9. Some Calculations Involving "Units," "µg/mg," and Other Measures of Potency

CALCULATIONS CAPSULE

Units of Activity

The potency of many pharmaceutical products derived from biological sources is based on *units of activity*. Units of activity are determined against specific biologic standards and vary between products. Generally, there is an established relationship between a product's units of activity and a measurable quantity (e.g., units per milligram; units per milliliter). This relationship may be used in a ratio and proportion to determine either the number of units of activity or the weight or volume containing a specified number of units:

$$\frac{\textit{Units of activity (given)}}{\textit{Weight or volume (given)}} = \frac{\textit{Units of activity (given or desired)}}{\textit{Weight or volume (given or desired)}}$$

- The potency of some antibiotics, endocrine products, vitamins, and biologies (e.g., vaccines):
  - is based on their activity,
  - is expressed in terms of units (of activity), in micrograms per milligram (μg/mg), or in other standardized terms of measurement.
  - meet standards approved by the Food and Drug Administration
  - are set forth in the United States Pharmacopeia.
  - conform also to international standards (e.g.. International Unit or I.U.).

- Measures of degrees of activity, as units of activity:
  - are determined by comparison against a suitable working standard, generally a USP Reference Standard.
- Reference standards:
  - are authentic specimens used as comparison standards in compendial tests and assays.
  - The number of USP Units of an antibiotic is based on a comparison of activity of a sample of that antibiotic on a milligram basis to the corresponding USP Reference Standard.
    - Eg: 1590 USP Units of penicillin G sodium per milligram of the USP Reference Standard of the antibiotic.

- Pharmaceutical products and preparations are allowed specific variances in potency:
  - Eg: the USP monograph for Sterile Penicillin G Sodium specifies a potency of not less than 1500 Penicillin G Units and not more than 1750 Penicillin G Units per milligram.
- The activity or potency of antibiotics is determined by their inhibitory effect on microorganisms.
- No relationship exists between the unit of potency of one drug and the unit of potency of another drug.

- The potency of antibiotics:
  - may also be designated in terms of "µg" (micrograms) of activity.
  - when reference standards for antibiotics were thought to consist entirely of single chemical entities and were therefore assigned potencies of "1000 µg/mg."
- As newer methods of antibiotic manufacture and purification were developed:
  - some highly purified antibiotics had greater than 1000 µg of activity per milligram compared to the original reference standard.
- Differences in potency were also found when comparing the chemical base versus the salt form.
  - ampicillin sodium has a potency equivalent to between 845 and 988 µg/mg of its parent compound ampicillin.

- A comparison of units and micrograms of potency of some official drugs and their respective weight equivalents is given in Table 9.1.
- potencies of certain drugs are designated in units, so too, the doses of these drugs and of their preparations are measured in units.
  - insulin and the penicillin antibiotics.
- Insulin:
  - The commercially available types vary according to
    - time of onset of action,
    - time of peak action,
    - duration of action,
  - all products are standardized to contain either 100 or 500 insulin units per milliliter of solution or suspension.
  - These strengths are designated as "U-100" and "U-500."

TABLE 9.1 EXAMPLES OF DRUG POTENCY EQUIVALENTS

DRUG	UNITS OR μg OF POTENCY PER WEIGHT EQUIVALENT*
Alteplase	580,000 USP Alteplase Units per mg of protein
Ampicillin Sodium	NLT (not less than) 845 μg and NMT (not more than) 988 μg of ampicillin per mg
Antihemophilic Factor	NLT 100 Antihemophilic Factor Units per g of protein
Bacitracin	NLT 40 Bacitracin Units per mg
Bacitracin Zinc	NLT 40 Bacitracin Units per mg
Cephalothin Sodium	NLT 850 μg of cephalothin per mg
Chymotrypsin	NLT 1000 USP Chymotrypsin Units per mg
Clindamycin Hydrochloride	NLT 800 μg of clindamycin per mg
Cod Liver Oil	In each gram: NLT 180 μg (600 USP Units) and NMT 750 μg (2500 USP Units) of Vitamin A and NLT 1.5 μg (60 USP Units) and NMT 6.25 μg (250 USP Units) of Vitamin D

TABLE 9.1 EXAMPLES OF DRUG POTENCY EQUIVALENTS

DRUG	UNITS OR μg OF POTENCY PER WEIGHT EQUIVALENT*
Colistimethate Sodium	390 μg colistin per mg
Digitalis	NLT 1 USP Digitalis Unit per 100 mg
Erythromycin Estolate	NLT 600 μg of erythromycin per mg
Gentamicin Sulfate	NLT 590 μg of gentamicin per mg
Heparin Calcium	NLT 140 USP Heparin Units per mg
Heparin Sodium	NLT 140 USP Heparin Units per mg
Insulin	NLT 26.5 USP Insulin Units per mg
Insulin Human	NLT 27.5 USP Insulin Human Units per mg
Insulin Lispro	NLT 27 USP Insulin Lispro Units per mg
Kanamycin Sulfate	NLT 750 μg of kanamycin per mg
Menotropins	NLT 40 USP Follicle-Stimulating Hormone Units and NLT 40 USP Luteinizing Hormone Units per mg
Minocycline Hydrochloride	NLT 890 μg and NMT 950 μg minocycline per mg
Mitomycin	NLT 970 μg mitomycin per mg
Neomycin Sulfate	NLT 600 μg of neomycin per mg
Nystatin	NLT 4400 USP Nystatin Units per mg
Pancreatin	NLT 25 USP Units of amylase activity, NLT 2 USP Units of lipase activity, and NLT 25 USP Units of protease activity per mg

TABLE 9.1 EXAMPLES OF DRUG POTENCY EQUIVALENTS

DRUG	UNITS OR μg OF POTENCY PER WEIGHT EQUIVALENT*
Penicillin G Benzathine	NLT 1090 and NMT 1272 Penicillin G Units per mg
Penicillin G Potassium	NLT 1440 and NMT 1680 Penicillin G Units per mg
Penicillin G Sodium	NLT 1500 and NMT 1750 Penicillin G Units per mg
Penicillin V	NLT 1525 and NMT 1780 Penicillin V Units per mg
Penicillin V Potassium	NLT 1380 and NMT 1610 Penicillin V Units per mg
Polymyxin B Sulfate	NLT 6000 Polymyxin B Units per mg
Sargramostim	5.6 million Sargramostim Units per mg of protein
Streptomycin Sulfate	NLT 650 μg and NMT 850 μg of streptomycin per mg
Thiostrepton	900 Thiostrepton Units per mg
Tobramycin	NLT 900 μg of tobramycin per mg
Trypsin, crystalized	NLT 2500 USP Trypsin Units per mg
Vancomycin	NLT 950 μg vancomycin per mg
Vasopressin	NLT 300 Vasopressin Units per mg
Vitamin A	1 USP Vitamin A Unit equals the biologic activity of 0.3 μg of the all-*trans* isomer of retinol

* Examples taken from the United States Pharmacopeia 31st Rev. National Formulary 26. Rockville, MD: United States Pharmacopeial Convention, 2008;2,3.

- dispensing errors can occur when a medication order abbreviates the term "units" with a "U" following the number of units, since a poorly written "U" can be mistaken for a zero; e.g., "100U" may be mistaken to be 1000 units.
- Thus, it is good practice to spell out the term "units" when used following the designated number; e.g., "100 units“ or "100 Units."
- Special syringes are available for measuring units of insulin, and the required dosage is then measured in milliliters, or directly in units, depending on the calibration of the syringe.
- **Figure 9.2** shows examples of insulin syringes calibrated in Units.

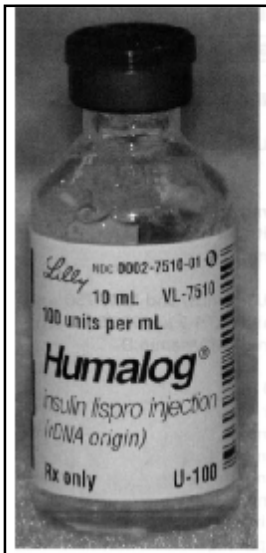

FIGURE 9.1 Example of a pharmaceutical product standardized in units of activity.

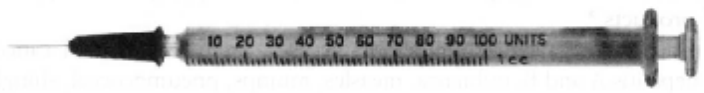

FIGURE 9.2 Example of an insulin syringe calibrated in Units. *(Courtesy of Becton, Dickinson and Company.)*

- Blood or blood serum levels of certain drugs may be expressed in the literature as "mU/mL," meaning milliunits of the agent per milliliter of blood or blood serum.
- Biologies:
  - are preparations produced from a living source.
    1. vaccines, toxoids, and immune sera, used for the development of immunity or resistance to disease;
    2. certain antitoxins and antivenins, used as treatment against specific antigens;
    3. toxins and skin antigens, used as diagnostic aids.
  - are prepared from human serum (e.g., immune globulin), horse serum (e.g., tetanus antitoxin), chick cell culture (e.g., measles virus vaccine).

- The strengths of the various biologic products are expressed in a number of ways.
  - a bacterial vaccine: micrograms (μg) or units of antigen per milliliter.
  - a viral vaccine: the tissue culture infectious dose (TCID50), which is the quantity of virus estimated to infect 50% of inoculated cultures.
  - Viral vaccines : units, micrograms of antigen, or number or organisms per milliliter.
  - a toxoid: flocculating units (Lf), 1 (one) Lf having the capacity to flocculate or precipitate one unit of standard antitoxin.
  - many immune sera and diagnostic antigens: Units of activity.

Calculating the amount of a drug or preparation equivalent to a dose expressed in units

- ***How many milliliters of U-100 insulin should be used to obtain 40 units of insulin?***

  U-100 insulin contains 100 units/mL

$$\frac{100(units)}{40(units)} = \frac{1(mL)}{x(mL)}, \quad x = 0.4\,mL, answer.$$

Or, solving by dimensional analysis:

$$40\,units \times \frac{1\,mL}{100\,units} = 0.4\,mL, answer.$$

A physician prescribed 100 units of insulin to be added to 500 mL of D5W in treating a patient with severe diabetic acidosis. How many milliliters of insulin injection concentrate, U-500, should be used?

- U-500 insulin contains 500 units/mL

$$\frac{500(units)}{100(units)} = \frac{1(mL)}{x(mL)}, \quad x = 0.2\,mL, answer.$$

Or, solving by dimensional analysis:

$$100\,units \times \frac{1\,mL}{500\,units} = 0.2\,mL, answer.$$

How many milliliters of a heparin sodium injection containing 200,000 units in 10 mL should be used to obtain 5,000 heparin sodium units that are to be added to an intravenous dextrose solution?

$$\frac{200,000(units)}{5,000(units)} = \frac{10(mL)}{x(mL)}, \quad x = 0.25mL, answer.$$

Calculating the equivalency of an antibiotic based on "µg" activity per milligram

- ***If neomycin sulfate has a potency of 600 µg of neomycin per milligram, how many milligrams of neomycin sulfate would be equivalent in potency to 1 mg of neomycin?***

$$\frac{600(ug\ of\ neomycin)}{1000(ug\ of\ neomycin)} = \frac{1(mg\ of\ neomycin\ sulfate)}{x(mg\ of\ neomycin\ sulfate)}$$

$$x = 1.67\,mg, answer.$$

Calculating the dose or antigen content of a biologic based on potency

- ***A biologic contains 50 Lf Units of diphtheria toxoid in each 2.5 mL of product. If a pediatric patient is to receive 10 Lf Units, how many milliliters of product should be administered?***

$$\frac{50(Lf\ Units)}{10(Lf\ Units)} = \frac{2.5(mL)}{x(mL)}$$

$$x = 0.5\,mg, answer.$$

- ***Measles Virus Vaccine Live is prepared to contain 1000 TClD50 per 0.5-mL dose. What is the TCID50 content of a 50-mL multiple dose vial of the vaccine?***

$$\frac{1000(TCID_{50})}{x(TCID_{50})} = \frac{0.5(mL)}{50(mL)}$$

$$x = 100{,}000\,TCID_{50}, answer.$$