

Comparison of Contrast Media Components with International Organization for Standardization (ISO) Standard Solvents to Determine Representative Patient Risk

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Medical devices are subject to rigorous testing during the biological evaluation process, including solvent extractions that are used to chemically characterize the device and for toxicological risk assessment (TRA). Per ISO-10993 guidelines, it is recommended that two extraction solvents of differing polarity (such as water or ethanol) are utilized to produce a robust extractables profile for the TRA process. As a case study, a contrast media injector system was evaluated by simulated use and exhaustive extraction using both water and a mixture of water and ethanol. TRA of water-extracted chemicals identified no unacceptable risks. Conversely, several chemicals in the ethanol extract were present above acceptable limits. Because of these findings, Gradient evaluated the physical and chemical properties of the individual components of two widely used contrast medias – Contrast Media A and B – in order to determine their extractive power compared to typical ISO 10993-18 polar solvents (such as water or saline), semi-polar solvents (such as ethanol, isopropanol, or methanol), and non-polar solvents (such as hexane or benzene). Specifically, the octanol-water partition coefficient (Log Kow) and relative electronegativities of CH, NH, and OH bonds of the contrast media components were compared to those of common solvents. Intravenous contrast media are solutions that utilize elements, typically iodine, organically bound in ionic or non-ionic compounds in aqueous solution. All of the components in Contrast Media A demonstrated negative Log Kow values (-10.42 to -0.77) and 3 out of 4 components in Contrast Media B had negative Log Kow values (-2.79 to -1.56), indicating high water solubility of these ingredients. The fourth component in Contrast Media B (Log Kow = 0.54) readily dissociates in water (exhibited by a relatively high water solubility value of 3.25E+4 mg/L) and other polar solvents. This analysis showed that highly polar solvents (such as water) represent the extractive powers of both contrast media A and B. Semi-polar solvents (such as isopropanol or alcohol-water solutions) and non-polar solvents (such as hexane or benzene) were concluded not to be representative of either contrast media. Based on this analysis, although the ethanol-extracted chemicals provided useful compositional data, it was concluded that the TRA of water-extracted chemicals best represented potential patient risk.