Summary report on tests performed on extracts of silicone gel filler material from PIP silicone breast implants. Commissioned by the MHRA in July 2010.

Objective

In July 2010 the MHRA commissioned a limited number of analyses intended to provide a preliminary evaluation of the filler material used in PIP silicone gel implants in advance of a more exhaustive testing programme that the French Regulatory Authority (AFFSAPS) was conducting.

The MHRA sought advice from toxicology experts to select the tests. The Ames test which gives an indication for presence of impurities in the gel filler material at high risk for genotoxicity, together with analytical chemistry, to make an assessment of a known chemical class of impurities with risks for toxicity, were selected.

Tests

Tests were conducted in compliance with the United Kingdom Good Laboratory Practice Regulations 1999, Statutory Instrument No. 3106 as amended by the Good Laboratory Practice (Codification Amendments Etc.) Regulations 2004 and the OECD Principles on Good Laboratory Practice (revised 1997, issued January 1998) ENVA4C/CHEM (98) 17. Extracts of the test article were prepared according to the principles of ISO10993, Part 3, 2003 and Part 12, 2007 (1).

1. AMES test

Samples of PIP silicone gel breast implants were assayed for mutation in five histidine-requiring strains of Salmonella typhimurium, both in the absence and in the presence of metabolic activation by an Aroclor 1254-induced rat liver post-mitochondrial fraction (S-9). Samples were extracted in one organic vehicle (dimethyl sulphoxide, DMSO) and one aqueous vehicle (water). A range of concentrations of extracts t (DMSO and Water) were tested with all strains in the absence and in the presence of S-9. There was no evidence for any toxicity. Nor was there any evidence for genotoxicity; the extracts failing to elicit positive responses in any of the strains of Salmonella typhimurium. The conclusion drawn was that extracts of the PIP silicone breast implants did not display genotoxic potential in the Ames test.

2. Extraction and organic analysis of implants

Extracts from the gel filler material were analysed for organic components using gas chromatography with mass selective detection (GC-MSD). Head-space GC-MSD was carried out directly on samples of the implant gel to assess volatile organic components.

Conclusions

The Ames test result did not indicate the presence of mutagenic chemicals in the PIP gel filler material. Identified volatile organic compounds were at levels below the USP <467> limits for Class 2 and Class 3 solvents (2).

The MHRA external expert opinion of the commissioned analyses was that the data demonstrated that extracts of PIP silicone were not mutagenic and did not show a potential to cause cancer. These conclusions were later supported by the results from the more extensive testing conducted by the French regulatory authority AFSSAPS. The details of their finding can be found in their Topical report: PIP silicone gel pre-filled implants' dated June 2011 published on the AFSSAPS website http://www.afssaps.fr

References

1. ISO10993, Part 3, 2003 and Part 12, 2007
ISO 10993-3:2003 Biological evaluation of medical devices Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
ISO 10993-12:2007 Biological evaluation of medical devices Part 12: Sample preparation and reference materials

2. US Pharmacopeia USP <467> limits for Class 2 and Class 3 solvents.
http://www.usp.org