

## WORKFLOW FOR IDENTIFYING AND MONITORING ANTIOXIDANT ADDITIVES IN SINGLE-USE SYSTEMS

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Single Use Systems (SUS) are increasingly used in biopharmaceutical industry. Despite their advantages, these polymeric assemblies receive attentions from end-users as well as regulatory agencies because they are a potential source of contamination due to extractable and leachable (E&L) compounds. One primary source of E&L compounds encountered during SUT product usage are antioxidants. When the SUS is in contact with processing liquid, excess antioxidants and their derivatives can migrate into the processing liquid. These substances could potentially jeopardize bioprocessing performance, cause cell growth inhibition, loss of expensive cell lines and reduce yields. This work represents our efforts in addressing this challenge via accelerated solvent extraction (ASE) technique coupled with ultra-fast separation and detection by high-resolution accurate mass (HRAM) LC-MS. Using common SU component materials e.g., polycarbonate (PC), polyvinyl chloride (PVC), polypropylene (PP), polyetherimide (PEI), etc. as testing samples, common antioxidants and their derivatives were extracted by ASE. The extraction efficiency of ASE is calculated to be 26 times higher than Soxhlet extraction. Followed by ASE, UHPLC-HRMS was utilized to characterize the extraction samples. Orbitrap-based HRAM analysis is found to be an efficient and powerful tool for extractables structural elucidation and identification. Under the optimized chromatographic separation conditions, more than 100 additives and degradation products were confidently identified by HRMS with Compound Discoverer against multiple data sources, such as spectral libraries and relevant compound databases. This UHPLC-HRAM-MS setup and associated data processing paves the way for the streamlining of risk assessment of antioxidant extractables and facilitates the design of next generation materials and process innovations.