

In principle, a surface area value can be calculated from particle size data; there are a variety of techniques that can give an approximate particle size distribution (PSD). Unfortunately, the PSD of many materials are broad and irregular. Three common descriptors are the mean, mode and median (d_{50}). These values can differ markedly as the PSD broadens. Which, then, is the most appropriate single value to calculate surface area? Figure 1 shows the PSD for a sample of a 2vol% aqueous suspension of a micro fine TiO_2 . The particle size is fairly uniformly distributed about the modal value (70nm) where the majority of the particles reside but the suspension contains a “tail” of agglomerates that skews the mean and median sizes. Table 1 lists the surface area values calculated from the three sizes. They are noticeably different.

Many real-world particles are far from round or uniform. Light scattering devices determine an equivalent spherical diameter (ESD) - the diameter of a sphere that would give the same result as the actual particle. Different techniques can yield very different ESD for the same particle; the more asymmetric the particle, the larger the difference in ESD.

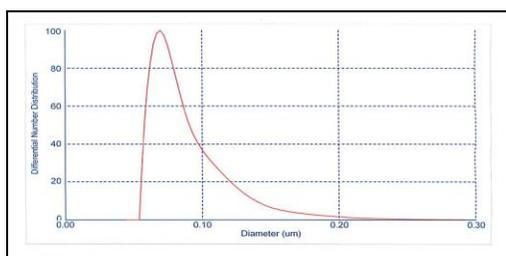


Figure 1

Particle Size (nm)	Surface Area (m^2/g)
91 (mean)	16
82 (median, d_{50})	18
70 (mode)	21

Any surface area value calculated from PSD data is, at best, only a crude approximation. In contrast to PSD devices, when calculating wetted surface area values from NMR relaxation data, there are no assumptions made regarding either particle size or shape. The Acorn Area™ can work with virtually any particle in any liquid at any concentration and since measurements typically take less than 5 minutes this makes it ideal for QC measurements.

Measuring the correct wetted surface area of active pharmaceutical ingredient (API) is vital because API surface area directly impacts not only bioavailability but also the rate of dissolution (Noyes-Whitney equation). There is also a growing body of evidence that, for any type of nanoparticle, it is the surface area and not particle size that is the defining metric controlling toxicological interaction. Figure 2 illustrates the difficulty where the PSD is bimodal. Here 10% of the API (the fraction at ca 200nm) accounts for 90% of the wetted surface area. Table 2 compares the wetted surface areas of six Lots of the same API that had passed QC by laser diffraction particle size measurements. The reproducibility of the NMR measurements was ca 1%. Lot#1 is clearly different (smaller SA).

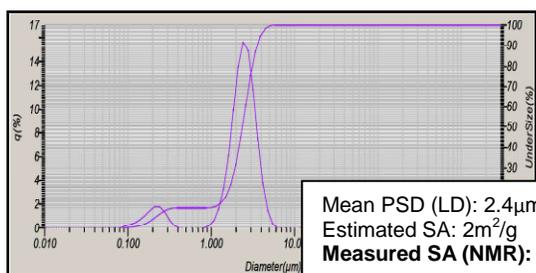


Figure 2

Lot#	1	2	3	4	5	6
SA (NMR)	4.4	5.3	5.6	5.4	5.2	5.4