Noninvasive Detection of Nanoparticle Clustering by Solvent NMR

Summary
Aggregation is a significant problem in the synthesis and long-term storage of nanoparticles. As the nanoparticles become significant ingredients in commercial products, the ability to determine nanoparticle quality becomes important. Nanoparticles have a much larger surface area per unit volume than traditional materials. This feature contributes to the unique properties exhibited by nanoparticles. However, this feature also contributes to their tendency to aggregate or cluster. Aggregation can have significant and detrimental effects of the nanoparticle properties and performance. UMB researchers have developed a magnetic resonance relaxometry method (solvent NMR) to reliably and non-invasively identify and determine nanoparticle aggregation.

Market
Aggregation can occur at any stage of product development and is one of the biggest hurdles in most processes, including production, administration, shipping, and storage. Technologies for analyzing complex solutions are invasive, requiring the solution to be drawn out of the container or a probe inserted into the solution to obtain quality control measurements. These approaches compromise product quality assurance. The cost of quality control can be significant. This noninvasive quality control tool has the potential to greatly reduce manufacturing costs and limit costs and pitfalls of product recalls. Solvent NMR is a simple, inexpensive, noninvasive and broadly applicable analytical tool for screening nanoparticle and micron-sized particle-containing formulation. It does not require sample preparation, can be optimized to take less than 1 minute per sample, has a strong and sensitive signal detection, and is adaptable for high-throughput screening. Compared to current quality control methods.

Technology
UMB researchers have discovered that the transverse relaxation rate \( R_2 \) of water increases depending on the extent of particle aggregation and the size distribution of the aggregates. Using magnetic resonance relaxometry, this can be measured and used to calculate aggregation in aqueous solutions using a non-destructive and non-invasive method. Solvent NMR allows for noninvasive measurement of NMR signals with a simple benchtop NMR instrument. It has the potential to be used during formulation research, for quality control during production, and long-term storage.

Technology Status
Solvent NMR has been tested in biological, nanoparticle-containing, and non-biological complex drug solutions, where it was found to quantify a change in concentration of a biopharmaceutical, detect surfactant micellization and monitor protein aggregation. The inventors have also recently shown that Solvent NMR outperforms conventional techniques such as SEC, DLS, and MFI. Solvent NMR was most consistently sensitive to increases in soluble and insoluble aggregates, including subvisible particles (Taraban et al. 2017).

Figure 1: Transverse relaxation rate of water \( R_2 \) measured in aqueous 5% w/v suspensions of PS nanoparticles vs. their average size. (a) Results from CPMG pulse sequence in a low magnetic field (0.47 T), interpulse delay \( \tau = 2 \text{ ms} \). (b) Results from CPMG pulse sequence in a high magnetic field (9.4 T), interpulse delay \( \tau = 1 \text{ ms} \). Red circles, 200 nm sample lacking surfactant; green circles, 200 nm sample with the corrected formulation.