EXTRACTABLES AND LEACHABLES IN CONTINUOUS PROCESSING SYSTEM

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Single-use system and continuous processing are two significant trends in biopharmaceutical production. The two techniques are parallel and complementary to each other thus together it can provide significant improvement on drug manufacturing quality assurance as well as efficiency. While single-use system had been widely implemented for decades, adoption of continuous processing in pharmaceutical production is still in its early stage. The rapid adoption of single use technologies complements the implementation of continuous bioprocess, providing facile and enclosed systems for bioprocess manufacturing. A new generation of single-use system has been developed to fit in a continuous processing platform. Since extractables and leachables remain a major concern for single-use system adoption, each individual key component of the continuous processing system was evaluated for extractables following BPOG protocol. Risk and toxicology assessment has been performed on the extractables from critical components particularly in downstream processing. Provision of comprehensive, BPOG-aligned extractables packages for each single use bioprocessing component helps frame what extrinsic compounds and degradants may potentially leach into the process flow. However, the robust nature of these studies coupled with high surface to volume ratios may exaggerate the number and level of compounds expected to leach and persist throughout the bioprocess. From a risk assessment perspective, many of these compounds may be expected to be diluted or readily cleared during typical continuous bioprocess application steps. To evaluate the capability of the downstream purification steps to remove extractables from upstream components, samples were collected after each step in continuous processing for extractables studies. This study tracks the emergence and clearance of extractables in model fluids observed at various stages throughout a typical continuous bioprocess implementation. Few extractables in model fluids from upstream components survived after downstream purification and diafiltration steps. Subsequent evaluation of extractables in drug product in continuous processing will be in future studies.