A REVIEW OF THE

CHEMICAL CHARACTERIZATION OF SILICONE GEL-FILLED BREAST PROSTHESIS MATERIALS

V. CONCLUSIONS

The chemical composition of extractable materials from the components of McGhan gel-filled, silicone breast prostheses is consistent with that which would be expected through a consideration of the chemistry involved in their manufacture. The use of powerful solvents to extract the shells resulted in extraction of mixtures of silicone chemicals at a level of based on weight of shell. The use of such powerful solvents was designed to produce a "worst case" analysis. Such solvents are unrealistic models for *in vivo* analogy. Many of the additional chemicals tentatively identified as being present in the extracts in trace amounts were likely to have arisen as artifacts of the techniques or during sample handling. Some of the materials present in the extracts at low concentrations can be attributed to trace-level cross-contamination either during manufacture of the raw materials, manufacture of the devices or during the analytical protocol. In any event, their presence is of little chemical consequence.

Of special interest is the determination of the level of lower molecular weight silicones in the shell extracts. Extractable silicones of molecular weight were analyzed at levels of the weight of the implant. Further, was extractable at levels of only implant, with some analyses showing no higher levels than the method blanks. Since most of the volatile components are removed from the raw materials used to produce the silicone elastomers, it is not surprising that extraction of the finished shell yields only very small quantities of these low molecular weight molecules.

Approximately by weight of the gel is extractable with hexane solvent, with methylene chloride solvent giving slightly higher levels and ethanol solvent giving a considerably lower amount of extractables. The extracts were identified as dimethylpolysiloxanes, or which only about by weight of the gel had molecular weights was identified at levels of only of gel (a level comparable to that for the solvent blanks associated with this technique).

Preliminary investigations of the "gel bleed" phenomenon indicated that prostheses employing a "barrier" shell showed an order of magnitude less silicone was transferred outside the shell than for "non-barrier" products. The material absorbed by the filter paper placed in contact with the prostheses was characterized as siloxanes. While very low levels of silicone were absorbed by the filter paper, the silicone contained a higher concentration of low molecular weight components than that found in the bulk composition of the gel. This is consistent with the theorical basis for low molecular weight components diffusing at a higher rate. This study is of itself inadequate to explain this complicated phenomenon, and attitional experiments will be required in order to provide further insight.

In conclusion of the toxicological considerations, the analysis of extracts of the silicone elastomer shell materials and the silicone gel from McGhan mammary implants indicates that the extractable materials are a PDMS polymers occasionally accompanied by minute quantities of residues and possible contaminating The potential toxicity of some of the individual constituents of the extractable materials has been extensively characterized in experimental animals. The lack of toxicity of the remaining constituents has been established by extensive testing of PDMS fluids in experimental animals. The quantities of low molecular weight PDMS constituents that are present in the extracts from shell materials and gel from McGhan mammary implants and which might hypothetically be mobilized from mammary implants are far below the amounts which have been shown to produce toxicity or which produced so-called "contradictory" results in reproductive toxicity studies. The minimum margin between a dose known to cause toxicity and the maximum hypothetical dose to a woman with bilateral implants provides a safety factor of at least 200, and this factor is more likely to be on the order of 3,500. Therefore, based on the results of this investigation no further investigation of the potential toxicity of constituents of extracts from the materials in Mcghan mammary implants is scientifically justifiable.

VI. TOXICOLOGY REFERENCES

Bates, H.R., Filler, R., and Kimmel, C. 1985. Developmental toxicity evaluation of polydimethylsiloxane injection in CD rats. Poster presented at the 1985 Annual Meeting of the Teratology Society.

Bates, H.K., Cunny, H.C., and LaBorde, J.B. 1992. Developmental toxicity evaluation of polydimethylsiloxane injection in the Sprague-Dawley rat. Proceedings of the Silicone in Medicine Conference, Baltimore, MD, February 1-2, 1991. HHS Publication FDA 92-424.

Cutler, M.G., Collings, A.J., Kiss, I.S, and Shatratt, M. 1974. A lifespan study of a polydimethylsiloxane in the mouse. Fd. Cosmet. Toxicol. 12:443-450.

Munson, A.E., White, K.L., Jr., and McCay, J.A. 1992a. Immunotoxicity of silicone in female B6C3F1 mice - 10 day exposure. Report to the National Toxicology Program from the Immunotoxicology Program, Medical College of Virginia/Virginia Commonwealth University, Richmond, VA. 71 pages.

Munson, A.E., White, K.L., Jr., McCay, J.A., and Stern, M.L. 1992b. Immunotoxicity of silicone in female B6C3F1 mice - 180 day exposure. Report to the National Toxicology Program from the Immunotoxicology Program, Medical College of Virginia/Virginia Commonwealth University, Richmond, VA. 96 pages.