

The Production Screen

The propensity for change in response to an externally applied stress is inherent in all solid forms. For products designed, manufactured and regulated to lie within a narrow range of performance specifications, any potential source of variability within the product can present a significant risk. With respect to pharmaceutical drug products, changes can occur at any stage during the drug production, packaging, shipping, storage and even in the hands of the doctor/patient. At any time stress is applied to a drug product, there exist the potential for induced change and hence variability in the drug properties.

From a patient care perspective the primary and obvious concern has to be whether the potential variability has any impact on bioavailability and ultimate drug efficacy. But changes induced in an API can have a broader impact on the pharmaceutical industry – for example, the physical changes may be sufficient such that the analytical response from the API in the drug product no longer matches the claims in the respective solid form patent. This can severely compromise a planned IP protection strategy and undermine the market performance of a drug product. Some induced changes can be very subtle and hardly influence the appearance of the analytical data yet still have a major influence on the final product performance. One such change is caused by matrix interactions between the API and excipients which can lead to wildly inaccurate quantitative analysis and a drug product that lies outside of the specified composition range.

The SSCI Production Screen has been specifically designed to characterize the propensity for change that exists within a drug product whether the changes originate within the API, the excipients or the excipient/API matrix.

At the basic level, the Production Screen consists of proprietary analytical software that accepts a broad range of analytical data (vibrational spectroscopy, thermal measurements and X-ray diffraction) looking for any systematic changes that have been introduced by the application of external stresses to the sample material. Any identified systematic changes in the analytical data are then interpreted by the software in terms of Thermodynamic and/or Kinetic material characteristics.

The pre-screen uses externally applied temperature, humidity (and/or solvent vapour) and physical stress (shear and/or compression) to map out a general risk space that establishes boundaries for the API

under study. These pre-screen measurements where possible are in-situ and dynamic to rapidly map out the risk boundaries. We also now will include excipients in the mix.

The more detailed screen builds on the pre screen and use point measurements at fixed values of humidity (solvent vapour), temperature and pressure. The only variable is therefore time which makes scaling up our results much easier. The point measurements can be used to map the risk boundaries in more detail or investigate the various solid phases that exist on each side of the boundary. The experimental design of the detailed Production Screen allows a partial transfer of the design space and risk assessment to a production scale.

Please contact us at info@ssci-inc.com for further details and questions.