**Minimum datasets for liquid endo-ocular tamponade agents**

Compiled by a working group of surgeons convened by the British and Eire association of Vitreo-retinal Surgeons (BEAVRS) and issued April 2021. There are 3 minimum datasets covering light silicone oils (lighter than water), heavy silicone oils, and perfluorocarbon liquids.

**Silicone Oils (lighter than water oils)**

In addition to the following table the manufacturer should also supply:

1. The intended surgical applications
2. The conditions of use
3. The maximum duration of contact recommended

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **TECHNICAL INFORMATION** | **EVALUATION** | **Proposed limits** | **Recommendations /Comment** |
| **1** | **Manufacturer of product** |  |  | NA |
| **2** | **Is the oil a mixture of two different viscosities? if yes what are the base oils and proportions?** |  |  | Some oils are a mixture of two different molecular weight oils |
| **2a** | **Molecular mass distribution of each constituent oil in final product** |  | Polydispersity  index Mw/Mn <1.9 | The range of molecular mass distribution and the polydispersity should be stated as listed in ISO 16672. We have chosen to use the polydispersity  index Mw/Mn as outlined by <https://doi.org/10.1167/tvst.8.5.9>. Polydispersity is a measure of purity, and although not proven to be important for toxicity, may relate to emulsification tendency. |
| **3** | **Shear viscosity (mPa)** |  | ±10% nominal value |  |
| **4** | **Specific gravity of product** |  |  | Typically, 0.967 – 0.975 g/ml at 25°C |
| **5** | **Refractive index** |  |  | Typically, 1.4013 - 1.4055 |
| **6** | **Oligosiloxanes (mw <1000g/mol) (ppm)** |  | <0.04% (or 400PPM) | Thought to be important for emulsification tendency, and may be important for long term (but not short term) toxicity but not proven. Ideally as close to 0 as possible. |
| **7** | **Silanol content** | Expressed in PPM |  | Silicone oil with a high silanol content can form oligosiloxanes and other by-products. Ideally less than 100ppm |
| **8** | **Cytotoxicity** |  | > 70% vitality,  < 2 morphology grade change | ISO standard 10993  specific immortalized murine fibroblast lines (BALB/c 3T3 and L929 cells) and on immortalized hamster pulmonary cells (V79). |
| **9** | **Methodology for toxicity testing** |  |  | The manufacturer should state the cell lines/tissue used, exposure time and contact/non-contact culture etc  See ISO 10993 |
| **10** | **Endotoxins** |  | < 0,2 EU/ml;  EU. Endotoxin units | Required for injected medical devices |
| **11** | **Acidity** |  | ≤ 0,15ml NaOH 0.01N |  |
| **12** | **Colour APHA** |  | ≤ 15 |  |
| **13** | **Total level of Ethylene Oxide (EO) or ethylene chlorohydrin (ECH) in the product if used** |  | <1,25 μg/dose for EO and <5,0 μg/dose for ECH |  |
| **14** | **Numbers in batch tested** | Number of individual ‘vials’ included in a ‘batch’ |  | The manufacturer should also supply their method of quality assurance for batch variability and individual batch testing to ensure consistency in their product |
| **15** | **Recommended shelf life** | In Months |  |  |

**Heavier than water silicone oils**

In addition to the following table the manufacturer should also supply:

1. The intended surgical applications
2. The conditions of use
3. The maximum duration of contact recommended

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **TECHNICAL INFORMATION** | **EVALUATION** | **Proposed limits** | **Recommendations/ Comment** |
| **1** | **Manufacturer of product** |  |  |  |
| **2** | **Is the oil a mixture of two different viscosities? if yes what are the base oils and proportions?** |  |  | Some oils are a mixture of two different molecular weight oils |
| **2a** | **Molecular mass distribution of each constituent oil in final product** |  | Polydispersity  index Mw/Mn <1.9 | The range of molecular mass distribution and the polydispersity should be stated as listed in ISO 16672. We have chosen to use the polydispersity  index Mw/Mn as outlined by <https://doi.org/10.1167/tvst.8.5.9>. Polydispersity is a measure of purity, and although not proven to be important for toxicity, may relate to emulsification tendency. |
| **3** | **Non silicone additive conferring heavier than water properties and proportion** |  |  | To assess what confers the heavier than water properties of the oil |
| **4** | **Shear viscosity (mPa)** |  | ±10% of nominal value |  |
| **5** | **Specific gravity of product** |  |  |  |
| **6** | **Refractive index** |  |  | Typically, 1.4013 - 1.4055 |
| **7** | **Oligosiloxanes (mw <1000g/mol) (ppm)** |  | <0.04% (or 400PPM) | May be important for emulsification tendency, and long term (but not short term) toxicity but not proven. Ideally as close to 0 as possible. |
| **8** | **Silanol content** | Expressed in PPM |  | Silicone oil with a high silanol content can form oligosiloxanes and other by-products. Ideally less than 100ppm |
| **9** | **Acidity** |  | ≤ 0,15ml NaOH 0.01N |  |
| **10** | **Colour APHA** |  | ≤ 15 |  |
| **11** | **Total level of Ethylene Oxide (EO) or ethylene chlorohydrin (ECH) in the product if used** |  | <1,25 μg/dose for EO and <5,0 μg/dose for ECH |  |
| **12** | **Cytotoxicity** |  | > 70% vitality,  < 2 morphology grade change | ISO standard 10993  specific immortalized murine fibroblast lines (BALB/c 3T3 and L929 cells) and on immortalized hamster pulmonary cells (V79). |
| **13** | **Methodology for toxicity testing** |  |  | The manufacturer should also state the cell lines/tissue used, exposure time and contact/non-contact culture etc |
| **14** | **Numbers in batch tested** | No. of individual ‘vials’ included in a ‘batch’ |  | \*\*The manufacturer should also supply their method of quality assurance for batch variability and individual batch testing to ensure consistency in their product |
| **15** | **Recommended shelf life** | Months |  |  |

**Perfluorocarbon liquids**

**To include: Decalin and Octane**

In addition to the following table the manufacturer should also supply:

1. The intended surgical applications
2. The conditions of use
3. The maximum duration of contact recommended

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **TECHNICAL INFORMATION** | **EVALUATION** | **Proposed limit** | **Recommendations/ Comment** |
| **1** | **Manufacturer of product** |  |  |  |
| **3** | **Viscosity (mPa)** |  |  |  |
| **4** | **Type of PFCL (Octane, Decalin etc)** |  |  |  |
| **5** | **Specific gravity of product** |  |  | Typically,  Perfluoro-n-octane🡪1.720 - 1.790 g/ml  Perfluorodecalin🡪1.879 – 1.955 g/ml |
| **7** | **Refractive index** |  |  | Typically, Perfluoro-n-octane A 25°C 🡪 1.27 + 0.01  Perfluorodecalin A 25°C 🡪 1.31 + 0.01 |
| **8** | **Boiling temperature (oC)** |  |  |  |
| **9** | **% of pure PFCL in product** |  |  | Recommended,  Perfluoro-n-octane : ≥ 99,0 % ;  Perfluorodecalin : ≥ 95,0 % |
| **10** | **The amount of reactive underfluorinated compounds and their degradation products including hydrogen fluoride (HF)** |  | <10 ppm |  |
| **11** | **Endotoxins** |  | < 0,2 EU/ml;  EU: Endotoxin units |  |
| **12** | **Acidity** |  | ≤ 0.02 µ equiv/ml |  |
| **13** | **Colour APHA** |  | ≤ 15 |  |
| **14** | **Total level of Ethylene Oxide (EO) or ethylene chlorohydrin (ECH) in the product if used** |  | <1,25 μg/dose for EO and <5,0 μg/dose for ECH |  |
| **15** | **Cytotoxicity** |  | > 70% vitality,  < 2 morphology grade change | ISO standard 10993  specific immortalized murine fibroblast lines (BALB/c 3T3 and L929 cells) and on immortalized hamster pulmonary cells (V79). |
| **16** | **Methodology for toxicity testing** |  |  | The manufacturer should also state the cell lines/tissue used, exposure time and contact/non-contact culture etc |
| **17** | **Numbers in batch tested**  (Number of individual ‘vials’ included in a ‘batch’) |  |  | \*\* The manufacturer should also supply their method of quality assurance for batch variability and individual batch testing to ensure consistency in their product |
| **18** | **Recommended shelf life** (months) |  |  |  |