428b High Throughput Solid Form Screening on Functionalized Nanoengineered Surfaces

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The ability of a chemical compound to exist in more than one solid state, polymorphism, is often observed in the pharmaceutical industry. It is essential to control and consistently produce the desired form as the physiochemical properties and bioavailability of a drug depends on the solid state structure. Thus, solid form screening is essential in the early phases of drug development as well as in the late stages due to its relevance to intellectual property management. In this work, a novel high-throughput polymorph screening method using functionalized nanoengineered surfaces, namely patterned self-assembled monolayers (SAMs) is discussed. Taking advantage of the contrasting wetting behavior (hydrophilic/hydrophobic regions) that SAMs offer, crystallization is constrained to uniform arrays of hydrophilic metallic gold islands. Crystallization proceeds due to solvent evaporation from the array of solution droplets, which are on the nano- and pico liter scale. Raman microscopy is utilized to characterize the crystalline form on each metallic island. This approach is applied to several pharmaceutical compounds. In one of the cases (glycine), it is observed that the polymorph distribution varies depending on the dimension of the islands and the concentration of the solution. Furthermore, an attractive feature of this technique is that it requires minute amounts of material and can be used to generate large number of uniform crystals under various crystallization conditions in a short period of time.