64

Head, Medical Devices Assessment Section, ODBT
Attention : [redacted]

[redacted]

APPLICATION FOR REGISTRATION

FILE NO	2003/03664 (off –file)
SUB NO	2003/098
PRODUCT	High cohesivity gel breast implant
SPONSOR	Medical Vision Australia P/L

Evaluation of Sponsor replies - BIOLOGICAL SAFETY

The company were asked to respond to an outstanding issue (bolded below) regarding the insufficient genotoxicity testing.

> **Satisfactory responses are still required regarding the genotoxicity testing. Although the company have determined the extractables based on the known manufacturing formulation, there has been no characterisation of the finished implant and the genotoxicity testing is insufficient as it stands.**
> **It is recommended that the following test be performed to fully demonstrate that there is no genotoxic potential. A gene mutation test with mammalian cells (ie OECD 476) incorporating both end points of clastogenicity and gene mutations. Both polar and non polar solvents (eg saline and DMSO) are to be used to prepare extracts of both the envelope and gel from a finished implant.**

The company have proposed in their fax dated 17 May 2004 to conduct an *in vivo* rodent micronucleus assay based on OECD 474 (1997) and ISO 10993-3 (2002) and have submitted a protocol for TGA approval. The protocol includes evaluation criteria which specify that micronucleated polychromatic erythrocytes are to be enumerated and this will judge clastogenicity effects in somatic cells. The test is appropriate and can be substituted for the previously recommended *in vitro* assay. The test sample in this assay should include envelope and gel from a finished implant – this has been confirmed by the company (p7 of fax).

RECOMMENDATION
The suggested test and submitted protocol is appropriate and pending satisfactory results will be sufficient to demonstrate a lack of genotoxic potential for this product.

[redacted]
Biocompatibility Stream
TGAL
3 June 2004