**Script for HSP Marketing PPT**

**SLIDE 1: The Use of HSP in Formulation Development**

Inorganic and organic pigments and dyes are important materials that are critical to the manufacture of many important commercial products such as paints, inks, cosmetics, pharmaceuticals, display devices, and ceramics.

The preparation of particle dispersions can be broken down into several steps, but the initial step is the incorporation of the dry powder into a liquid which can be water, an oil or a non-aqueous solvent.

So, it would seem that a predictive method for selecting appropriate solvent or solvent mixtures in wetting and dispersion of powders would have practical and economic benefits.

Some 40 years ago, Charles Hansen suggested that what is termed the Hansen Solubility Parameters (HSP) might be used to select the most appropriate solvents for wetting and dispersing nanoparticulate powder materials

**SLIDE 2: HSP applied to dispersion of particles**

In applying this approach to the dispersion of particles, Hansen used - as a suitable metric - the visual observation of sedimentation time, where settling was observed to be slowest in a good solvent.

He proposed that solvent blends – even mixtures of individually poor solvents – having an HSP value similar to that for the material particle surface will be most effective in wetting the material and producing high quality dispersions.

This approach is somewhat analogous to using the hydrophile-lipophile balance (HLB) method to choose the most appropriate blend of surfactants in the emulsification of oil(s).

Unfortunately, the procedure is subjective, very time-consuming – certainly for nanoparticles - and there is no standard methodology.

Analytical centrifugation (AC) does provide a quantitative approach for solvent selection. Here, the measurement of relative sedimentation times (RST) is demonstrably faster and less error prone.

However, AC still has some practical limitations. For example, for very small nanoparticles (< 30 nm), the settling time - even under high-speed centrifugation - can be very long. More critically, AC is influenced by the hydrodynamics of the particle settling and the details of the sample preparation as it is based on the application of Stokes Law. AC performs best for spherical particles under what are called laminar flow conditions, but this is not always achievable.

AC also needs dilute dispersions of spherical particles with reasonably narrow particle size distributions. Unfortunately, many industrial materials comprise broad particle size distributions with non-spherical particles; large particles can create turbulence as they move past the smaller particles.

Solid’s concentrations above about 1.5% v/v lead to hindered settling and hence inaccurate measurements. Industrial slurries are often prepared at high volume fraction and must therefore go through a dilution step (which can also lead to errors) prior to AC measurement. AC also requires knowledge of both density and viscosity of the different solvents employed in order to calculate an RST value.

**SLIDE 3: Mageleka’s *M*agno*M*eter**

NMR solvent relaxation measurements are sensitive to the same intermolecular forces (as well as the dynamics) between solvent and surfaces with which HSP are concerned but they do not suffer from the limitations of the AC technique.

NMR relaxation measurements made using Mageleka’s *M*agno*M*eter are fast, direct and quiescent; the size and shape of the powder material is immaterial. Importantly, from a practical perspective any industrially relevant solids concentration can be used. Further, the total amount of sample needed is typically ca 0.1 mL and can be as little as 250 μL.

**SLIDE 4: Examples**

This Slide summarizes the characteristics of two different materials used to demonstrate the utility of measurements with the *M*agno*M*eter.

The first set comprised three different microfine grade zinc oxide powders. All three materials are typically used in the formulation of sunscreens. One was a base (uncoated) material and the other two were coated versions *of the same zinc oxide*. One was coated with silica (SiO2) to change the surface chemistry but remain hydrophilic; the other was coated with a silane (specifically a tricapryl silane) to render the surface hydrophobic, so that it could be readily dispersed in a non-aqueous fluid, such as the oil phase of a sunscreen emulsion.

The second set comprised two different aluminas. Again, one was a base (uncoated) material and one was coated with a tricapryl silane.

**SLIDE 5: Solvents**

This Slide summarizes the wide range of solvents used in the study.

Hansen recommends that a minimum of twelve probe solvents be used in order to ensure maximum interrogation of a material.

As a note of caution, the NMR relaxation time of any liquid is sensitive to both the water content and the presence of any dissolved oxygen (which is paramagnetic). Thus, the purity and source of a solvent is critical when making comparisons. Indeed, it has long been recognized that traces of polar impurities and, especially, water play a key role in any non-aqueous application. Hence, this sensitivity of NMR relaxation suggests that the measurement can also be used as a fast quality control (QC) tool to fingerprint solvents for industrial applications.

**SLIDE 6: Experimental Results: ZnO**

What we show here is a comparison between the relative relaxation rates for the (hydrophilic) silica-coated zinc oxide and the (hydrophobic) silane-coated zinc oxide.

The relative relation rate, Rsp, is the rate for the suspension divided by that for the solvent alone minus one. The larger the value for Rsp the more efficient is the wetting.

It is seen that the relaxation rates have a significant dynamic range across the selection of solvents and also that the magnitude of the relaxation rate itself is markedly higher for the silica-coated material compared with the silane-coated material (approximate a factor of 8).

These NMR data demonstrate two points. First, the solvents clearly differ in their ability to separate and disperse the particles. Second, the solvent-surface interaction is an important determinant of dispersibility.

As can be seen, the silane-coating makes the surface of the zinc oxide powder so hydrophobic it is difficult to wet even with non-polar solvents. Thus, unless a wetting agent is used, it might not be possible to prepare a well-dispersed stable suspension using the non-polar solvents tested.

**SLIDE 7: Teas Plots: Comparing Hydrophilic ZnO and Al2O3 *vs* their hydrophobic derivatives**

TEAS plots comparing the hydrophilic and hydrophobic versions of the same particle provide useful information regarding the nature of the surface chemistries.

The two hydrophilic zinc oxides – bare (uncoated) and silica-coated - have similar HSP. Thus, wetting and dispersibility would be comparable. As expected, the hydrophobic, silane-coated zinc oxide is demonstrably different.

However, there is an even much larger difference between the hydrophilic, silica-coated alumina and the hydrophobic, silane-coated version.

**SLIDE 8: Comparing ZnO and Al2O3 and their hydrophobic derivatives**

Here we can also see that the two uncoated oxides have a similar HSP. While ZnO and Al2O3 are clearly different chemical materials, the HSP data suggest that the interaction of solvents having strong affinity with the surface of these materials is comparable. This can be understood by considering that both materials are hydrophilic, cationic in water, and with similar zeta potentials.

Conversely, the type of silane coating of the oxides must be quite different, either in chemical nature or coating density. Such a marked difference affects the choice not only of the solvent used but also any other moiety – such as a surfactant, dispersant or stabilizer - that might subsequently be used in the formulation of a suspension, since it will impact the interaction (e.g., adsorption) with the surface.

Thus, the HSP can be used to probe and discriminate the surface chemical nature of materials. Understanding this allows a formulator to more efficiently and better optimize the preparation of a suspension.

**SLIDE 15: NMR Results: Wetting and Dispersibility**

The NMR relaxation rate can also be used as a fast screening experiment for solvent selection.

We have demonstrated above how the relaxation rate can be used as a quantitative measure of the appropriateness of a solvent. Thus, it is possible to use high relaxation rates to indicate good solvents and low relaxation rates to identify poor solvents directly, without completing the entire HSP process.

This is illustrated with the example of the silica-coated zinc oxide dispersed in toluene, methanol or *N*-methyl pyrollidone (NMP). The relaxation rates were found to be 0.12, 2.89 and 7.10 respectively and we would thus predict that a longer term stability experiment would conclude that the NMP dispersion be the most stable and the toluene dispersion the least stable.

The Slide shows photographs taken of samples of silica-coated zinc oxide dispersed in these solvents as part of a simple stability test.

Visual inspection of the dispersions immediately after preparation shows that there is poor wetting of the glass vial by the toluene suspension but, initially, both the methanol and NMP suspensions look good.

However, after four hours standing at room temperature it is obvious that the toluene suspension has – as might be expected – completely separated and, indeed, appears flocculated. There is also noticeable settling in the methanol suspension but very little in the NMP suspension which still looks well dispersed.

The *initial* relaxation rate was thus a good index of the *propensity* of a suspension to settle and so can provide the formulator with useful information. Since the measurement of a relaxation time takes only minutes, it can quickly provide a formulator with a measure of dispersibility well before there are any visible signs of change in concentrated suspensions.

**SLIDE 10: Conclusion**

*M*agno*M*eter measurements provide a quick way to screen solvents for suitability with various particles and, further, that they can be used to quantitatively measure Hansen Solubility Parameters for particulate materials.

*M*agno*M*eter measurements can help in the selection of the most suitable solvent for initial wetting and dispersing of powders, can quickly distinguish between concentrated suspensions that, initially, appear to be similar and so can provide the formulator with time-saving information.