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AN INVESTIGATIONAL STUDY ON THE IMPACT OF AN INCOMPATIBLE FILTRATION OF BENZYL ALCOHOL USING A POLYETHERSULFONE MEMBRANE

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Chemical compatibility of a process stream with a disposable component is a critical element of determining the suitability of the single-use system. Chemical compatibility is often a collection of data on the physical interactions of a disposable with a solution, including but not limited to filter integrity, membrane swelling, and hardware deformations. Compatibility conditions recommended by the disposable manufacturer such as solvent concentration, temperature, and contact time should be compared to actual process use conditions. An incompatible filtration operation can impact the integrity of the filter, in addition to introducing material-derived impurities to a process stream that may not be understood. A case study is presented on the investigation and impact assessment of an incompatible filtration of a polyethersulfone (PES) membrane with 100% benzyl alcohol. The filtration of 100% benzyl alcohol using a PES membrane filter has the potential to introduce material-derived impurities to a process stream by dissolution of the membrane. Laboratory samples were prepared by filtering the 100% benzyl alcohol through the PES filter. LC-MS and FT-IR were utilized to screen the benzyl alcohol filtrate for PES derived compounds and other known wetting agents utilized in the production of the PES membrane. The FT-IR analysis confirmed the presence of PES in the benzyl alcohol filtrate. An additional analysis of the 100% benzyl alcohol filtrate was compared to the 100% unfiltered benzyl alcohol control using LC-MS, and a number of compounds (including the slip agent erucamide, several cyclic PES oligomers, and stearic and palmitic acid) were observed only in the benzyl alcohol filtrate. When compared to the control samples, cyclic PES oligomers were present in greater amounts in the filtered solution. A commercial reference standard was not available for quantiying tricyclic ether sulfone; as a result, a reference standard was generated internally and a limit test method was established at 0.9 ng/mL. Sample retains from three chromatography product pools were obtained, and tricyclic ether sulfone at less than 0.9 ng/mL was identified in three separate production lots. A toxicological assessment was completed to determine impact to patient safety resulting from the entirety of the tricyclic ether sulfone forward processing into a single dose of injectable drug product. The permissible daily exposure (PDE) of tricyclic ether sulfone was determined to be 160 µg/day, while the worst case estimated daily exposure to tricyclic ether sulfone was 0.027 µg/day. This results in an exposure 5,926 times lower than the PDE. A hazard or risk to patient safety is therefore not anticipated based on these findings. As a result of this investigation, several corrective actions/preventative actions were identified, including a materials gap assessment as a prerequisite for a technical process transfer.