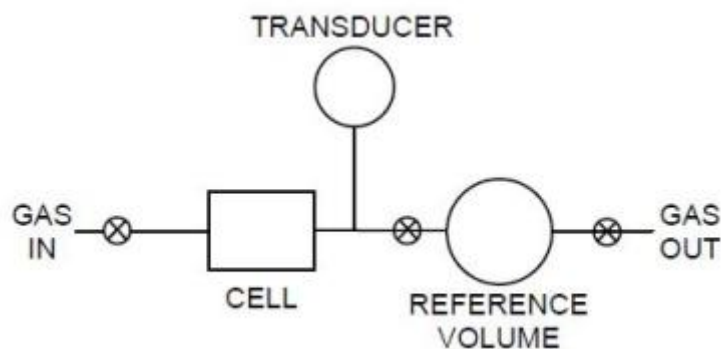


## Helium Pycnometry

### Overview

Gas pycnometry is a technique used to measure the apparent density of particles in a powder. A sample of known mass is placed in one of two chambers of known volume, maintained at a constant temperature. Helium is then added to the system. The resulting equilibrium pressures are used in conjunction with the ideal gas law to determine the apparent density of the particles.



**Figure 1: Schematic of helium pycnometry method**

### ASTM Standard Testing Procedure

ASTM B923-10: Standard Test Method for Metal Powder Skeletal Density by Helium or Nitrogen Pycnometry describes the basic procedure for performing an apparent density measurement on metal powders using helium pycnometry. These specifications can be extended for use with pharmaceutical excipients. Though the basic procedure is outlined in this document, specific operation may vary depending on the equipment used.

### Test Specimen

The ASTM standard does not give any specifications on the size of the sample. However, care should be taken with sampling to ensure that the test specimen is representative of the bulk material.

### Procedure

1. Weigh sample cup
2. Add sample to cup
  - a. Ensure that enough material is used to satisfy the requirements of the equipment.
3. Weigh the filled cup, and determine the mass of the sample.
4. Place sample in pycnometer chamber.
5. Input process parameters as required by the equipment.
6. Specific operation of the equipment will vary with the manufacturer.
  - a. ASTM B923-10 requires that a minimum of 5 skeletal volume measurements be made on each sample.
7. The method of obtaining results depends on the equipment used. For some equipment, the resulting skeletal density and skeletal volume are output automatically.

*Results Report*

The report of the results should contain the following information, as defined by ASTM B923-10:

1. Sample ID
2. Measured skeletal volume and associated statistics
3. Calculated skeletal densities
4. Sample mass
5. Gas used
6. Outgassing method

***USP-NF Standard Testing Procedure***

Chapter <699> of USP32-NF27 provides a description of the testing method for the measurement of the apparent density of a powder by the gas pycnometry method. While this standard does not provide a specific testing procedure, it does specify requirements for operating parameters and the selection of a dispersant fluid. These requirements are as follows.

1. Utilize an appropriate method to calibrate the test chamber.
2. The surrounding temperature should be maintained between 15 and 30 °C ± 2 °C during testing.
3. If appropriate, the specimen may need to be dried prior to testing.
4. The sample size should be selected based on the requirements of the equipment used.
5. Repeat the measurement sequence until the results for the volume, V<sub>s</sub>, of the sample agree to within 0.2%.
6. The final mass of the sample, w, should be measured and the apparent density of the sample calculated as:

$$\rho = \frac{w}{V_s}$$

**Test Methods: Pros and Cons**

<b>Test Method</b>	<b>Pros</b>	<b>Cons</b>
Helium pycnometry	<ol style="list-style-type: none"><li>1. Small sample size</li><li>2. Reproducible, not operator dependent</li></ol>	