properties. Open pores are connected to the external surface and are therefore accessible to fluids, depending on the pore nature/size and the nature of fluid. Open pores can be further divided in dead-end or interconnected pores. Further classification is related to the pore shape, whenever is possible to determine it. The characterization of solids in terms of porosity consists in determining the following parameters:

- **Pore size:** Pore dimensions cover a very wide range. Pores are classified according to three main groups depending on the access size.
  - Micropores: less than 2 nm diameter
  - Mesopores: between 2 and 50 nm diameter
  - Macropores: larger than 50 nm diameter
- **Specific pore volume and porosity:** The internal void space in a porous material can be measured. It is generally expressed as a void volume (in cm^3 or mL) divided by a mass unit (g).
- **Pore size distribution:** It is generally represented as the relative abundance of the pore volume (as a percentage or a derivative) as a function of the pore size.
- **Bulk density:** Bulk density (or envelope density) is calculated by the ratio between the dry sample mass and the external sample volume.
- **Percentage porosity:** The percentage porosity is represented by ratio between the total pore volume and the external (envelope) sample volume multiplied by 100.
- **Surface area:** See above for discussion.

LVI. TRUE DENSITY

Density is the ratio of the mass of an object to its volume, and for solids this term describes the arrangement of molecules. The study of compaction of powders is described by the Heckel equation. The densities of molecular crystals can be increased by compression. Information about the true density of a powder can be used to predict whether a compound will cream or sediment in a suspension such as metered dose inhaler (MDI) formulation. Therefore, suspensions of compounds that have a true density less than these figures will cream (rise to the surface), and those that are denser will sediment. It should be noted, however, that the physical stability of a suspension is not merely a function of the true density of the material. The true density is thus a property of the material and is independent of the method of determination. In this respect, the determination of the true density can be determined using three methods: displacement of a liquid, displacement of a gas (pycnometry), or floatation in a liquid. The liquid displacement is tedious and tends to underestimate the true density; displacement of a gas is more accurate but needs relatively expensive instrumentation. As an alternative, the floatation method is simple to use and inexpensive.

Gas pycnometry is probably the most commonly used method in the pharmaceutical industry for measuring true density. Gas pycnometers rely on the measurement of pressure changes, as a reference volume of gas, typically helium, added to, or deleted from, the test cell.

LVII. FLOW AND COMPACTION OF POWDERS

The flow properties of a powder will determine the nature and quantity of excipients needed to prepare a compressed or powder dosage form. This refers mainly to factors such as ability to process the powder through machines. To make a quick evaluation, the compound is compressed using an infrared (IR) press and die under 10 tons of pressure with variable dwell times, and the resulting tablets are tested with regard to their crushing strength after storing the tablets for about 24 hours. If longer dwell times result in higher crushing strength then the material is likely plastic; elastic material will show capping at low dwell times; the brittle material will not show any effect of dwell times. It is recommended that the compressed tablets be subject to XPRD to record any changes in the polymorphic forms.

There appears to be a relationship between indentation hardness and the molecular structure of organic materials. However, a prerequisite for predicting indentation hardness is knowledge of the crystal structure. As a result, highly sophisticated, computational methods and extensive crystallography libraries have recently become available to study the. For example, the Pfizer Research relies on the The Cambridge Structural Database (http://www.ccdc.cam.ac.uk/), the world repository of small molecule crystal structures. The Cambridge Structural Database (CSD) is the principal product of the CCDC. It is the central focus of the CSD System, which also comprises software for database access, structure visualization and data analysis, and structural knowledge bases derived from the CSD. The CSD records bibliographic, chemical, and crystallographic information for organic molecules and metal-organic compounds whose 3D structures have been determined using X-ray diffraction or neutron diffraction. The CSD records results of single crystal studies and powder diffraction studies which yield 3D atomic coordinate data for at least all non-H atoms. In some cases, the CCDC is unable to obtain coordinates, and incomplete entries are archived to the CSD. The CSD is distributed as part of the CSD System, which includes software for search and information retrieval (ConQuest), structure visualization (Mercury), numerical analysis (Vista), database creation (PreQuest). The CSD System also incorporates IsoStar, a knowledge base of intermolecular interactions, contains data derived from both the CSD and the PDB. Some software listed above are available for free use.

X-ray microtomography such as available from Skyscan (http://www.skyscan.be/next/home.htm) is used to analyze the effect of compaction on powder particles. It allows for the noninvasive 3D analysis of resulting structures, and has shown that the structure may be controlled by choice of pyrogen and the method of solvent removal. Simple seeding of the substrate surface with drug crystals can be used initially with a view to incorporating more sophisticated substrate polymorph approaches. The Skyscan-1172 represents a new generation in desk-top X-ray micro-CT scan systems. A novel architecture in which both the sample stage and the x-ray camera are moveable allows an unprecedented combination of image resolution, sample size accommodation, scan speed, and sample throughput. This innovative flexible scanner geometry of the Skyscan-1172 is particularly advantageous over intermediate resolution levels, where scans are around 10 times faster (to obtain the same or better image quality) compared to previous scanners with a fixed source-detector design. The Skyscan-1172 features two X-ray camera options: the high-performance 10 megapixel option, and the economy 1.3 megapixel option. The former, 10 megapixel camera allows the maximum scanning versatility, with an image field width of 68 mm (in dual image camera shift mode) or 35 mm (in standard single camera image mode). A nominal resolution (pixel size) of lower than 1 μm is attainable. A scannable height of around 70 mm allows for