185

Biomaterials Stream – CONFORMITY ASSESSMENT

13

[redacted]

TO:	[redacted]
FROM:	
COMPONENT EVALN.:	Biological Safety Information
SPONSOR:	Medical Vision Australia P/L
ENT ID	29703
PRODUCT:	1 IMGHC-LS-S 2 IMGHC-LS-H 3 IMGHC-TX-S 4 IMGHC-TX-H 5 IMGHC-TX-R 6 IMGHC-TX-AL 7 IMGHC-TX-AR 8 IMGHC-LS-EH 9 IMG
DATE:	~~8~~ February
SUB NO.:	2003/098
FILE NO:	2003/0036
DUE DATE:	27 Februa

Duplicate of Doc 9. Pg 8 (2)
Not in main Doc. Pg 7 (1)
...pleted 19/3/04 -
...leted 19.4.04

[redacted] we have recently received more information from PIP. Please find attached responses to the recommendations arising from the Biocompatiblity evaluation for the PIP breast implants. See pg 3

Your assessment of the information would be appreciated.

If additional information is required, please advise the recommendations.

Thanks

[redacted]

Returned 13/4/04 –

Comments from [redacted] were that they have not characterised the FINAL material but what went into it. Commented to [redacted] that at audit in Nov. P.I.P. were given a copy of the draft ISO 10993-18 which is chemical characterisation. Although the company have attemped to do a characterisation this is not sufficient. Would still recommend they do the genotox tests as required

[redacted] 13.4.04.

184

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

ADDITIONAL NOTES – NOT TO BE SENT TO COMPANY

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

Regarding evaluation request dated 26th February 2004:

Q1 It has recently been brought to this evaluator's attention that the Breast Implant Panel of the Therapeutic Devices Evaluation Committee determined in November 2001 that silicone dosage was not an issue with respect to effects on reproductive toxicity. A similar question had been raised by an evaluator regarding the maximum implantable dosage in reproductive testing of components of the Mentor Siltex implant. The Panel deemed that there was sufficient evidence in the submission, clinical experience and in the literature to show that there reproductive toxicity is not an issue of concern.

Q2 Regarding the approach of the company, this is generally not acceptable for the finished device as a characterisation of the materials in the finished device should be included as evidence. This would be a characterisation such as that in Part 18 of ISO 10993 "Chemical Characterisation of Materials" to determine the chemicals which possibly leach into surrounding tissue. As far as this evaluator is aware this has not been conducted. The company have determined levels of extractables of the known formulation inputs and have verified that these levels in the finished implant are acceptable. However the company have not considered the extractables from the point of view of characterising the finished material fully and then conducting actual extractable studies.

Currently the tests submitted for the finished device are an AMES test (saline extract only) and a chromosome aberration test. The justification for using a polar solvent only is that biological fluids and tissues are polar. The company may not fully comprehend the purpose of using a non-polar solvent for extraction that is recommended, where possible, in both the MEDDEV document, the FDA document and ISO 10993. A non polar solvent, such as DMSO, would be capable of extracting and solubilising material that is incapable of being extracted or solubilised by saline alone. Body fluids and tissues are not similar to saline or tissue culture fluid alone, they contains lipids which could extract material that saline cannot.

If the company's approach is not acceptable then the company should be asked to submit outstanding data. The test that remains outstanding that would offer the best information would be an in vitro gene mutation test with mammalian cells (ie OECD 476) which incorporates both end points (clastogenicity and gene mutations). This test can be conducted with two extractants such as saline and DMSO.

RECOMMENDATION

It is this evaluator's understanding that OECD 476 is the minimum genotoxicity testing that has also been requested for recent silicone gel implants (Paragel). The report headed Application for Registration and dated 19 April 2004 should be conveyed to the company in it's entirety so as to facilitate understanding of this issue.

[redacted]
Biocompatibility Stream, TGAL
19 April 2004