



Determination of Leachable Species- IOL

Overview:

For a wide range of applications, it is important to quantify the amount of material that can be easily extracted from a polymer under physiological conditions. This is especially true for any materials that come into contact with the human body including contact lenses and more importantly implantable devices such as intraocular lenses. It is vital that such devices are essentially free of extractable substances, which will ensure their safe and effective use. The polymerisation process used to produce such polymers will always result in the potential for extractable species in the form of unreacted monomer. Since hydrogel materials become swollen in water, unreacted monomer is usually eluted from the material and the finished device is rendered free of extractable material. In the case of PMMA the material is hard and glassy which effectively stops the migration of unreacted monomer to the surface of the material.

The amount of leachable species present in finished intraocular lenses can be determined by extraction as detailed in the following standard.

ISO 11979-5:2006 Ophthalmic Implants - Intraocular lenses - Part 5: Biocompatibility.

Specifically this corresponds with Annex B - Test for Leachables. The intraocular lenses are dried to constant mass and then extracted at a specific ratio of test material to solvent. The difference between the original dry mass of the lenses and the extracted dry mass determines the quantity of leachable substances.

Knowledge of the quantity and identity of extractable substances is helpful in evaluating new materials and in determining the subsequent pre-clinical examination programme. The material extracted from the intraocular lenses may be examined by appropriate chromatographic methods to identify residual monomers, cross-linking agents and catalysts that were employed in the polymerization process.

Procedure:

Test samples should be representative of the finished product and be in finished intraocular lens form or representative samples weighing approximately 4g. The method of preparing and finishing the lenses shall reflect as far as possible the normal production processes including sterilization.

Hydrophilic lenses are usually packaged in a solution containing inorganic salts. An adjustment in the calculation should be made for the contribution of the inorganic salt of the packaging solution. The water content of the lenses will be required in order to accurately calculate the contribution of the



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inorganic salt to the extractables. Alternatively, the lenses may be equilibrated

in at least two changes of water each for 24 hours at room temperature prior to the beginning of the test.

Two different extraction media are selected, one aqueous and one lipophilic solvent, selected with relevance to the test material. The material is divided into two equal parts for incubation in the extraction media. Each of these is then divided into two again so that at least two vials are used for each medium. The mass of each portion of samples is then determined accurately. The test material is placed into glass vials containing a sufficient volume of medium to achieve a ratio of 10g of test material per 100ml of medium. Vials containing just the solvents are also prepared to act as a control during analysis. The vials are agitated to ensure all surfaces of the test material are available for extraction during the entire period of extraction. The material is extracted at $35^{\circ}\text{C} \pm 2^{\circ}\text{C}$ for $72 \text{ h} \pm 1 \text{ h}$.

The vials are allowed to equilibrate to room temperature after the extraction period has been completed. The test materials are removed from the vial and their spectral transmittance is obtained and compared to that of the untreated material and any changes are noted. Each vial is subject to analysis for leachable substances using gas chromatography and UV/Vis spectrophotometry as appropriate. The results for the analysis of the extracts of the test material should be compared to those of the solvent blank, and any findings should be interpreted in the context of possible material changes.