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# ⟨1176⟩ PRESCRIPTION BALANCES AND VOLUMETRIC APPARATUS USED IN COMPOUNDING





## 1. BALANCES

Pharmacies that perform materials measurements for compounding and dispensing should have access to a well-maintained National Institute of Standards and Technology (NIST) Class III torsion prescription balance or superior balance (preferably an electronic balance) to weigh masses accurately. The pharmacy should have a set of calibration weights, or the balance should have internal calibration capability to standardize the precision and accuracy of the balance.

For more information regarding standards for weights and balances, see *Balances* ⟨41⟩. The standards in NIST Handbook 44 called "Specifications, Tolerances, and Other Technical Requirements for Weighing and Measuring Devices" may also be useful to compounders.[1] Some balances offer digital or direct-reading features and printing capabilities, which may be desirable for ease of use. All balances should be calibrated or verified and tested frequently using appropriate test weights.

### 1.1 Mechanical Prescription Balances

A Class III (formerly Class A) prescription balance is a device designed to accurately weigh drugs and other substances and materials required in pharmaceutical compounding and dispensing practice.[1] It is constructed to support its full weighing capacity without developing undue stresses, and its adjustment is not altered by repeated weighing of the capacity load. The removable pans or weighing vessels should be of equal weight and shape. The balance should have leveling feet or screws and a built-in means to observe its level. The balance may feature dial-in weights and also a precision spring and dial instead of a weighbeam. A balance that has a graduated weighbeam must have a stop that halts the rider or poise at the zero reading, and the reading edge of the rider must be parallel to the graduations on the weighbeam. The distance from the face of the index plate to the indicator pointer or pointers should be NMT 1.0 mm; the points should be sharp; and when there are two pointers, the ends should be separated by NMT 1.0 mm when the scale is in balance. The indicating components and the lever system should be protected against drafts; the balance lid should permit free movement of the loaded weighing pans when the lid is closed; and the balance must have a mechanical arresting device.

#### BALANCE TESTING PROCEDURE

A Class III prescription balance meets the criteria in the following four tests using an ANSI/ASTM E617 set of Class 6 or better test weights. A typical apothecary weight set contains weights ranging from 10 mg to 50 g in sizes of 10 mg, 20 mg, 50 mg, 100 mg, 200 mg, 500 mg, 1 g, 2 g, 5 g, 10 g, 20 g, and 50 g.

Four tests are required to evaluate the suitability of a Class III prescription balance. A balance is acceptable if it passes all four tests. If the balance fails any test, it should not be used until it has been repaired to meet specifications and retested. The four tests are:

1. Sensitivity requirement
2. Arm ratio test

3. Shift test
4. Rider and graduated beam

**Sensitivity requirement test:** The following requirements are based on (1) the NIST standard that a 6-mg load must displace the pointer 2 mm,[1] and (2) the absence of a 6-mg weight in a typical apothecary weight set.

1. For balances with pointer scale division marks 2 mm apart, a 10-mg weight on one pan and no weight on the other pan, dial, or rider beam of a leveled balance should displace the pointer 1.5-scale division marks, or approximately 6.7 mg/mark, as observed visually. This same 1.5-scale division mark displacement shall be observed with a 10-g weight on one pan and 10-g plus 10-mg weights on the other pan of a level balance.
2. For balances on which the pointer scale division marks are 1 mm apart, a 10-mg weight on one pan and no weight on the other pan, dial, or rider beam of a leveled balance should displace the pointer 3-scale division marks, or approximately 6.7 mg/two marks, as observed visually. This same 3-scale division marks displacement shall be observed with a 10-g weight on one pan and 10-g plus 10-mg weights on the other pan of a level balance.
3. NLT 0.12 g (120 mg) shall be weighed on a Class III prescription to reduce reading errors of less than one mark and two marks in cases (a) and (b), respectfully, to NMT 5% weighing error.

When a balance has been observed or suspected to have been moved, unleveled, contaminated, or otherwise damaged, misaligned, or misused, then its sensitivity must be tested and confirmed to be accurate.

**Arm ratio test:** The arm ratio test will determine whether both arms of the balance are of equal length.

1. Level the balance.
2. With the pans empty, adjust the balance until the pointer is in the middle of the marker plate.
3. Place a 30-g weight in the center of each pan.
4. When the balance comes to rest, record the rest point.
5. If the rest point has changed from the middle of the marker plate, place a 30-mg weight on the lighter side.
6. When the balance comes to rest, this new rest point should either return to or go farther than the middle of the marker plate.

**Shift test:** The shift test checks the mechanics of the arm and lever components of the balance.

1. Level the balance.
2. With the pans empty, adjust the balance until the pointer is in the middle of the marker plate.
3. Place a 10-g weight in the center of the left pan and place another 10-g weight successively toward the right, left, front, and back side of the right pan, noting the rest point in each case.
4. In any case where the rest point has changed from the center of the marker plate, add a 10-mg weight to the lighter side.
5. When the balance comes to rest, this new rest point either should return to or go farther than the middle of the marker plate.
6. Level the balance and adjust the balance until the pointer is in the middle of the marker plate.
7. Repeat the procedure with the 10-g weight in the center of the right pan, and vary the position of the 10-g weight on the left pan.
8. Level the balance and adjust the balance until the pointer is in the middle of the marker plate. Make several observations in which both 10-g weights are shifted simultaneously to off-center positions on their pans (i.e., both toward the inside, both toward the outside, one front and the other back). In any case where the rest point is shifted from the middle of the marker plate, the addition of a 10-mg weight on the lighter side should equalize or overcome the shift.

**Rider and graduated beam test:** The rider and graduated beam test checks the accuracy of the calibrated dial or rider on the balance.

1. Level the balance.
2. With the pans empty, adjust the balance until the pointer is in the middle of the index plate.
3. Place a 500-mg weight on the left pan and move the dial or rider to the 500-mg point.
4. When the balance comes to rest, record the rest point.
5. If the rest point has changed from the middle of the index plate, place a 10-mg weight on the lighter side.
6. When the balance comes to rest, this new rest point should either return to or go farther than the middle of the index plate.
7. Follow the same procedure using a 1-g weight on the left pan and the dial or rider on the 1-g point. If the new rest point is shifted from the middle of the index plate, a 10-mg weight to the lighter side should equalize or overcome the shift.

### 1.2 Electronic Balances

A typical electronic prescription balance is an instrument that provides essential readability for materials weighed within the range of capacities for the balance. The display should have prompts to guide users through the balance function, as well as an output port for printing if necessary. Most balances sold for prescription compounding meet or exceed Class I or II accuracy requirements according to NIST Handbook 44 and come with certificates issued under the National Type Evaluation Program (NTEP) of the National Conference on Weights and Measures.

Calibration/certification of the balance should be performed according to the standard operating procedures of the facility. Many electronic balances contain internal calibration programs that automatically calibrate the balance daily. If there is no internal calibration feature, external calibration may be conducted using a calibration weight, according to the procedure supplied by the manufacturer. Weights for use in calibrating an electronic balance should be kept in a special rigid and compartmentalized box and handled with plastic or plastic-tipped forceps, or gloves that are provided with the weights, to prevent scratching or soiling. These calibration weights should meet or exceed ASTM Class 1 criteria. In addition, there are companies that offer calibration services to certify that the balance is performing adequately. For more information regarding the use of electronic balances, see ⟨41⟩ and *Weighing on an Analytical Balance* ⟨1251⟩.

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### 1.3 Minimum Accurately Weighable Quantity on the Balance

The minimum accurately weighable quantity (MAWQ) is the smallest weight or mass that will produce no greater than a predetermined fraction of error on a properly calibrated, situated, and operated balance. The predetermined weighing error is assigned based on either a professional standard (such as NMT 0.05 or 5% error in the weight of any prescription ingredient) or scientific rigor, for example, NMT 0.005 or 0.5% error in the weight of an ingredient that is in limited supply. The compounder should use professional judgment when assigning the acceptable error for each process.

The formula for determining MAWQ for a typical Class III torsion balance is:

MAWQ = Sensitivity requirement/Acceptable error

Example: Calculate the MAWQ for a Class III torsion balance with a sensitivity requirement of 6 mg and an acceptable error of 5% or 0.05.

MAWQ = 6 mg/0.05 = 120 mg

For electronic balances, the MAWQ is calculated using the linearity or the absolute error over the range of the balance. This value is provided by the balance manufacturer. Note that the balance linearity and the readability of the smallest mass unit may not be the same.

Example: Calculate the MAWQ for an electronic balance with a linearity of 0.002 g and an acceptable error of 5% or 0.05.

MAWQ = 0.002 g/0.05 = 0.04 g or 40 mg

▲The MAWQ equation in this section should be used if the linearity of an electronic balance is known. If the linearity of an electronic balance is not known, the minimum weight of an analytical balance equation described in *Weighing on an Analytical Balance ⟨1251⟩, Qualification, Minimum Weight* should be used and verified at regular intervals as described in the facility's standard operating procedures (SOPs) or at least annually and after any repairs.▲ (USP 1-May-2019)

## 2. VOLUMETRIC APPARATUS

An assortment of appropriate volumetric devices should be available to accurately measure fluids and liquids of different volumes and densities. Pharmaceutical devices approved for measuring volumes of liquids, including burets, pipets, and cylindrical graduates marked in metric or metric and apothecary units, are to meet the standard specifications for glass volumetric apparatus described in "Specifications and Tolerances for Reference Standards and Field Standard Weights and Measures, 2. Specifications and Tolerances for Field Standard Measuring Flasks".[2] Conical graduates are to meet the standard specifications described in NIST Handbook 44.[1] There are ASTM standards (ASTM E542) for the calibration of laboratory volumetric apparatus that may be useful to compounders as well.[3]

### 2.1 Selection and Use of Graduates

CAPACITY

The capacity of a cylindrical graduate is the volume at the maximum graduation mark at the specified temperature. Volumes for prescription compounding and dispensing that are measured in cylindrical graduates should be adequate to not exceed 5% error.

CYLINDRICAL AND CONICAL GRADUATES

The error in a measured volume caused by a deviation of ±1 mm in reading the lower meniscus in a graduated cylinder remains constant along the height of the uniform column. The same deviation of ±1 mm causes a progressively larger error in a conical graduate, the extent of the error being further dependent upon the angle of the flared sides to the perpendicular of the upright graduate. A deviation of ±1 mm in the meniscus reading causes an error of approximately 0.5 mL in the measured volume at any mark on the uniform 100-mL cylinder graduate. The same deviation of ±1 mm can cause an error of 1.8 mL at the 100-mL mark on an acceptable conical graduate marked for 125 mL.

A general rule for selection of a graduate for use is to use 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 errors, because the larger diameter increases the volume error in a deviation of ±1 mm from the mark. The relation of the volume error to the internal diameters of graduated cylinders is based on the equation:

$$V = \pi r^2 h$$

$V$ = volume

$r$ = radius

$h$ = height

An acceptable 10-mL cylinder having an internal diameter of 1.18 cm holds 109 µL in 1 mm of the column. Reading 4.5 mL in this graduate with a deviation of ±1 mm from the mark causes an error of about ±2.5%, and the same deviation in a volume of 2.2 mL in the same graduate causes an error of about ±5%. *Table 1* shows the accuracy limits for cylindrical graduates.

**Table 1. Tolerance or Accuracy Limits for Class A Cylindrical Graduates[a]**

| Capacity (mL) | Smallest Graduation Mark Interval (mL) | Tolerance (±mL)[b] | Minimum Volume for 5% Error (mL)[c] |
|---|---|---|---|
| 5 | 0.1 | 0.05 | 1.0 |
| 10 | 0.1 or 0.2 | 0.10 | 2.0 |
| 25 | 0.2 or 0.5 | 0.17 | 3.4 |
| 50 | 1 | 0.25 | 5.0 |
| 100 | 1 | 0.50 | 10.0 |
| 250 | 2 | 1.00 | 20.0 |
| 500 | 5 | 2.00 | 40.0 |
| 1000 | 10 | 3.00 | 60.0 |
| 2000 | 20 | 6.00 | 120.0 |
| 4000 | 50 | 14.50 | 290.0 |

[a] Adapted from ASTM E1272-02. Standard specification for laboratory glass graduated cylinders. West Conshohocken, PA: ASTM International; 2012. www.astm.org. Some brands exceed the ASTM limits; for example, one source of a Class A 10-mL graduate lists the tolerance as ±0.08 mL.

[b] The constant volume error in each measurement.

[c] The minimum volume for *N*% error = [Tolerance (mL) × 100]/*N* (%); e.g., for *N* = 5% for a 10-mL graduate, the minimum volume is 2.0 mL. [The minimum volume for 5% error = (0.1 mL × 100)/5 = 2.0.]

There is an inverse relationship between the temperature and density of liquids. For compounding and dispensing purposes, deviations will be negligible when volume measurements are performed at temperatures NMT 5° from that specified on the particular cylindrical graduate, which is usually 20°. For example, the densities in g/mL of water, ethanol, and glycerin vary, respectively, from 0.999 to 0.997, 0.791 to 0.785, and 1.265 to 1.262 over the temperature range of 15°–25°. The accuracy of each cylindrical graduate used in pharmacy practice is recommended to be verified as follows, at a measuring temperature of 20°–25° with the assumption that deviations follow a normal or Gaussian distribution:

1. Tare a clean, dry graduate on a properly calibrated balance of adequate capacity, linearity, and readability for the volumes to be measured.
2. Fill the tared, dry graduate identically five or more times on a level surface to the smallest, a mid-range, and the maximum capacity graduation marks with *Purified Water* or deionized water, precluding and wiping spills and splashes from the exterior and interior above the target fill line.
3. Record the weight of each filling.
4. Calculate the mean weight of each set of fillings.
5. Calculate the percent deviation of each weight from the theoretical weight as follows:

$$\text{Percent deviation weight} = \{[\text{Actual weight} - (\text{intended volume} \times 0.9975)]/(\text{Intended volume} \times 0.9975)\} \times 100\%$$

6. Calculate the percent mean deviation weight as follows:

$$\text{Percent mean deviation weight} = \{[\text{Mean actual weight} - (\text{intended volume} \times 0.9975)]/(\text{Intended volume} \times 0.9975)\} \times 100\%$$

Deviations for cylindrical graduates used in compounding and dispensing should not exceed 5.0% for individual weights or 2.5% for mean weights of the corresponding volumes of *Purified Water*. *Table 1* and *Table 2* show that a wider range of volumes can be measured in Class A cylindrical graduates compared to Class B. According to ASTM standards, Class A cylindrical graduates must be marked with the letter “A” to designate compliance with applicable construction and accuracy requirements. Class B cylindrical graduates are the same basic design as Class A cylindrical graduates and are considered to be for general purpose use. However, volumetric tolerances may be up to twice the allowable range for Class A cylindrical graduates.

**Table 2. Tolerance or Accuracy Limits for Class B Cylindrical Graduates[a]**

| Capacity (mL) | Smallest Graduation Mark Interval (mL) | Tolerance (±mL)[b] | Minimum Volume for 5% Error (mL)[c] |
|---|---|---|---|
| 5 | 0.1 | 0.10 | 2.0 |
| 10 | 0.1 or 0.2 | 0.2 | 4.0 |
| 25 | 0.2 or 0.5 | 0.34 | 6.8 |
| 50 | 1 | 0.50 | 10.0 |
| 100 | 1 | 1.00 | 20.0 |
| 250 | 2 | 2.00 | 40.0 |
| 500 | 5 | 4.00 | 80.0 |
| 1000 | 10 | 6.00 | 120.0 |
| 2000 | 20 | 12.00 | 240.0 |
| 4000 | 50 | 29.00 | 580.0 |

[a] Adapted from ASTM E1272-02. Standard specification for laboratory glass graduated cylinders. West Conshohocken, PA: ASTM International; 2012. www.astm.org.

[b] The constant volume error in each measurement.

[c] The minimum volume for *N*% error = [Tolerance (mL) × 100]/*N* (%); e.g. for *N* = 5% for a 5-mL graduate, the minimum volume is 2.0 mL. [The minimum volume for 5% error = (0.1 mL × 100)/5 = 2.0.]

### 2.2 Medicine Droppers

Medicine droppers meet the specifications in *Packaging and Storage Requirements* ⟨659⟩. Medicine droppers should be used only for qualitative purposes, such as pH adjustment with an acid, alkali, or buffer, and visual identification testing with reagents. Medicine droppers are not approved for volumetric measurements for compounding. Calibrated medicine droppers have markings to guide delivery of the prescribed quantity of medication. Their purpose should be limited to the measurement of a dose for administration.

### 2.3 Dispensing Bottles

Some dispensing bottles may be supplied by the manufacturer as part of the packaging, whereas others may be selected and supplied by the pharmacist. These containers are not necessarily accurately calibrated and should not be used for measurement during compounding and dispensing unless they are appropriately calibrated by the compounder.

### 2.4 Syringes

Syringes are available in a variety of sizes with calibrated increments used for measuring and may be used to accurately measure and deliver a wide range of liquid volumes. For viscous liquids, measurements made with syringes are usually more accurate than those made with cylindrical graduates.

#### ORAL SYRINGES

Oral syringes are available as a device for accurately providing a dose of liquid medication to a patient. The performance of the syringes may be user dependent. For this reason, it is important that suitable operating procedures are documented and followed, and that operators are specifically trained in the correct use of the instruments. Users should be cautious about relying on manufacturers' performance figures. It is more appropriate to perform calibration, taking into account the variation between different users. Oral syringes provide an improvement in dosing accuracy for viscous medications, compared with medication droppers.

#### SYRINGE CALIBRATION

Syringe calibration is based on the gravimetric determination of the quantity of water either contained or delivered, and the conversion of this value to true volume at the standard temperature of 20°. At 80% of the nominal syringe volume, 5–10 measurements should be performed.

Calibration procedure:

1. Aspirate and dispense an exact volume of deionized water that is 80% of the nominal syringe volume.
2. Determine the mass of the dispensed water.
3. Calculate the volume of the dispensed water using mass and density.
4. Document the measurement values.
5. Calculate the accuracy (*R*).

Calibration formula:

$$\text{Accuracy } (R) = [(\text{Average value} - \text{target value})/\text{Target value}] \times 100$$

### 2.5 Pipets

Pipets are thin glass tubes used to deliver volumes <25 mL. The two types of pipets are the single-volume pipet and the calibrated pipet. The single-volume pipet is the most accurate and the simplest to use, but the single-volume pipet is limited to the measurement of a single fixed volume; it is not capable of partial volume measurements.

The calibrated pipet has graduation marks from a point near the tip of the pipet to the capacity of the pipet. In addition to delivering its entire contents, the calibrated pipet can be used to deliver partial volumes with good volumetric precision.

Micropipets generally are used when very small volumes (<1 mL) are required; micropipets are available in a variety of sizes. Each micropipet can be adjusted, usually by turning a dial, to deliver a volume within a limited range. For example, one micropipet may deliver volumes of 0–20 µL, another delivers 0–100 µL, and yet another delivers 0–1000 µL. The pipet selected should provide the greatest accuracy for the volume to be measured. Pipets should be calibrated/certified periodically as specified in the facility's standard operating procedures. Calibrating micropipets is a very specialized process that requires adequate training and appropriate equipment. There are companies that offer contract calibration services to certify that pipets are performing correctly.

### 2.6 Volumetric Flasks

Volumetric flasks have a slender neck and wide, bulb-like base. They are single-volume glassware and come in a variety of sizes. Only one calibration mark is etched on the neck of the flask. When the flask is filled to that mark, the flask contains the volume indicated on the flask. Volumetric flasks are difficult to use if dissolving solids in liquid because of the narrowness of the neck. If solids are to be dissolved, the flask should be partially filled with liquid, the solid material added and completely dissolved, and then the flask should be filled to the calibration mark.

### 2.7 Additional Considerations When Using Volumetric Apparatus

The use of volumetric apparatus requires some working knowledge of viscosity, density, surface tension, and adhesion. Each of these properties may affect measurement accuracy. For example, higher-viscosity liquids will be drawn into the vessel at a slower rate, and the operator should allow time for complete filling. Delivery can also be slow, because higher-viscosity fluids travel through the orifice at a slower rate. Density can affect filling and emptying in a manner similar to viscosity. In addition, liquids with very low surface tension may tend to “crawl up” the vessel wall or leak from the tip of a syringe or pipet. Adhesion can affect accuracy by resulting in a slow rate of vessel emptying. The operator should confirm that all of the liquid has been drained from the vessel if performing a quantitative transfer.

Understanding the terms “To Contain (TC)” and “To Deliver (TD)” is important, because they apply to glassware. TC and TD glassware consists of vessels that range from 1 to about 100 mL and are individually marked to indicate whether they are TC or TD vessels. A TC vessel is designed to deliver the entire measured content of the operation, and it may require forced air to expel the final quantity. A TD vessel is designed to deliver the entire measured amount via gravity flow.

## GLOSSARY

**Accuracy:**

The closeness of the displayed weight, as measured by the balance, to the true weight, as known by the use of a calibration weight or weights.

**Balance indicator:**

A combination of elements, one or both of which will oscillate with respect to the other, to indicate the equilibrium state of the balance during weighing.

**Capacity:**

Maximum weight, including the weight of tares to be placed on one pan. The nominal capacity of a prescription scale (Class III prescription balance) is assumed to be one-half apothecary ounce (15.55 g), unless otherwise marked.

[Note—This is applicable only to scales not marked with an accuracy class. Past and currently available Class III prescription balances typically have a capacity of either 60 or 120 g and bear a label stating such.]

**Linearity:**

The ability to maintain the same sensitivity over the entire weighing range of the balance. This is the constant weighing error in every amount weighed within the capacity range of the balance. This term is used only with electronic balances. Analogous terms are “absolute error” or “linear accuracy”. The linearity is determined by the balance manufacturer.

**Minimum accurately weighable quantity (MAWQ):**

The smallest weight or mass that will produce no greater than a predetermined fraction of error on a properly calibrated, situated, and operated balance.

**Precision:**

The reproducibility of the weighing measurement as expressed by a standard deviation. A similar term, “repeatability”, is sometimes used in specifications for electronic balances.

**Readability:**

The smallest division at which the balance increments.

**Repeatability:**

An instrument's ability to consistently deliver the same weight reading for a given object, and to return to a zero reading after each weighing cycle. This is tested by repeatedly weighing the same test weight.

**Rest point:**

The point on the index plate at which the indicator or pointer stops when the oscillations of the balance cease, or the index plate position of the indicator or pointer calculated from recorded consecutive oscillations in both directions past the zero of the index plate scale. If the balance has a two-pointer indicating mechanism, the position or the oscillations of only one of the pointers need to be recorded or used to determine the rest point.

**Sensitivity requirements (SR):**

The maximum change in load that will cause a specified change, such as a particular quantity of pointer scale division marks, of the pointer or indicating component of the balance.

**Tare bar:**

An auxiliary ungraduated weighbeam bar with a movable poise. It can be used to correct for variations in weighing glasses or papers.

**Weighbeam** or **Beam:**

A graduated bar equipped with a movable poise or rider. Metric graduations are in 0.01-g increments up to a maximum of 1.0 g.

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[1] NIST Handbook 44 (2015) Specifications, Tolerances, and Other Technical Requirements for Weighing and Measuring Devices. Section 2.2.0 Scales (http://www.nist.gov/pml/wmd/pubs/h44-11.cfm).

[2] Harris GL. Specifications and tolerances for reference standards and field standard weights and measures. 2. Specifications and tolerances for field standard measuring flasks. 1996. NTIS Order Number: PB96-178926. National Technical Information Service, Alexandria, Virginia 22312 (http://www.ntis.gov).

[3] ASTM E542-01. Standard practice for calibration of laboratory volumetric apparatus. West Conshohocken, PA: ASTM International; 2012. www.astm.org.

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