

BPOG MODEL SOLVENT COMPARISON FOR EXTRACTABLES TESTING FOR SINGLE USE SYSTEMS

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Regulatory guidance requires an extractables based evaluation for drug manufacturing processes. Concerns about the increasing use of hybrid and fully single use systems in manufacturing processes and what they may contribute to the bulk drug substance and final drug product has highlighted the need for thorough risk assessments and safety evaluations. Awareness of the risk each unit operation represents a strategy to deal with the risk is crucial.

An outline of a manufacturing process will be presented along with each unit operations potential risk. This discussion will define an extractables testing strategy based upon the Biophorum Operations Group (BPOG) Extractables Protocol for the highest risk process step - sterilizing filtration in a point of use filling line application that is in direct contact with drug product. Analytical results from multiple methods for six model solvent streams will be shown: water, 0.5N NaOH, 0.1 M Phosphoric Acid, 50% Denatured Ethanol/ 50% Water mixture, 1% Polysorbate 80 and 5M NaCl; using time points of <30 minutes, 24 hours and 7 days. A comparison of the compounds identified by each method, solvent and time point will be presented. The extractables data from the sterilizing grade filter will be used to perform a patient safety evaluation for a typical process and a representative drug product. The calculated extractables concentration per dose will be compared to the Permissible Daily Exposure (PDE) level for individual compounds.