Stage 4 Harmonization
Official: August 1, 2025

⟨699⟩ DENSITY OF SOLIDS

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▲Portions of the chapter text that are national *USP* text, and are not part of the harmonized text, are marked with symbols (♦) to specify this fact.

The density of solids corresponds to their average mass per unit volume and typically is expressed in grams per cubic centimeter (g/cm^3).

Unlike gases and liquids whose density depends only on temperature and pressure, the density of a solid also depends on molecular packing (polymorphism, degree of crystallinity) and porosity. Solid density could further depend upon the history of preparation, treatment, and storage if the solid is partially crystalline or partially amorphous. Therefore, the densities of two chemically equivalent solids may be intrinsically different and this difference reflects a difference in solid-state structure, which may include voids that are considered part of the solid material.

The density of solids may be expressed differently, depending on the criteria used to define the volume occupied by the solid material:

- The *material density* is based on the solid volume of the material excluding any voids.
- The *particle density* includes the solid volume of the material together with the void volume of intraparticulate pores.
- The *bulk density* includes the solid volume of the material, the intraparticulate and interparticulate voids within the powder bed; hence, the bulk density depends on the particle density and the spatial arrangement of particles in the powder bed and thus on the degree of powder consolidation.

Note that the term "true density" is also commonly used in the literature but its usage is quite inconsistent (for example, sometimes reflecting the density measured by gas pycnometry and sometimes being defined as the density for crystalline samples only). For this reason, the term "true density" is not used in this general chapter.

The following density terms relate to various experimental techniques used to determine the density of solids:

- The *crystal density* is an intrinsic property of a specified crystal structure of a substance and is best calculated from crystallographic data (volume and composition of the unit cell) commonly determined by X-ray diffraction. In some of the materials, the unit cell may include voids, such as open channels, as part of the crystal structure.
- The *gas pycnometric density* is determined by measuring the volume occupied by a known mass of solid, which is equivalent to the volume of gas displaced by the solid using a gas displacement pycnometer (see *Gas Pycnometry for the Measurement of Density*). In gas pycnometric density measurements, the volume determined excludes the volume occupied by open pores; but includes the volume occupied by sealed pores or pores inaccessible to the gas. Due to the small molecular size of helium, which is the preferred choice of gas, most open pores are accessible to the gas. Therefore, the gas pycnometric density of a powder is often not very different from the material density. This density is often the best approximation of the material density of an amorphous or partially crystalline sample and it is therefore widely used for pharmaceutical powder samples. This procedure is, however, not suitable for solids that release gas due to sublimation, desolvation, or desorption (such as sorbed water) when exposed to gas.
- The *mercury porosimeter density*, sometimes called the *granular density*, is determined by measuring the volume occupied by the solid, the sealed pores, and any pores inaccessible to mercury (see *Porosimetry by Mercury Intrusion* ⟨267⟩). The poresize limit or minimal access diameter depends on the maximal mercury intrusion pressure applied during the measurement, and under normal operating pressures, the mercury does not penetrate the finest pores that are accessible to helium. Various granular densities can be obtained from one sample as, for each applied mercury intrusion pressure, a density can be determined that corresponds to the poresize limit at that pressure.
- The *untapped bulk density* (minimum consolidation) of a powder is determined by measuring the volume of a known mass of powder sample, which may have been passed through a sieve, in a graduated cylinder. Alternatively, it can be determined by measuring the mass of known volume of powder sample that has been passed through a volumeter into a cup or measuring vessel.

The untapped bulk density and the tapped bulk density are determined as described in *Bulk Density of Powders* ⟨616⟩.▲ (USP 1-Aug-2025)

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▲♦▲ (USP 1-AUG-2025)GAS PYCNOMETRY FOR THE MEASUREMENT OF DENSITY

Gas pycnometry is a convenient and suitable method for the measurement of the density of powder particles. A simple schematic of one type of gas pycnometer is shown in *Figure 1*.

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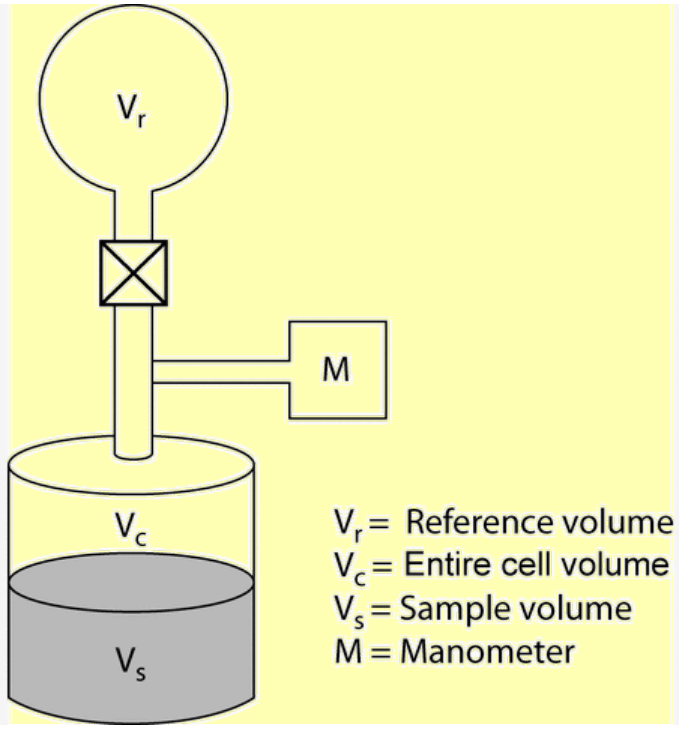

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Figure 1. Schematic of gas pycnometer.

▲ (USP 1-Aug-2025)

The sample, with mass *w* and volume V_s, is placed inside a sealed test cell with an empty cell volume of V_c. The system reference pressure, P_r, is determined at the manometer while the valve that connects the reference volume with the test cell is open. The valve is closed to separate the reference volume, V_r, from the test cell. The test cell is pressurized with the measurement gas to an initial pressure, P_i. Then the valve is opened to connect the reference volume, V_r, with the test cell, and the pressure drops to the final pressure, P_f. If the measurement gas behaves ideally under the conditions of measurement, the sample volume, V_s, is given by the following expression:

$$V_s = V_c - \frac{V_r}{\left[\frac{P_i - P_r}{P_f - P_r}\right] - 1} \quad (1)$$

The density, ρ, is given by the equation:

$$\rho = \frac{w}{V_s} \quad (2)$$

Details of the instrumental design may differ, but all gas pycnometers rely on the measurement of pressure changes as a reference volume is added to, or deleted from, the test cell.

The measured density is a volume-weighted average of the densities of individual powder particles. The density will be in error if the test gas sorbs onto the powder or if volatile contaminants are evolved from the powder during the measurement. Sorption is prevented by an appropriate choice of test gas. Helium is the common choice. Volatile contaminants in the powder are removed by degassing the powder under a constant purge of helium prior to the measurement. Occasionally, powders may have to be degassed under vacuum. Two consecutive readings should yield sample volumes that are equal within 0.2% if volatile contaminants are not interfering with the measurements. Because volatiles may be evolved during the measurement, the weight of the sample should be taken after the pycnometric measurement of volume.

Method

Ensure that the reference volume and the calibration volume have been determined for the gas pycnometer by an appropriate calibration procedure. The test gas is helium, unless another gas is specified in the individual monograph. The temperature of the gas pycnometer should be between 15° and 30° and should not vary by more than 2° during the course of the measurement. Load the test cell with the substance under examination that has been prepared according to the individual monograph. Where ⟨699D⟩ is indicated, dry the substance under examination as directed for *Loss on Drying* in the monograph unless other drying conditions are specified in the monograph *Density of Solids* test. Where ⟨699U⟩ is indicated, the substance under examination is used without drying. Use a quantity of powder recommended in the operating manual for the pycnometer. Seal the test cell in the pycnometer, and purge the pycnometer system with the test gas according to the procedure given in the manufacturer's operating instructions. If the sample must be degassed under vacuum, follow the recommendations in the individual monographs and the instructions in the operating manual for the pycnometer.

The measurement sequence above describes the procedure for the gas pycnometer shown in *Figure 1*. If the pycnometer differs in operation or in construction from the one shown in *Figure 1*, follow the operating procedure given in the manual for the pycnometer.

Repeat the measurement sequence for the same powder sample until consecutive measurements of the sample volume, V_s, agree to within 0.2%. Unload the test cell and measure the final powder weight, *w*. Calculate the pycnometric density, ρ, of the sample according to *Equation*

2.▲ (USP 1-Aug-2025)

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