Pharmaceutical calculation

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COURSE OUTLINE

- Balance sensitivity, significant figures, accuracy and percentage of errors
- Measurement of volume and weight
- Aliquot method of weighing and measuring
- Density, specific gravity, specific volume

introduction

- Pharmaceutical calculations is
  - the area of study that applies the **basic principles** of **mathematics** to the **preparation** and **safe** and **effective** use of pharmaceuticals.

Some fundamentals of measurement and calculations

Balance sensitivity

- The sensitivity of balance (SOB) is the **smallest amount** that the balance can measure.

significant figures

- When we count objects accurately, every figure in the numeral expressing the total number of objects must be taken at its face value.
- When we record a measurement, the last figure to the right must be taken to be an approximation, an admission that the limit of possible precision or of necessary accuracy has been reached and that any further figures to the right would not be significant—that is, either meaningless or, for a given purpose, needless.

- A denominate number, like 325 grams, is interpreted as follows:
  - The 3 means 300 grams, neither more nor less, and
  - the 2 means exactly 20 grams more;
  - the final 5 means approximately 5 grams more, i.e., 5 grams plus or minus some fraction of a gram
- Whether this fraction is, for a given purpose, negligible depends on how precisely the quantity was (or is to be) weighed.

- Significant figures, then, are consecutive figures that express the value of a denominate number accurately enough for a given purpose.
- The accuracy varies with the number of significant figures, which are all absolute in value except the last, and this is properly called *uncertain*

- Any of the digits in a valid denominate number must be regarded as significant. Whether zero is significant, however, depends on its position or on known facts about a given number.
- Digits other than zero are significant.
- A zero between digits is significant.
- Final zeros after a decimal point are significant.
- Zeros used only to show the location of the decimal point are not significant.

- The interpretation of zero may be summed up as follows:

1. Any zero **between** digits is significant.
2. **Initial zeros to the left** of the first digit are never significant; they are included merely to show the location of the decimal point and thus give place value to the digits that follow.
3. One or more **final zeros to the right** of the decimal point may be taken to be significant

Examples:
Assuming that the following numbers are all denominate:

1. In 12.5, there are three significant figures; in 1.256, four significant figures; and in 102.56, five significant figures.
2. In 0.5, there is one significant figure. The digit 5 tells us how many tenths we have. The nonsignificant 0 simply calls attention to the decimal point.
3. In 0.05, there is still only one significant figure, as there is in 0.005.

4. In 0.65, there are two significant figures, and likewise two in 0.065 and 0.0065.

5. In 0.0605, there are three significant figures.

The first 0 calls attention to the decimal point,

the second 0 shows the number of places to the right of the decimal point occupied by the remaining figures, and

the third 0 significantly contributes to the value of the number. In 0.06050, there are four significant figures, because the final 0 also contributes to the value of the number.

PRACTICE PROBLEMS

- State the number of significant figures in each of the *italicized quantities:*

(a) One fluidounce equals *29.57 milli-liters*

(b) One liter equals *1000 mililiters*

(c) One inch equals *2.54 centimeters.*

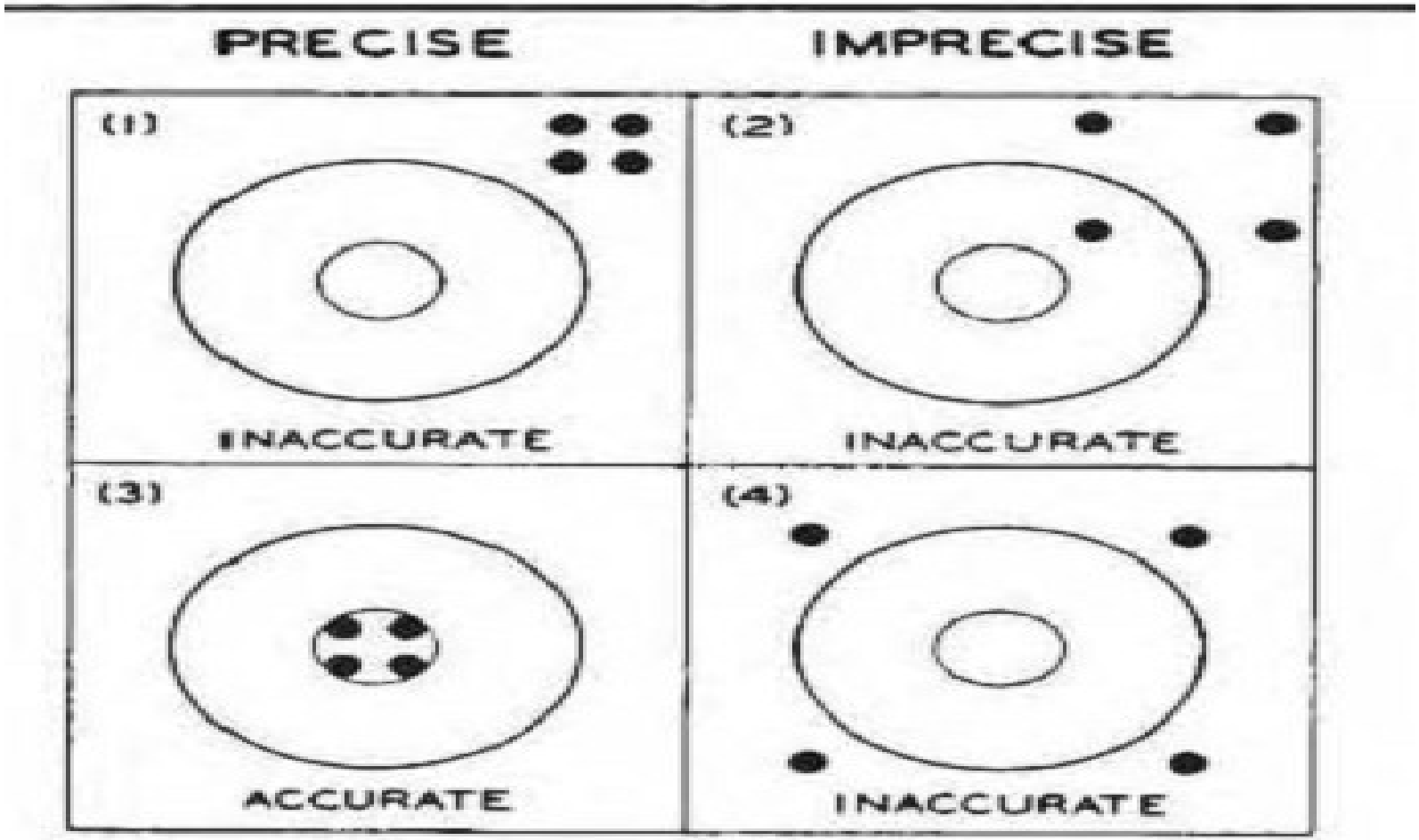
(d) The chemical costs *$1.05per pound.*

(e) One gram equals *1,000,000 micrograms*

(f) One microgram equals 0.001 milligram.

Accuracy

- The **accuracy** of a measurement system is the degree of closeness of a measurement of a quantity to that quantity's actual (true) value.
- The **precision** of a measurement system, also called reproducibility or repeatability, is the degree to which repeated measurements under unchanged conditions show the same results.
- If the values are very close to each


PRECISE
IMPRECISE
(1)
INACCURATE
(2)
INACCURATE
(3)
ACCURATE
(4)
INACCURATE

- For example, if a tablet contains exactly 200 mg of drug, and three analyses show a drug content of 205, 205, and 206 mg, it might be concluded that the analysis is precise, but not accurate.

Percentage of Error

- When a pharmacist measures a volume of liquid or weighs a material, two quantities become important:

(1) the apparent weight or volume measured, and

(2) the possible excess or deficiency in the actual quantity obtained.

- **Percentage of error** may be defined as the maximum potential error multiplied by **100** and divided by the quantity desired. The calculation may be formulated as follows

$$\frac{\text{Error} \times 100\%}{\text{Quantity desired}} = \text{Percentage of error}$$

example

- Using a graduated cylinder, a pharmacist measured 30 milliliters of a liquid. On subsequent examination, using a narrow-gauge burette, it was determined that the pharmacist had actually measured 32 milliliters.
- What was the percentage of error in the

32 milliliters − 30 milliliters = 2 milliliters, the volume of error

$$\frac{2 \text{ mL} \times 100\%}{30 \text{ mL}} = 6.7\%, \textit{answer.}$$

Cont...

- When the maximum potential error is 4 milligrams in a total of 100 milligrams, what is the percentage of error?

$$\frac{4 \text{ mg} \times 100\%}{100 \text{ mg}} = 4\%, \textit{ answer.}$$

A prescription calls for 800 milligrams of a substance. After weighing this amount on a balance, the pharmacist decides to check by weighing it again on a more sensitive balance, which registers only 750 milligrams. Because the first weighing was 50 milligrams short of the desired amount, what was the percentage of error?

$$\frac{50 \text{ mg} \times 100\%}{800 \text{ mg}} = 6.25\%, \textit{ answer.}$$

Measurement of Volume

- Common instruments for the pharmaceutical measurement of volume range from micropipets and burettes used in analytic procedures to large, industrial-size calibrated vessels.
- The selection of measuring instrument should be based on the level of precision required.
- In pharmacy practice, the most common instruments for measuring volume are cylindric and conical (cone-shaped) graduates


FISHER
20°C
0 ML
10
20
30
40
50
60
70
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90
50
ml
40
30
20
10
250
200
150
100
50
5 1/10

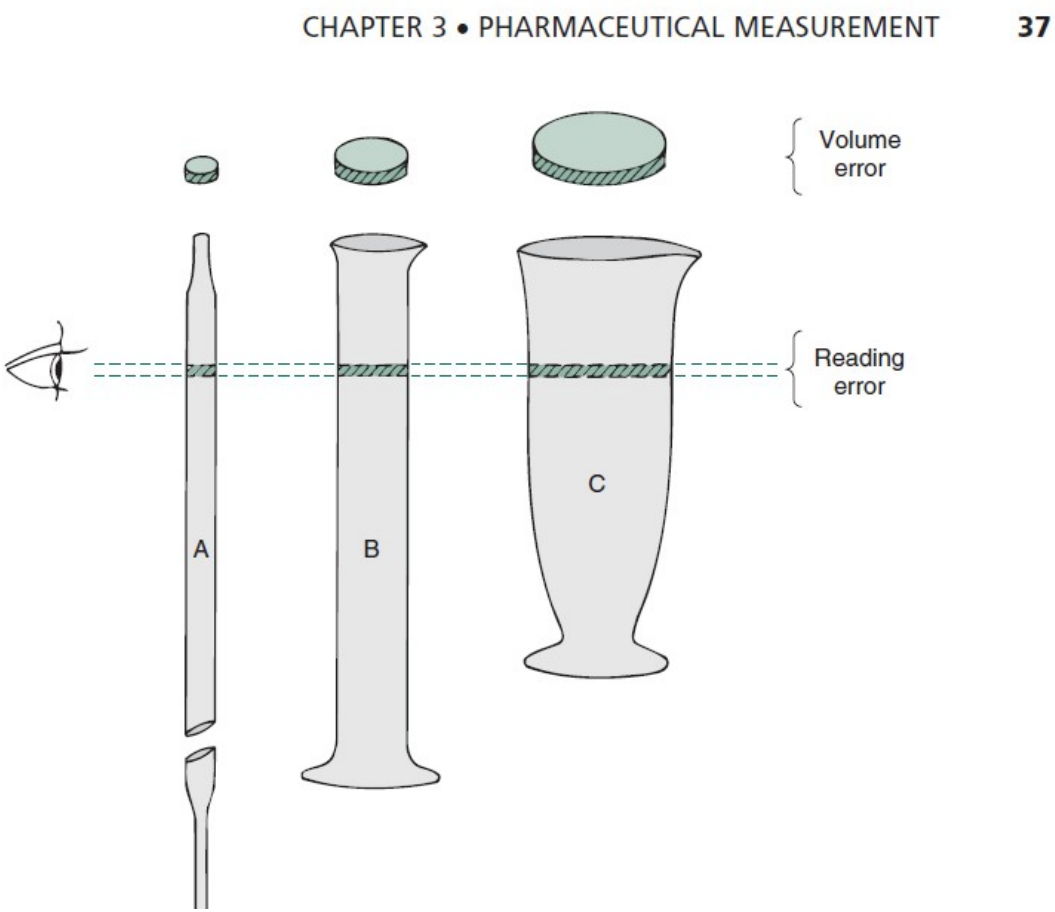
- As a general rule, it is best to select the graduate with a capacity equal to or just exceeding the volume to be measured.

- Measurement of **small volumes in large** graduates tends to increase the size of the error

- the **narrowe**r the bore or chamber, the lesser the error in reading the meniscus and the more accurate the measurement

- According to the *United States Pharmacopeia, a* deviation of 1 mm in the meniscus reading causes an error of approximately 0.5 milliliter when a 100-milliliter cylindric graduate is used and an error of 1.8 milliliters at the 100-milliliter mark in a comparable conical graduate

FIGURE 3.2 Volume error differentials due to instrument diameters.
(A), volumetric pipette; (B), cylindrical graduate; and **(C), conical graduate.**



Cont…

- It is essential for the pharmacist
- to select the proper type and capacity of instrument for volumetric measure and
- to carefully observe the meniscus at eye level to achieve the desired measurement.

Measurement of Weight

- The selection of implements from the wide range of available weights, balances, and scales for pharmaceutical measurement depends on the task at hand
- from highly sensitive electronic analytic balances and prescription balances in extemporaneous compounding procedures to
- large-capacity scales in the industrial manufacturing and production of pharmaceutical products.

- Class A prescription balances (Fig. 3.3) are designed for the weighing of medicinal or pharmaceutical substances required in the filling of prescriptions or in small-scale compounding
- Minimally, a Class A prescription balance should be used in all prescription compounding procedures.
- Most commercially available Class A balances have a maximum capacity of 120 grams.

- Balances of this type have a **sensitivity requirement (SR) of 6 milligrams or less** with no load and with a load of 10 grams in each pan.
- To avoid errors of greater than 5% when using this balance, the pharmacist should not weigh less than 120 milligrams of material (i.e., a 5% error in a weighing of 120 milligrams = 6 milligrams).

FIGURE 3.3 Torbal torsion balance and Ohaus electronic balance.



- The term ***sensitivity requirement is defined as the load that will cause a change of one division*** on the index plate of the balance. It may be determined by the following procedure:

1. Level the balance.
2. Determine the rest point of the balance.
3. Determine the smallest weight that causes the rest point to shift one division on the index plate.

- For greater accuracy than a Class A prescription balance, many pharmacies utilize high-precision electronic analytical balances to weigh very small quantities

Cont…

- these balances are capable of weighing accurately 0.1 milligram, are self-calibrating, and are equipped with convenient digital readout features.
- The usual maximum capacities for balances of this precision range from about 60 grams to 210 grams depending upon the model.

FIGURE 3.4 Sartorious BasicLite analytical balance.

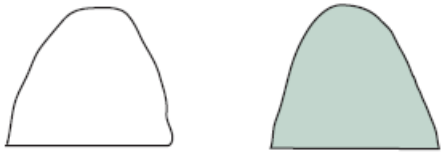
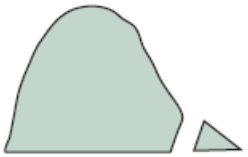


Aliquot Method of Weighing and Measuring

- When a degree of precision in measurement that is beyond the capacity of the instrument at hand is required, the pharmacist may achieve the desired precision by calculating and measuring in terms of aliquot parts.
- An aliquot is a **fraction, portion,** or part that is contained an exact number of times in another.

Weighing by the Aliquot Method

- The aliquot method of weighing is a method by which small quantities of a substance may be obtained within the desired degree of accuracy by weighing a larger-than-needed portion of the substance, diluting it with an inert material, and then weighing a portion (aliquot) of the mixture calculated to contain the desired amount of the needed substance.
- A stepwise description of the procedure is depicted in the next Figure and is described as follows:

Step 1	Step 2	Step 3
 5 mg [drug needed] × 25 [multiple factor] = 125 mg [quantity actually weighed]	 Add 2875 mg [diluent] = 3000 mg mixture [125 mg drug + 2875 mg diluent]	 Weigh $\frac{1}{25}$ of 3000 mg = 120 mg [5 mg drug + 115 mg diluent]

- *Preliminary Step. Calculate the smallest quantity of a substance that can be weighed on* the balance with the desired precision.
- The equation used:

$$\frac{100\% \times \text{Sensitivity Requirement (mg)}}{\text{Acceptable Error (\%)}} = \text{Smallest Quantity (mg)}$$

Example:

On a balance with an SR of 6 mg, and with an acceptable error of no greater than 5%, a quantity of not less than 120 mg must be weighed.

$$\frac{100\% \times 6 \text{ mg}}{5\%} = 120 \text{ mg}$$

.

Step 1. Select a multiple of the desired quantity that can be weighed with the required precision

If the quantity of a required substance is *less than the minimum weighable amount, select a* ‘‘multiple’’ of the required quantity that will yield an amount equal to or greater than the minimum weighable amount. (A larger-than-necessary multiple may be used to exceed the minimum accuracy desired.)

Example:

- *If the balance in the example in the preliminary step is used, and if 5 mg of a drug substance is required on a prescription, then a quantity at least* ***25 times (the multiple) the desired amount, or*** *125 mg (5 mg 25), must be weighed for the desired accuracy.*
- *(If a larger multiple is used,* say 30, and 150 mg of the substance is weighed [5 mg 30], then a weighing error of only 4% would result.)

Step 2. Dilute the multiple quantity with an inert substance.

- *The amount of inert diluent to use is determined by the fact that the aliquot portion of the* drug-diluent mixture weighed in *Step 3 must be equal to or greater than the minimum* weighable quantity previously determined.
- By multiplying the amount of the aliquot portion to weigh in *Step 3 by the multiple selected* in *Step 1, the total quantity of the mixture to prepare is determined.*
- *Example:*
- *According to the preliminary step, 120 milligrams or more must be weighed for the desired accuracy.*
- *If we decide on 120 mg for the aliquot portion in Step 3, and multiply it by the multiple selected in Step 1 (i.e., 25), we arrive at 3000 mg for the total quantity of the drug-diluent mixture to prepare.*
- *Subtracting the 125 mg of drug weighed in Step 1, we must add 2875 mg of diluent to prepare the 3000 mg of drug-diluent mixture.*

Step 3. Weigh the aliquot portion of the dilution that contains the desired quantity.

- Since ***25 times the needed amount of drug substance was weighed (Step 1), an aliquot part*** equal to 1⁄25 of the 3000-mg drug-diluent mixture, or 120 mg, will contain the required quantity of drug substance

Proof: $\frac{1}{25} \times 125$ mg (drug substance weighed in *Step 1*) = 5 mg

$\frac{1}{25} \times 2875$ mg (diluent weighed in *Step 2*) = 115 mg

120 mg aliquot part

- *A torsion prescription balance has a sensitivity requirement of 6 milligrams. Explain how you would*
- *weigh 4 milligrams of atropine sulfate with an accuracy of 5%, using lactose as the diluent.*

Cont…

- Because 6 milligrams is the potential balance error, 120 milligrams is the smallest amount that should be weighed to achieve the required precision.
- If 120 milligrams, or 30 times the desired amount of atropine sulfate, is chosen as the multiple quantity to be weighed in Step 1, and if 150 milligrams is set as the aliquot to be weighed in Step 3, then:

Cont...

1. Weigh 30 × 4 mg, or 120 mg of atropine sulfate
2. Dilute with 4380 mg of lactose
   to make 4500 mg of dilution
3. Weigh $\frac{1}{30}$ of dilution, or 150 mg of dilution, which will contain 4 mg of atropine sulfate, *answer*.

Proof: $$\frac{4500 \text{ mg (dilution)}}{150 \text{ mg (dilution)}} = \frac{120 \text{ mg (atropine sulfate)}}{x \text{ mg (atropine sulfate)}}$$

$= 4$ mg, *answer*.

In this example, the weight of the aliquot was arbitrarily set as 150 mg, which exceeds the weight of the multiple quantity, as it preferably should. If 120 mg had been set as the aliquot, the multiple quantity should have been diluted with 3480 mg of lactose to get 3600 mg of dilution, and the aliquot of 120 mg would have contained 4 mg of atropine sulfate. On the other hand, if 200 mg had been set as the aliquot, the multiple quantity of atropine sulfate should have been diluted with 5880 mg of lactose to get 6000 mg of dilution.

Cont…

- ***NOTE: It is important to recognize that answers to aliquot calculations may vary, but still be correct, depending on the multiple factors arbitrarily chosen for use.***

Measuring Volume by the Aliquot Method

- The aliquot method of measuring volume, which is identical in principle to the aliquot method of weighing, may be used when relatively small volumes must be measured with great precision:
- Step 1. Select a multiple of the desired quantity that can be measured with the required precision.
- Step 2. Dilute the multiple quantity with a compatible diluent (usually a solvent for the liquid to be measured) to an amount evenly divisible by the multiple selected.
- Step 3. Measure the aliquot of the dilution that contains the quantity originally desired

Examples:

- A formula calls for 0.5 milliliter of hydrochloric acid. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1-milliliter divisions, explain how you would obtain the desired quantity of hydrochloric acid by the aliquot method.
- If 4 is chosen as the multiple, and if 2 milliliters is set as the volume of the aliquot, then:

Cont…

1. Measure 4 × 0.5 mL, or 2 mL of the acid
2. Dilute with 6 mL of water
   to make 8 mL of dilution
3. Measure ¼ of dilution, or 2 mL of dilution, which will contain 0.5 mL of hydrochloric acid, *answer*.

A prescription calls for 0.2 mL of clove oil. Using a 5-mL graduate calibrated in units of 0.5 mL, how would you obtain the required amount of clove oil using the aliquot method and alcohol as the diluent?

If 5 is chosen as the multiple, then:

1. Measure 5 × 0.2 mL, or 1 mL of clove oil
2. Dilute with 4 mL of alcohol
   to make 5 mL of dilution
3. Measure ⅕ of the dilution, or 1 mL, which contains 0.2 mL of clove oil, *answer*.

Density

- Density(d) is mass per unit volume of a substance.
- It is usually expressed as grams per cubic centimeter (g/cc).
- Because the gram is defined as the mass of 1 cc of water at 4C, the density of water is 1 g/cc.
- For our purposes, because the United States Pharmacopeia1 states that 1 mL may be used as the equivalent of 1 cc, the density of water may be expressed as 1 g/mL.
- In contrast, one milliliter of mercury weighs 13.6 g; hence, its density is 13.6 g/mL.

Density may be calculated by dividing mass by volume, that is:

$$\text{Density} = \frac{\text{Mass}}{\text{Volume}}$$

Thus, if 10 mL of sulfuric acid weighs 18 g, its density is:

$$\text{Density} = \frac{18\ (\text{g})}{10\ (\text{mL})} = 1.8 \text{ grams per milliliter}$$

Specific Gravity

- **Specific gravity** (sp gr) is a ratio, expressed decimally, of the weight of a substance to the weight of an equal volume of a substance chosen as a standard, both substances at the same temperature or the temperature of each being known.
- Water is used as the standard for the specific gravities of liquids and solids; the most useful standard for gases is hydrogen.

Cont...

Specific gravity may be calculated by dividing the weight of a given substance by the weight of an equal volume of water, that is:

$$\text{Specific gravity} = \frac{\text{Weight of substance}}{\text{Weight of equal volume of water}}$$

Thus, if 10 mL of sulfuric acid weighs 18 g, and 10 mL of water, under similar conditions, weighs 10 g, the specific gravity of the acid is:

$$\text{Specific gravity} = \frac{18\ (\text{g})}{10\ (\text{g})} = 1.8$$

TABLE 5.1 SOME REPRESENTATIVE SPECIFIC GRAVITIES AT 25°C

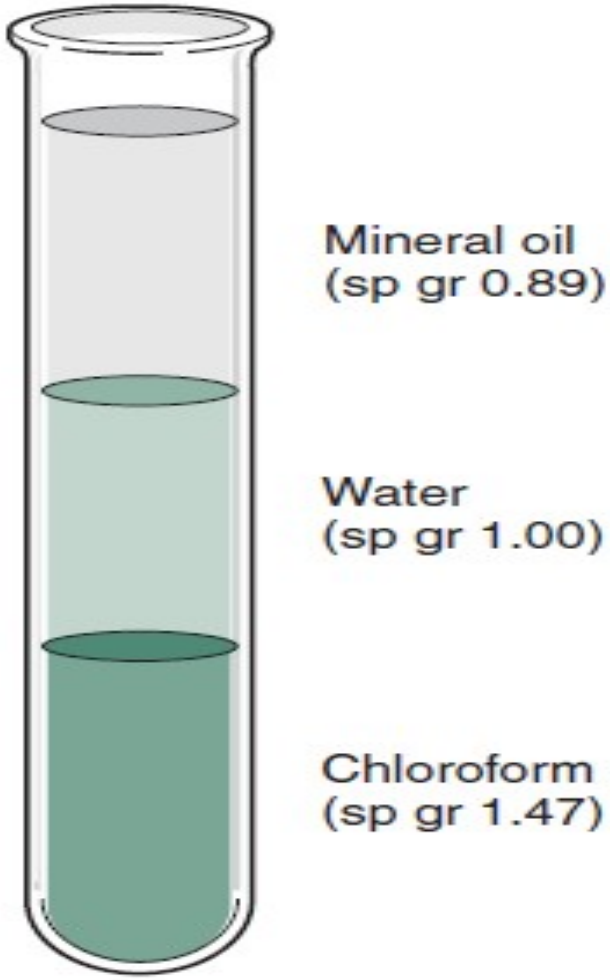
AGENT	SP GR
Ether (at 20°C)	0.71
Isopropyl alcohol	0.78
Acetone	0.79
Alcohol	0.81
Liquid petrolatum	0.87
Peppermint oil	0.90
Olive oil	0.91
Peanut oil	0.92
Cod liver oil	0.92
Castor oil	0.96
Water	1.00
Propylene glycol	1.03

- Substances that have a specific gravity less than 1 are lighter than water.
- Substances that have a specific gravity greater than 1 are heavier than water.
- In the United States Pharmacopeia, the standard temperature for specific gravities is 25C, except for that of alcohol, which is 15.56C by government regulation.

Density Versus Specific Gravity

- The density of a substance is a concrete number (1.8 g/mL in the example), whereas specific gravity, being a ratio of like quantities, is an abstract number (1.8 in the example).
- Whereas density varies with the units of measure used, specific gravity has no dimension and is therefore a constant value for each substance (when measured under controlled conditions).
- Thus, whereas the density of water may be variously expressed as 1 g/mL, 1000 g/L, or 62½ lb/cu ft, the specific gravity of water is always 1.

Depiction of layering of immiscible liquids in a test tube, mineral oil being lighter than water and chloroform being heavier.



Calculating the Specific Gravity of Liquids

- Known Weight and Volume
- Calculating the specific gravity of a liquid when its weight and volume are known involves the use of the equation:

$$\text{Specific gravity} = \frac{\text{Weight of substance}}{\text{Weight of equal volume of water}}$$

Examples:

If 54.96 mL of an oil weighs 52.78 g, what is the specific gravity of the oil?

54.96 mL of water weighs 54.96 g

$$\text{Specific gravity of oil} = \frac{52.78\ (g)}{54.96\ (g)} = 0.9603, \textit{ answer.}$$

If a pint of a certain liquid weighs 601 g, what is the specific gravity of the liquid?

1 pint = 16 fl. oz.
16 fl. oz. of water weighs 473 g

$$\text{Specific gravity of liquid} = \frac{601\ (g)}{473\ (g)} = 1.27, \textit{ answer.}$$

Pycnometer or Specific Gravity Bottle

- A **pycnometer** is a special glass bottle used to determine specific gravity .
- Pycnometers are generally available for laboratory use in volumes ranging from 1 mL to 50 mL.
- Pycnometers have fitted glass stoppers with a capillary opening to allow trapped air and excess fluid to escape.
- Some pycnometers have thermometers affixed, because temperature is a factor in specific gravity determinations.

Cont...

- In using a pycnometer, it is first weighed empty and then weighed again when filled to capacity with water.
- The weight of the water is calculated by difference. Since 1 g of water equals 1 mL, the exact volume of the pycnometer becomes known.
- Then, when any other liquid subsequently is placed in the pycnometer, it is of *equal volume to the water, and its specific* gravity may be determined.

pycnometer



Cont...

Example:

A 50 mL pycnometer is found to weigh 120 g when empty, 171 g when filled with water, and 160 g when filled with an unknown liquid. Calculate the specific gravity of the unknown liquid.

Weight of water: 171 g − 120 g = 51 g

Weight of unknown liquid: 160 g − 120 g = 40 g

$$\text{Specific gravity} = \frac{\text{Weight of substance}}{\text{Weight of equal volume of water}}$$

$$\text{Specific gravity of unknown liquid} = \frac{40\ (\text{g})}{51\ (\text{g})} = 0.78, \textit{ answer.}$$

Use of Specific Gravity in Calculations of Weight and Volume

- When specific gravity is used as a factor in a calculation, the result should contain no more significant figures than the number in the factor.
- It is important to remember that specific gravity is a factor that expresses how much heavier or lighter a substance is than water, the standard with a specific gravity of 1.0.
- For example, a liquid with a specific gravity of 1.25 is 1.25 times as heavy as water, and a liquid with a specific gravity of 0.85 is 0.85 times as heavy as water.
- Thus, if we had 50 mL of a liquid with a specific gravity of 1.2, it would weigh 1.2 times as much as an equivalent volume of water. An equivalent

Calculating Weight, Knowing the Volume and Specific Gravity

Based on the explanation in the previous paragraphs, we can derive the following equation:

$$\text{Grams} = \text{Milliliters} \times \text{Specific gravity}$$

Although it is both obvious and true that one cannot multiply milliliters by specific gravity and have a product in grams, the equation "works" because the volume of the liquid in question is assumed to be the same volume as water for which milliliters equal grams. So, in essence, the true equation would be:

$$\text{Grams (other liquid)} = \text{Grams (of equal volume of water)} \times \text{Specific gravity (other liquid)}$$

Examples:

What is the weight, in grams, of 3620 mL of alcohol with a specific gravity of 0.820?

3620 mL of water weigh 3620 g

3620 g × 0.820 = 2968 g, *answer.*

What is the weight, in grams, of 2 fl. oz. of a liquid having a specific gravity of 1.118?

In this type of problem, it is best to convert the given volume to its metric equivalent first and then solve the problem in the metric system.

2 × 29.57 mL = 59.14 mL

59.14 mL of water weigh 59.14 g

59.14 g × 1.118 = 66.12 g, *answer.*

Calculating Volume, Knowing the Weight and Specific Gravity

By rearranging the previous equation, we can calculate the volume of a liquid using the equation:

$$\text{Milliliters} = \frac{\text{Grams}}{\text{Specific gravity}}$$

Examples:

What is the volume, in milliliters, of 492 g of nitric acid with a specific gravity of 1.40?

492 g of water measure 492 mL

$$\frac{492 \text{ mL}}{1.40} = 351 \text{ mL}, \textit{ answer.}$$

Calculating Specific Volume

- Specific volume, in pharmaceutical practice, is usually defined as an abstract number representing the ratio, expressed decimally, of the volume of a substance to the volume of an equal weight of another substance taken as a standard, both having the same temperature. Water is the standard.
- Whereas specific gravity is a comparison of weights of equal volumes, specific volume is a comparison of volumes of equal weights

- Because of this relationship, specific gravity and specific volume are reciprocals; that is, if they are multiplied together, the product is 1.
- Specific volume tells us how much greater (or smaller) in volume a mass is than the same weight of water.
- It may be calculated by dividing the volume of a given mass by the volume of an equal weight of water. Thus, if 25 g of glycerin measures 20 mL and 25 g of water measures 25 mL under the same conditions, the specific vol

$$\frac{\text{Volume of 25 g of glycerin}}{\text{Volume of 25 g of water}} = \frac{20\ (\text{mL})}{25\ (\text{mL})} = 0.8$$

Calculating the specific volume of a liquid, given the volume of a specified weight, involves the following type of calculation.

Example:

Calculate the specific volume of a syrup, 91.0 mL of which weighs 107.16 g.

107.16 g of water measures 107.16 mL

$$\text{Specific volume of syrup} = \frac{91.0\ (\text{mL})}{107.16\ (\text{mL})} = 0.849, \textit{ answer.}$$

- Because specific gravity and specific volume are reciprocals, a substance that is heavier than water will have a higher specific gravity and a lower specific volume, whereas a substance that is lighter than water will have a lower specific gravity and a higher specific volume.
- It follows, therefore, that we may determine the specific volume of a substance by dividing 1 by its specific gravity, and we may determine the specific gravity of a substance by dividing 1 by its specific volume.

Examples:

What is the specific volume of phosphoric acid having a specific gravity of 1.71?

$$\frac{1}{1.71} = 0.585, \textit{ answer.}$$

If a liquid has a specific volume of 1.396, what is its specific gravity?

$$\frac{1}{1.396} = 0.716, \textit{ answer.}$$

quiz

1,define accuracy and precision.(2%)

2, A prescription calls for 50 milligrams of chlorpheniramine maleate. Using a prescription balance with a sensitivity requirement of 6 milligrams, explain how you would obtain the required amount of chlorpheniramine maleate with an error not greater than 5%.(2%)

3, A pharmacist weighed 475 milligrams of a substance on a balance of dubious accuracy. When checked on a balance of high accuracy, the weight was found to be 445 milligrams. Calculate the percentage of error

4,determine the number of significant numbers(2%)

- 0.1010, 0.001, 12.005, 1001, 10.00, 101.002

5, If 150 mL of a sorbitol solution weigh 170 g, what is its specific gravity?(1%)

6, If 73.42 g of a liquid measures 81.5 mL, what is its specific volume?(1%)

7,If chloroform has a specific gravity of 1.476, what is its specific volume?(1%)

Chapter two

Course outline

- Percentage, ratio and proportion
- Percentage preparations (percentage W/V, V/V, W/W)
- Conversions of concentration to mg/mL, Parts per million (ppm)

- The term percent and its corresponding sign (%) mean ‘‘by the hundred’’ or ‘‘in a hundred,’’ and percentage means ‘‘rate per hundred’’; so 50 percent (or 50%) and a percentage of 50 are equivalent expressions.
- A percent may also be expressed as a ratio, represented as a common or decimal fraction.
- For example, 50% means 50 parts in 100 of the same kind, and may be expressed as 50⁄100 or 0.50.

- For the purposes of computation, percents are usually changed to equivalent decimal fractions.
- This change is made by dropping the percent sign (%) and dividing the expressed numerator by 100.

$$\text{Thus, } 12.5\% = \frac{12.5}{100}\text{, or } 0.125\text{; and } 0.05\% = \frac{0.05}{100}\text{, or } 0.0005.$$

Cont…

- We must not forget that in the reverse process (changing a decimal to a percent), the decimal is multiplied by 100 and the percent sign (%) is affixed.

Ratio

- The relative magnitude of two quantities is called their **ratio.**
- Since a ratio relates the relative value of two numbers, it resembles a common fraction except in the way in which it is presented.

Whereas a fraction is presented as, for example, ½, a ratio is presented as 1:2 and is not read as "one half," but rather as "one is to two."

All the rules governing common fractions equally apply to a ratio. Of particular importance is the principle that if the two terms of a ratio are multiplied or are divided by the same number, the value is unchanged, the value being the quotient of the first term divided by the second

example, the ratio 20:4 or 20/4 has a value of 5; if both terms are divided by 2, the ratio becomes 10:2 or 10/2, again the value of 5.

- The terms of a ratio must be of the same kind, for the value of a ratio is an abstract number expressing how many times greater or smaller the first term (or numerator) is than the second term (or denominator)
- Thus, we can have a ratio of 20 to 4 (20⁄4) or 20 grams to 4 grams (20 grams/4 grams).

- When two ratios have the same value, they are *equivalent.*
- *An interesting fact about equivalent* ratios is that the *product of the numerator of the one and the denominator of the other always equals the product of the denominator of the one and the numerator of the other; that is, the cross products are equal:*

Cont...

Because $^{2}/_{4} = {}^{4}/_{8}$,

2×8 (or 16) $= 4 \times 4$ (or 16).

It is also true that *if two ratios are equal, their reciprocals are equal:*

Because $^{2}/_{4} = {}^{4}/_{8}$, then $^{4}/_{2} = {}^{8}/_{4}$.

We discover further that the *numerator of the one fraction equals the product of its denominator and the other fraction:*

If $^{6}/_{15} = {}^{2}/_{5}$,

then $6 = 15 \times {}^{2}/_{5} \left(\text{or } \frac{15 \times 2}{5} \right) = 6,$

and $2 = 5 \times {}^{6}/_{15} \left(\text{or } \frac{5 \times 6}{15} \right) = 2.$

And the denominator of the one equals the quotient of its numerator divided by the other fraction:

$$15 = 6 \div {}^{2}\!/_{5} \text{ (or } 6 \times {}^{5}\!/_{2}) = 15,$$

$$\text{and } 5 = 2 \div {}^{6}\!/_{15} \text{ (or } 2 \times {}^{15}\!/_{6}) = 5.$$

An extremely useful practical application of these facts is found in *proportion.*

Proportion

- A ***proportion is the expression of the equality of two ratios. It may be written in any one of***
- three standard forms:

(1) $a:b = c:d$

(2) $a:b :: c:d$

(3) $\frac{a}{b} = \frac{c}{d}$

Cont...

- Each of these expressions is read: a is to b as c is to d, and a and d are called the extremes (meaning ‘‘outer members’’) and b and c the means (‘‘middle members’’).
- In any proportion, the product of the extremes is equal to the product of the means.
- This principle allows us to find the missing term of any proportion when the other three terms are known.
- If the missing term is a mean, it will be the product of the extremes divided by the given mean, and if it is an extreme, it will be the product of the means divided by the given extreme.

- Using this information, we may derive the following fractional equations:

$$\text{If } \frac{a}{b} = \frac{c}{d}, \text{ then}$$

$$a = \frac{bc}{d}, b = \frac{ad}{c}, c = \frac{ad}{b}, \text{ and } d = \frac{bc}{a}.$$

The application of ratio and proportion enables the solution to many of the pharmaceutical calculation problems in this text and in pharmacy practice.

Examples:

If 3 tablets contain 975 milligrams of aspirin, how many milligrams should be contained in 12 tablets?

$$\frac{3\ (\text{tablets})}{12\ (\text{tablets})} = \frac{975\ (\text{milligrams})}{x\ (\text{milligrams})}$$

$$x = \frac{12 \times 975}{3}\ \text{milligrams} = 3900\ \text{milligrams},\ \textit{answer.}$$

If 3 tablets contain 975 milligrams of aspirin, how many tablets should contain 3900 milligrams?

$$\frac{3\ (\text{tablets})}{x\ (\text{tablets})} = \frac{975\ (\text{milligrams})}{3900\ (\text{milligrams})}$$

$$x = 3 \times \frac{3900}{975}\ \text{tablets} = 12\ \text{tablets},\ \textit{answer.}$$

Percentage Preparations

- The percentage concentrations of active and inactive constituents in various types of pharmaceutical preparations are defined as follows by the *United States Pharmacopeia:*
- ***Percent weight-in-volume (w/v) expresses the number of grams of a constituent in 100 mL*** of solution or liquid preparation and is used regardless of whether water or another liquid is the solvent or vehicle. Expressed as: *% w/v.*

- **Percent volume-in-volume (v/v) expresses the number of milliliters of a constituent in 100** mL of solution or liquid preparation. Expressed as: % v/v.
- **Percent weight-in-weight (w/w) expresses the number of grams of a constituent in 100 g of** solution or preparation. Expressed as: % w/w.
- The term percent, or the symbol %, when used without qualification means: for solutions or suspensions of solids in liquids, percent weight-in-volume;
- for solutions of liquids in liquids, percent volume-in-volume;
- for mixtures of solids or semisolids, percent weight-in-weight; and
- for solutions of gases in liquids, percent weight-in-volume.

- Based on these considerations, if the designation of the term of a calculation (e.g., w/v, w/w, or v/v) is not included in a problem, the appropriate assumption must be made.

TABLE 6.1 EXAMPLES OF PHARMACEUTICAL DOSAGE FORMS IN WHICH THE ACTIVE INGREDIENT IS OFTEN CALCULATED AND EXPRESSED ON A PERCENTAGE BASIS

PERCENTAGE BASIS	EXAMPLES OF APPLICABLE DOSAGE FORMS
Weight-in-volume	Solutions (e.g., ophthalmic, nasal, otic, topical, large-volume parenterals), and lotions
Volume-in-volume	Aromatic waters, topical solutions, and emulsions
Weight-in-weight	Ointments, creams, and gels

- *Specific gravity may be a factor in a number of calculations involving percentage concentration.* Many formulations are presented on the basis of weight, even though some of the ingredients are liquids. Depending on the desired method of measurement, it may be necessary to convert weight to liquid or, in some instances, vice versa. Thus, the student should recall the equations from the p y:

$$g = mL \times sp\ gr$$

$$mL = \frac{g}{sp\ gr}$$

Percentage Weight-in-Volume

- In a true expression of percentage (i.e., parts per 100 parts), the percentage of a liquid preparation (e.g., solution, suspension, lotion) would represent the grams of solute or constituent in 100 g of the liquid preparation.
- However, in practice, the pharmacist most frequently uses a different definition of percentage for solutions and for other liquid preparations, one in which the parts of the percentage represent grams of a solute or constituent in 100 mL of solution

Cont...

- Indeed, in weight-in-volume expressions, the ‘‘correct’’ strength of a 1% (w/v) solution or other liquid preparation is defined as containing 1 g of constituent in 100 mL of product.
- This variance to the definition of *true percentage is based on an assumption that the solution/liquid preparation has a specific gravity of 1, as if it were water.*

- It is on this assumption that each 100 mL of solution/liquid preparation is presumed to weigh 100 g and thus is used as the basis for calculating percentage weight-in-volume (e.g., 1% w/v 1% of [100 mL taken to be] 100 g =1 g in 100 mL).
- Taking water to represent any solvent or vehicle, we may prepare weight-in-volume percentage solutions or liquid preparations by the SI metric system if we use the following rule.

- Multiply the required number of milliliters by the percentage strength, expressed as a decimal, to obtain the number of grams of solute or constituent in the solution or liquid preparation.
- *The volume, in milliliters, represents the weight in grams of the solution or liquid*

Volume (mL, representing grams) X % (expressed as a decimal) = grams (g) of solute or constituent

Examples of Weight-in-Volume Calculations

How many grams of dextrose are required to prepare 4000 mL of a 5% solution?

4000 mL represents 4000 g of solution
5% = 0.05
4000 g × 0.05 = 200 g, *answer.*

Or, solving by dimensional analysis:

$$\frac{5\text{ g}}{100\text{ mL}} \times 4000\text{ mL} = 200\text{ g, } \textit{answer.}$$

How many grams of potassium permanganate should be used in compounding the following prescription?

℞ Potassium Permanganate 0.02%
Purified Water ad 250 mL
Sig. as directed.

250 mL represents 250 g of solution
0.02% = 0.0002
250 g × 0.0002 = 0.05 g, *answer.*

- To calculate the percentage weight-in-volume of a solution or liquid preparation, given the weight of the solute or constituent and the volume of the solution or liquid preparation, it should be remembered that the volume, in milliliters, of the solution represents the weight, in grams, of the solution or liquid preparation as if it were pure water.

What is the percentage strength (w/v) of a solution of urea, if 80 mL contains 12 g?

80 mL of water weighs 80 g

$$\frac{80\ (\text{g})}{12\ (\text{g})} = \frac{100\ (\%)}{\text{x}\ (\%)}$$

$$\text{x} = 15\%, \textit{answer.}$$

Calculating the volume of a solution or liquid preparation, given its percentage strength weight-in-volume and the weight of the solute or constituent, involves the following:

How many milliliters of a 3% solution can be made from 27 g of ephedrine sulfate?

$$\frac{3\ (\%)}{100\ (\%)} = \frac{27\ (g)}{x\ (g)}$$

$x = 900$ g, weight of the solution if it were water

Volume (in mL) = 900 mL, *answer.*

Percentage Volume-in-Volume

- Liquids are usually measured by volume, and the percentage strength indicates the number of parts by volume of an ingredient contained in the total volume of the solution or liquid preparation considered as 100 parts by volume.
- If there is any possibility of misinterpretation, this kind of percentage should be specified: e.g., *10% v/v.*

Examples of Volume-in-Volume Calculations

℞ Liquefied Phenol 2.5%
Calamine Lotion ad 240 mL
Sig. For external use.

Volume (mL) × % (expressed as a decimal) = milliliters of active ingredient

240 mL × 0.025 = 6 mL, *answer.*

Or, solving by dimensional analysis:

$$\frac{2.5 \text{ mL}}{100 \text{ mL}} \times 240 \text{ mL} = 6 \text{ mL, } \textit{answer.}$$

- In preparing 250 mL of a certain lotion, a pharmacist used 4 mL of liquefied phenol. What was the percentage (v/v) of liquefied phenol in the lotion?

$$\frac{250\ (\text{mL})}{4\ (\text{mL})} = \frac{100\ (\%)}{x\ (\%)}$$

$$x = 1.6\%, \textit{ answer.}$$

What is the percentage strength v/v of a solution of 800 g of a liquid with a specific gravity of 0.800 in enough water to make 4000 mL?

800 g of water measures 800 mL

800 mL ÷ 0.800 = 1000 mL of active ingredient

$$\frac{4000\ (\text{mL})}{1000\ (\text{mL})} = \frac{100\ (\%)}{x\ (\%)}$$

$$x = 25\%, \textit{ answer.}$$

- The volume of a solution or liquid preparation, given the volume of the active ingredient and its percentage strength (v/v), may require first determining the volume of the active ingredient from its weight and specific gravity.

Peppermint spirit contains 10% v/v of peppermint oil. What volume of the spirit will contain 75 mL of peppermint oil?

$$\frac{10\ (\%)}{100\ (\%)} = \frac{75\ (\text{mL})}{x\ (\text{mL})}$$

$$x = 750\ \text{mL},\ \textit{answer.}$$

Percentage Weight-in-Weight

- Percentage weight-in-weight (true percentage or percentage by weight) indicates the number of parts by weight of active ingredient contained in the total weight of the solution or mixture considered as 100 parts by weight.

Examples of Weight-in-Weight

How many grams of phenol should be used to prepare 240 g of a 5% (w/w) solution in water?

Weight of solution (g) × % (expressed as a decimal) = g of solute

240 g × 0.05 = 12 g, *answer.*

How many grams of a drug substance are required to make 120 mL of a 20% (w/w) solution having a specific gravity of 1.15?

120 mL of water weighs 120 g

120 g × 1.15 = 138 g, weight of 120 mL of solution

138 g × 0.20 = 27.6 g plus enough water to make 120 mL, *answer.*

Or, solving by dimensional analysis:

$$120 \text{ mL} \times \frac{1.15 \text{ g}}{1 \text{ mL}} \times \frac{20\%}{100\%} = 27.6 \text{ g, } \textit{answer.}$$

- Sometimes in a weight-in-weight calculation, the weight of one component is known but not the total weight of the intended preparation. This type of calculation is performed as demonstrated by the following example.
- How many grams of a drug substance s

100% − 4% = 96% (by weight) of water

n 240 mL of water weighs 240 g

$$\frac{96\ (\%)}{4\ (\%)} = \frac{240\ (\text{g})}{x\ (\text{g})}$$

$$x = 10\ \text{g},\ \textit{answer}.$$

How should you prepare 100 mL of a 2% (w/w) solution of a drug substance in a solvent having a specific gravity of 1.25?

100 mL of water weighs 100 g

100 g × 1.25 = 125 g, weight of 100 mL of solvent

100% − 2% = 98% (by weight) of solvent

$$\frac{98\ (\%)}{2\ (\%)} = \frac{125\ (g)}{x\ (g)}$$

$$x = 2.55\ g$$

Therefore, dissolve 2.55 g of drug substance in 125 g (or 100 mL) of solvent, *answer.*

Simple Conversions of Concentration to ‘‘mg/mL’’

- To convert product percentage strengths to mg/mL, multiply the percentage strength,

Example:

Convert 4% (w/v) to mg/mL.

$4 \times 10 = 40$ mg/mL, *answer.*

Proof or alternate method: 4% (w/v)
= 4 g/100 mL
= 4000 mg/100 mL
= 40 mg/mL

To convert *product ratio strengths to mg/mL*, divide the ratio strength by 1000.

Example:

Convert 1:10,000 (w/v) to mg/mL.

$10{,}000 \div 1000 = 1$ mg/10 mL, *answer.*

Proof or alternate method: 1:10,000 (w/v)
= 1 g/10,000 mL
= 1000 mg/10,000 mL
= 1 mg/10 mL

- To convert product strengths expressed as grams per liter (g/L) to mg/mL, convert the numerator to milligrams and divide by the number of milliliters in the denominator.

Example:

Convert a product concentration of 1 g per 250 mL to mg/mL.

1000 ÷ 250 = 4 mg/mL, *answer.*

Proof or alternate method: 1 g/250 mL = 1000 mg/250 mL = 4 mg/mL

Parts per Million (PPM) and Parts per Billion (PPB)

- The strengths of very dilute solutions are commonly expressed in terms of parts per million (ppm) or parts per billion (ppb), i.e., the number of parts of the agent per 1 million or 1 billion parts of the whole.
- For example, we are all familiar with fluoridated drinking water in which fluoride has been added at levels of between 1 to 4 parts per million (1:1,000,000 to 4:1,000,000) for the purpose of reducing dental caries.

Example Calculations of Parts per Million and Parts per Billion

- Express 5 ppm of iron in water in percentage strength and ratio strength.
- 5 ppm = 5 parts in 1,000,000 parts = 1:200,000, ratio strength, and 0.0005%, percentage strength, answers.
- The concentration of a drug additive in an animal feed is 12.5 ppm. How many milligrams of the drug should be used in preparing 5.2 kg of feed?
- 12.5 ppm = 12.5 g (drug) in 1,000,000 g (feed) Thus,

$$\frac{1{,}000{,}000\ \text{g}}{12.5\ \text{g}} = \frac{5{,}200\ \text{g}}{x\ \text{g}}$$

$$x = 0.065\ \text{g} = 65\ \text{mg},\ \textit{answer.}$$