topics as drug stability and product formulation of injectable drug products. You may be able to answer questions about which injectable drugs can be mixed together or diluted in which IV fluids by using either of these two references. Unfortunately, all of the possible combinations of drugs and IV fluids are not listed. Most often, these references are used to answer drug compatibility questions. For example, you may receive a call from a nurse who needs to know whether several of a patient’s IV lines can be run together or if two different IV drugs can be mixed together in the same IV bag. You can use these references to look up the answer.

Pharmacy Law Digest

This reference was first published in 1965. Since that time, it has been recognized as a leading book in the field of pharmacy law. Updated annually, *Pharmacy Law Digest* provides a general overview of the legal system as it affects the practice of pharmacy. The book addresses federal laws regulating controlled substances, constitutional considerations in dealing with governmental inspections, regulation of pharmaceuticals, civil liability, and business law. *Pharmacy Law Digest* also includes a condensed review of actual civil and criminal cases involving the practice of pharmacy as well as reprints of the National Association of Boards of Pharmacy (NABP) Survey of Pharmacy Law. Also included is discussion of the Federal Freedom of Information Act, the FDA’s current regulations for professional package labeling and for labeling of over-the-counter (OTC) products, a section on the Internet and controlled substances, and information on the distribution of methadone. This text is great for anyone needing an overview of the legal system as it affects the practice of pharmacy.

Drug topics Red Book

The *Red Book* provides complete pricing information as well as summaries of pricing changes and new product introductions. Alphabetical product entries and changes are highlighted in red to enable quick and easy retrieval of information. There are also expanded listings of products from the top generic manufacturers.

American Hospital Formulary Service Drug Information

American Hospital Formulary Service (AHFS®) Drug Information (DI) contains detailed information on drug products. It includes data about drug doses, dosage forms and ingredients, and general drug classifications. Drugs are arranged by target organ system and therapeutic category. Most of the information is arranged in paragraph form, which can make quick referencing difficult. *AHFS DI* is published yearly and updated periodically with supplements prepared by pharmacists for the purpose of disseminating drug information to the entire medical community. It is a tested and proven source of comparative, unbiased, and evaluative drug information and contains a monograph on virtually every drug entity available in the US. Drug monographs are arranged by pharmacologic-therapeutic classification.

American Drug Index

This reference is prepared for the identification, explanation, and correlation of the many pharmaceuticals in concise dictionary format with extensive cross-referencing. The comprehensive drug listing includes composition, strength, dosage form, packaging, schedule, and use for thousands of brand and official *USP* generic drugs. Appendices include cancer chemotherapy regimens and new drugs available to the medical, pharmaceutical, and allied health professions.

Drug Facts and Comparisons

This reference book is very useful to technicians. It contains information about drug doses, dosage forms and ingredients, and general drug classifications. Available drug products, their formulations, and brand names are listed. Manufacturer names, addresses, and phone numbers are included in an appendix. Pharmaceuticals are presented in sections based on their therapeutic category/target organ system for ease of comparison. The section “Gastrointestinal Drugs,” for example, is broken down into subsections on H-Pylori agents, Proton Pump Inhibitors, Sucralfate, Antacids, Gastrointestinal Anticholinergics/Antispasmodics, Histamine Antagonists, Laxatives, and Antidiarrheals and Antiflatuents, just to name a few. Much of the information is arranged in easy-to-read, well-organized tables and charts. *Drug Facts and Comparisons* is published annually and updated monthly. The updates provide information about newly released drugs and new or revised information about currently marketed drugs.

To find information in *Drug Facts and Comparisons*, you should use the four steps in the following table:

Drug Facts and Comparisons Steps and Descriptions	
Steps	Description
Step 1. Refer to the INDEX.	Always check the Monthly Index Supplement (gray pages) first; then refer to the Quarterly Index.
Step 2. Check the ORGANIZATION.	Each chapter is a therapeutic category of drugs; these categories are marked by “tabs” throughout the reference: <ul style="list-style-type: none"> • Cardiovascular Agents • Respiratory Agents • Central Nervous System Agents • Gastrointestinal Agents • Ophthalmic and Otic Agents • Antineoplastic Agents • Diagnostic Aids <p>NOTE: This is not the complete index list, but it is intended to provide several examples.</p>
Step 3. Check the DRUG MONOGRAPHS.	Group monographs provides general prescribing information on a group of drugs; individual monographs provide specific information on individual agents.
Step 4. Check the PRODUCT LISTINGS.	Products are arranged by dosage form and strength; combination products are arranged by similarity of formula.

You will find this reference useful in providing objective information in a format that enhances comparisons of drug products. These comparisons can help in determining suitable substitutions.

The Review of Natural Products

The Review of Natural Products: Published by Drug Facts & Comparisons is the most comprehensive, scientifically based publication about natural products on the market. Monographs are based on scientific and clinical studies with complete citations contained within the monograph and are peer-reviewed by experts in a variety of fields. A clinical overview is included with each monograph.

More than 300 monographs on natural products include scientific and common names, botany or source, history, chemistry, pharmacology, interactions, toxicology, patient information, references,

and appendices. The text includes valuable appendices including an evidence-based herb/drug interaction table, sources of natural product information, pregnancy and lactation information, and therapeutic and alphabetic indexes.

The U.S. Pharmacopoeia-National Formulary

The *USP–NF* is a single-volume combination of two official compendia containing public pharmacopeial standards. It contains standards for medicines, dosage forms, drug substances, excipients, medical devices, and dietary supplements.

Monographs for drug substances and preparations, as well as dietary supplements and ingredients, are featured in the *USP*. Excipient monographs are in the *NF*. A monograph includes the name of the ingredient or preparation; the definition; packaging, storage, and labeling requirements; and the specification. The specification consists of a series of tests, procedures for the tests, and acceptance criteria. These tests and procedures require the use of official *USP* reference standards. Medicinal ingredients and products will have the stipulated strength, quality, and purity if they conform to the requirements of the monograph.

The US Federal Food, Drug, and Cosmetics Act designates the *USP–NF* as the official compendia for drugs marketed in the US. A drug product in the US market must conform to the standards in the *USP–NF* to avoid possible charges of adulteration and misbranding. The *USP–NF* is also widely used by manufacturers wishing to market therapeutic products worldwide. Meeting *USP–NF* standards is accepted globally as assurance of high quality.

Remington: The Science and Practice of Pharmacy

The *Remington: The Science and Practice of Pharmacy* publication was originally created in 1886 and is touted as the definitive textbook and reference on the science and practice of pharmacy. *Remington* covers wide-ranging subjects such as pharmacogenomics, application of ethical principles to practice dilemmas, technology and automation, professional communication, medication errors, re-engineering pharmacy practice, management of special risk medicines, specialization in pharmacy practice, disease state management, emergency patient care, and wound care. Even though this is a hard-bound reference, the publication strives for a five-year life cycle and acknowledges the challenge in doing so in a world of Internet information and primary publications.

Physicians' Desk Reference

The *Physician's Desk Reference (PDR)* is basically a compilation of drug product package inserts. Therefore, it includes the latest product information prepared by the manufacturers. This information includes indications, dosages, descriptions, contraindications, and adverse reactions. It also includes a drug product identification section that pictures drug products in full color. Manufacturer names, addresses, and phone numbers are also provided. It is published annually with periodic updates. One disadvantage of the *PDR* lies in the fact that the information is the “package insert” from the companies who chose to pay for “advertisement” in the book. Not all products of the company may be listed, and not all companies choose to advertise in this manner.

Goodman & Gilman's: The Pharmacological Basis of Therapeutics

This reference, first published in 1941, is written to physicians and clinical pharmacists as its main audience. The book's chapters are grouped into easily read sections categorized by specific systems. Also included are specific drug classes and therapeutic strategies. Appendices on prescription-writing, patient compliance and the design of dosage regimens are found at the end of the book. Clinicians who frequently face difficult decisions regarding dosage can refer to the table of pharmacokinetic data relevant to dosage adjustment. This reference is updated approximately every five years.

Lexicomp's Drug Information Handbook

This reference covers over 4,000 US and Canadian medications containing up to 39 key fields of information within each drug monograph. The information is alphabetically organized by brand and

generic drug name (like a dictionary) and fully cross-referenced by page number. Dosing information is provided for both labeled and unlabeled indications. This reference includes drug-herb interactions where applicable. The appendices contain comparative drug charts, tables, and treatment guidelines covering a variety of clinical topics. Lexicomp also makes this product available electronically for computers or smart phones. The *Drug Information Handbook* is just one of many reference resources available through this company, two other resources are the *Pediatric Dosage Handbook*, and *Poisoning and Toxicology Handbook*.

Package insert

One of the most immediately available references for information about a particular drug is individual package inserts. The FDA requires that every drug has a package insert (PI) included in the packaging by the manufacturer and that every PI identifies drug dosage forms, dosages, use, side effects, drug stability, and other related information.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

617. Adverse events reporting

1. Who sponsors the adverse events and products defects programs in which all personnel are encouraged to participate?
2. What is the emphasis of a QA program?
3. What is the pharmacy technician's role in patient monitoring?

618. Compatibilities and stability principles

1. What is one of the most widely used references for researching incompatibility and stability information?
2. What type of incompatibility has occurred if two drugs are combined in a solution and they produce a change in the appearance of that solution?
3. What is the most common cause of incompatibilities in intravenous admixtures?
4. What is beyond-use dating?
5. What is an "assay?"

6. According to *USP 795*, up to how many days can a water-containing formulation be stored in a refrigerator?

619. Requirements for compounding cytotoxic and biological agents

1. When is the term “cytotoxic” used?
2. According *USP 797*, hazardous drugs should be stored in what type of room?
3. What type of gloves are preferred when handling hazardous drugs?
4. What is a BSC?
5. What type of BSC sends air from the work zone through a HEPA filter and then to the outside of the building through an auxiliary exhaust system?
6. How often should BSCs be inspected and certified?
7. Due to air quality, how far away from the wall of a BSC should you handle any materials?
8. What items should a spill kit contain?
9. Into what type of container should you place broken glass from a hazardous product?
10. How should you clean your eyes if you become exposed to a hazardous chemical?

620. Reference library

1. What are three basic ways pharmacy reference material is used?

2. What is TJC's requirement in regard to the availability of knowledge-based information resources?
3. List four types of reference media that can be found in our pharmacy reference library.
4. Which pharmacy periodical is a monthly publication that is practitioner focused and dedicated to the promotion of best practices and medication safety?
5. What is an advantage to using online services to access pharmacy references?
6. Who is tasked with making sure all drugs in the United States are safe and effective?
7. What pharmaceutical reference identifies drug products approved on the basis of safety and effectiveness by the FDA?
8. List each volume of the *United States Pharmacopoeia-Dispensing Information*.
9. Which two pharmacy references contain drug stability and product formulation of injectable drug products?
10. Which text provides complete pricing information as well as summaries of pricing changes and new product introductions?
11. What drug data does the *AHFS® DI* contain?
12. Which drug reference lists pharmaceuticals by section based on their therapeutic category/target organ system for ease of comparison?
13. Which pharmacy reference is touted as the most comprehensive, scientifically-based publication about natural products on the market?

14. What reference book is basically a compilation of drug product package inserts?
15. Who is the main audience of Goodman & Gilman's: *The Pharmacological Basis of Therapeutics*?
16. What are the FDA's requirements for package inserts?

Answers to Self-Test Questions

613

1. Solutions ready for injection; dry, soluble products (combined with a solvent prior to use); suspensions ready for injection; dry, insoluble products (combined with a vehicle prior to use); emulsions; and liquid concentrates ready for dilution prior to administration.
2. Sub-Q, IM and IV.
3. Drugs that are very soluble and potent enough to be effective in small volumes.
4. The gluteal muscle of the buttock or in the deltoid muscle (shoulder joint and upper part of the arm area).
5. Intravenous.
6. IV push.
7. IV piggyback.
8. The IV administration of nutrients needed to sustain life, which include carbohydrates, protein, fats, water, electrolytes, vitamins, and trace elements.
9. Dextrose (carbohydrates) and amino acids (protein) and may also include fat and water.
10. To prevent essential fatty acid deficiency and as a source of calories.
11. There are two ways to mix the base components: FAD, or DAF.
12. A system of checks and balances must be built into each step of the TPN ordering, preparation, and administration process. Calculations must be verified and double-checked; solutions and their ingredients should be checked and rechecked.

614

1. The personnel who compound the products.
2. An individual's ability to make a clean product or their aseptic technique.
3. It is the term frequently used to describe the method for handling sterile parenteral dosage forms. Aseptic technique requires that personnel who prepare IV solutions handle these products in clean environments without introducing microorganisms into the product.

615

1. Touch, air, and water.
2. Thorough hand washing.
3. A bacterial or viral contaminant.
4. A gown.

616

1. In an ISO class 5 environment.
2. Refrigerators, computers, and printers.
3. Monthly.

4. Low, medium, and high.
5. The result of comparing the guidance from *USP 797* against your pharmacy's current practices; the differences between the two are the gaps, or areas that aren't in compliance with the *USP 797*.
6. At least every six months.
7. Horizontal and vertical.
8. Thirty minutes.

617

1. The FDA.
2. Maintaining and improving the quality of systems.
3. Monitoring patients for any effects, either appropriate or adverse.

618

1. ASHP's *Handbook on Injectable Drugs*, 18th Edition.
2. Physical.
3. pH of the admixture.
4. The time by which a preparation must be used before it is at risk for chemical degradation or contamination.
5. An analytical procedure that tests the properties, composition, and/or strength of drugs (and a variety of other substances) by chemical means.
6. Up to 14 days.

619

1. To refer to any agent that may be genotoxic, oncogenic, mutagenic, teratogenic, or hazardous in any way.
2. Negative pressure.
3. Surgical latex gloves.
4. A type of vertical laminar flow hood that is designed to protect workers from exposure as well as to help maintain sterility during preparation.
5. Type B.
6. Annually.
7. Three inches.
8. Protective gear such as eye protection, a respirator, utility and latex gloves, a disposable gown or coveralls, and shoe covers. They should also contain the equipment needed to clean up the spill. These include a disposable scoop and a puncture and leak-resistant plastic container for disposing of glass fragments; absorbent spill pads; gauze and disposable toweling; absorbent powder; and sealable, thick plastic waste disposal bags.
9. A puncture- and leak-resistant container.
10. Flush the affected eye or eyes with large amounts of water or use an eye flush kit.

620

1. Current awareness, research, and education.
2. Knowledge-based information resources should be readily available, current, and authoritative.
3. Current texts, periodicals, indexes, abstracts, reports, documents, databases, directories, discussion lists, successful practices, equipment and maintenance user manuals, standards, protocols, practice guidelines, clinical trials, and other resources such as videotapes, audiotapes, package inserts, pamphlets and booklets, and advertising as well as other promotional materials.
4. *Hospital Pharmacy (Journal)*.
5. Quick access to specific information.
6. The Center for Drug Evaluation and Research.
7. *The Orange Book*.

8. *Volume I, Drug Information for the Health Care Professional; Volume II, Advice for the Patient; Volume III, Approved Drug Products and Legal Requirements.*
9. *Trissel's Handbook on Injectable Drugs* and *King's Guide to Parenteral Admixtures.*
10. *Drug Topics Red Book.*
11. Drug doses, dosage forms and ingredients, and general drug classifications.
12. Drug Facts and Comparisons.
13. The Review of Natural Products.
14. The Physician's Desk Reference.
15. Physicians and clinical pharmacists.
16. That every drug has a PI included in the packaging by the manufacturer and that every PI identifies drug dosage forms, dosages, use, side effects, drug stability, and other related information.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter. When you have completed all unit review exercises, transfer your answers to the Field Scoring Answer Sheet.

Do not return your answer sheet to AFCDA.

36. (613) The purpose of *United States Pharmacopeia (USP) 797* is to protect the
 - a. pharmacy personnel.
 - b. pharmacist.
 - c. pharmacy.
 - d. patient.
37. (613) What is an *advantage* of administering medication to a patient via intravenous injection (VI)?
 - a. Immediate physiological action.
 - b. Undesirable effects are easily reversed.
 - c. Simplicity of combining parenteral solutions.
 - d. Absorption more gradual than intestinal tract.
38. (613) What term *best* describes an injection of a small quantity of fluid given through the layers of the skin and into the underlying tissue?
 - a. Intradermal.
 - b. Intravenous.
 - c. Intramuscular.
 - d. Subcutaneous.
39. (613) What type of intravenous (IV) administration is used to administer large volumes of IV solutions over long periods of time?
 - a. IV drip.
 - b. IV push.
 - c. IV piggyback.
 - d. Total parenteral nutrition (TPN).
40. (613) What is a *base* component of a total parenteral nutrition (TPN) solution?
 - a. Trace elements.
 - b. Amino acids.
 - c. Electrolytes.
 - d. Vitamins.
41. (613) What is the proper mixing order for a 3-in-1 total parenteral nutrition (TPN) solution?
 - a. Fats, amino acids, then dextrose.
 - b. Amino acids, fats, then dextrose.
 - c. Fats, dextrose, then amino acids.
 - d. Dextrose, fats, then amino acids.

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42. (614) What type of testing does *United States Pharmacopeia (USP) 797* direct pharmacy departments to perform on their personnel?
- a. Hepatitis C testing of personnel compounding intravenous admixtures.
 - b. Sterility testing to check the competency of personnel compounding intravenous admixtures.
 - c. Semi-annual blood test for personnel compounding intravenous admixtures containing cytotoxic agents.
 - d. Random urinalysis testing of personnel compounding intravenous admixtures containing controlled substances.
43. (614) The absence of disease-causing microorganisms is known as
- a. asepsis.
 - b. sterility.
 - c. culture-free.
 - d. contaminant-free.
44. (614) How often must personnel be re-evaluated for competency in high-risk level compounding?
- a. Monthly.
 - b. Quarterly.
 - c. Semiannually.
 - d. Annually.
45. (615) What is the first essential step in aseptic technique?
- a. Donning a gown.
 - b. Donning a mask.
 - c. Donning gloves.
 - d. Hand washing.
46. (615) Which of the following is *most likely* to give a false sense of security when preparing sterile products?
- a. Gown.
 - b. Goggles.
 - c. Sterile gloves.
 - d. Hand washing.
47. (615) During compounding, you must re-sterilize your gloves every
- a. 10 minutes.
 - b. 20 minutes.
 - c. 30 minutes.
 - d. 40 minutes.
48. (615) Most multiple-dose vials have a beyond-use date of how many days after initially being opened?
- a. 27 days.
 - b. 28 days.
 - c. 29 days.
 - d. 30 days.
49. (616) Which types of activities take place in pharmacy clean rooms?
- a. Disinfecting supplies.
 - b. Sterile compounding.
 - c. Order processing.
 - d. Stock handling.

50. (616) What International Organization for Standardization (ISO) class environment must be maintained in the direct compounding area of a clean room?
- 5.
 - 6.
 - 7.
 - 8.
51. (616) The purpose of sticky mats in a sterile product clean room is to
- minimize traffic flow.
 - remove particles from shoes.
 - catch rodents and insects in the clean room.
 - catch floating particulate matter from the air.
52. (616) How often should counters and floors within an International Organization for Standardization (ISO) class 8 environment be cleaned?
- Daily.
 - Every other day.
 - Three times per week.
 - Weekly.
53. (616) Risk levels for compounding is determined in the pharmacy by the
- size of your pharmacy.
 - specific number of technicians who compound.
 - number of patients who receive compounded products.
 - likelihood of contamination affecting a compounded sterile product (CSP) prepared at your facility.
54. (616) Which document is used to prove to agencies, such as the Joint Commission, that a facility is compliant or is working towards compliance with *United States Pharmacopeia (USP) 797*?
- Written action plan.
 - Microbial risk analysis.
 - Clinic self-inspection reports.
 - Last Unit Environmental Inspection (UEI) report.
55. (616) *United States Pharmacopeia (USP) 797* requires air quality be sampled by electronic means at least once every
- month.
 - 3 months.
 - 6 months.
 - 12 months.
56. (617) *United States Pharmacopeia (USP) 797* encourages any personnel who work in a facility that dispenses sterile products to participate in
- adverse event reporting.
 - blogs regarding sterile product information.
 - quarterly health screenings for compounding personnel.
 - peer-reviews from other local facilities regarding sterile products.
57. (617) As part of the Food and Drug Administration (FDA) and the *United States Pharmacopeia (USP)* guidelines, who must investigate any complaints of adverse events involving compounded sterile products (CSP)?
- Compounding supervisors.
 - Chief of pharmacy services.
 - State or federal pharmacy association officials.
 - Infection control office personnel or related service personnel.

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58. (617) A Quality Assurance (QA) Program must include objective, measurable indicators for monitoring activities that are identified as
- no-risk.
 - low-risk.
 - medium-risk.
 - high-risk.
59. (618) Which type of incompatibility occurs when two drugs combined in a solution produce a change in the appearance of that solution?
- Aseptic.
 - Physical.
 - Chemical.
 - Therapeutic.
60. (618) A theoretical beyond-use date must never be assigned to a dating period of over
- 10 days.
 - 20 days.
 - 30 days.
 - 40 days.
61. (618) Which types of formations may occur the longer a compounded sterile product is stored?
- Pyrogen.
 - Calcium chloride.
 - Petroleum hydrocarbons.
 - Plastic or metal shavings.
62. (619) The term “cytotoxic” is used to refer to any agent that may be genotoxic, oncogenic, mutagenic, teratogenic, or
- sterile.
 - unsterile.
 - biological.
 - hazardous.
63. (619) A biological safety cabinet (BSC) is a type of
- vertical laminar flow hood designed to protect workers from exposure only.
 - horizontal laminar flow hood designed to protect workers from exposure only.
 - vertical laminar flow hood designed to protect workers from exposure as well as to help maintain sterility during preparation.
 - horizontal laminar flow hood designed to protect workers from exposure as well as to help maintain sterility during preparation.
64. (619) What percentage of air is pumped back into the room after it passes through a high efficiency particulate air (HEPA) filter for a Type A biological safety cabinet (BSC)?
- 0.
 - 15.
 - 30.
 - 45.
65. (619) According to *United States Pharmacopeia (USP) 797* standards, the anteroom must maintain what type of air pressure?
- Zero.
 - Positive.
 - Negative.
 - Anti-gravity.

66. (619) How can you prevent vial pressure buildup causing the drug to spray out around the needle when preparing chemotherapy products?
- Use a chemotherapy dispensing pin.
 - Maintain a slight positive pressure inside the vial.
 - Maintain a great negative pressure inside the vial.
 - Eliminate all air from the vial before injecting the needle.
67. (619) With which type of gloves should you *handle the outside* of a hazardous waste container?
- Contaminated gloves.
 - Powdered latex gloves.
 - Uncontaminated gloves.
 - Outer pair of surgical latex gloves.
68. (619) The proper method for cleaning hazardous spills with detergent is to start at the
- center of the spill and work toward the outside.
 - outside of the spill and work toward the center.
 - front of the spill and work toward the back.
 - back of the spill and work toward the front.
69. (620) Which statement best reflects The Joint Commission's (TJC) standard for reference libraries?
- Military pharmacies are not required to maintain reference libraries.
 - Military pharmacies are required to maintain hard-bound references.
 - All pharmacies, no matter what size they are, must have a full-scale drug information center.
 - Knowledge-based information resources can be made available to clinical staff through electronic means.
70. (620) When a patient needs information regarding a new medication just prescribed, which reference is considered the best to use to educate your patient?
- United States Pharmacopoeia-Dispensing Information (USP DI)[®] Volume I, Drug Information for the Health Care Professional.*
 - USP DI[®] Volume II, Advice for the Patient.*
 - USP DI[®] Volume III, Approved Drug Products and Legal Requirements.*
 - Trissel's Handbook on Injectable Drugs and King's Guide to Parenteral Admixtures.*
71. (620) Which reference would you choose to locate prices as well as summaries of pricing changes and new product introductions?
- Drug Topics Red Book.*
 - Physician's Desk Reference.*
 - Remington's Pharmaceutical Sciences.*
 - United States Pharmacopoeia-Dispensing Information.*
72. (620) How often is *Drug Facts and Comparisons* published?
- Every two months.
 - Semi-annually.
 - Annually.
 - Every 5 years.
73. (620) Which reference is the most comprehensive, scientifically based publication about natural products on the market?
- Drug Topics Red Book.*
 - Natural Products Reference.*
 - Physician's Desk Reference.*
 - The Review of Natural Products.*

74. (620) Which statement best reflects the requirement of the Food and Drug Administration (FDA) regarding package inserts (PI)?
- a. There is no FDA requirement regarding PIs.
 - b. Drug dosage forms and doses are the only items a PI must include within the packaging by the manufacturer.
 - c. Side effects and drug stability are the only items a PI must include within the packaging by the manufacturer.
 - d. Every drug must include a PI that identifies drug dosage forms, dosages, uses of the drug, side effects, drug stability, and other related information.

Student Notes

Glossary

Symbols

%	percent
+	positive
–	negative
CO ₂	carbon dioxide
°C	degrees Celsius
$\frac{1}{2}$	fluid dram
$\frac{1}{2}$	fluid ounce
$\frac{1}{2}$	one-half fluid ounce
H ⁺	hydrogen ion
H ₂	Hydrogen
H ₂ CO ₃	carbonic acid
H ₂ O	water
μm	microns
OH ⁻	hydroxide ion

Abbreviations and Acronyms

AFI	Air Force instruction
AHFS® DI	<i>American Hospital Formulary Service Drug Information</i>
ASHP	American Society of Health-system Pharmacists
AV	avoirdupois system
bid	two times a day
BSC	biological safety cabinet
C	concentration
cc	cubic centimeter
CDC	Centers for Disease Control
CDER	Center for Drug Evaluation and Reserach
CSP	compounded sterile product
CSTD	closed-system vial-transfer devices
D5W	dextrose 5% in water
DAF	dextrose, amino acids, then fats
dL	deciliter
FAD	fats, amino acids, then dextrose
FDA	Food and Drug Administration

fl oz	fluid ounce
g or gm	gram
gal	gallon
GMW	gram molecular weight
gr	grain
gtt	drops
HEPA	High-efficiency particulate air
IM	intramuscular
IPA	isopropyl alcohol
ISO	International Organization for Standardization
IV	intravenous
KCL	potassium chloride
kg	kilogram
L	liter
lb	pound
LVP	large volume parenteral
MAJCOM	major command
mcg	microgram
mEq	milliequivalent
mg	milligram
min	minute
mL	milliliter
MTF	medical treatment facility
MVI	multi-vitamin
NABP	National Association of Boards of Pharmacy
NaCl	sodium chloride
NIOSH	National Institute for Occupational Safety and Health
NS	normal saline
OTC	over-the-counter
oz	ounce
PDR	<i>Physician's Desk Reference</i>
pH	scaled measurement of acidity or alkalinity
PI	package insert
PPE	personnel protective equipment
pt	pint
PVC	polyvinyl chloride
QA	quality assurance
q.i.d.	four times per day
QSAD	add quantity sufficient to make total amount
qt	quart

r	refrigerated
SC, SQ, or Sub-Q	subcutaneous
SVP	small volume parenteral
tbsp	tablespoonful
TJC	The Joint Commission
TMC	triamcinolone acetone cream
TPN	total parenteral nutrition
tsp	teaspoonful
USP	<i>United States Pharmacopeia</i>
USP DI[®]	<i>United States Pharmacopeia Dispensing Information</i>
USP–NF	<i>United States Pharmacopeia–National Formulary</i>
V	volume
v/v	volume-in-volume
w/v	weight-in-volume
w/w	weight-in-weight

Student Notes

Student Notes

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