Date : 17-19 Nov 2003

Manufacturer: Poly Implants Prostheses, 337 Avenue De Bruxelles, 83507 La Seyne sur Mer, FRANCE

Products:

Document Review	Audit observations
Clarification of identity of material components **1 Technical File D.1.2 : "raw material and manufacturing processes for both envelopes is the same"** In relation to material equivalency, testing the envelope from the saline filled envelope was used for some testing for the gel filled implant : **envelope from saline implant:** MED 6400 : xylene dispersion (envelope & patch) MED2 6400: 1,1,1 trichloroethane (tex envelope last layer & patch) **envelope from gel implant** **MED6 6400 : xylene dispersion (envelope, closure & patch)** **MED 6400: xylene dispersion for 1st gluing layer** **How are these equivalent?** **2** Biological safety testing of the envelope was conducted on the main shell component MED6 6400 and did not include the patch closure component – you replied recently that the closure patch was less that 3% of the total so you did not need to test **How have you determined that the main shell and the closure patch are chemically equivalent?**	MED2 6400 is the 1,1,1 trichloroethane dispersion (CTCE) → typo error in data we had – no longer using 1,1,1 trichloroethane in MED2 6400 as of Feb 2001 → use as eg of Design changes for QMS. – when questioned the Q.C. leader? (Mr Bossie) answered that the saline + gel envelopes are exactly the same, since TCE not used anymore – advised they need to inform TOA of this change – they said they would send to TOA. – DIFF. btwn MED 6400 – has phenyl groups and MED6 6400 – has vinyl groups instead of phenyl. → Advised that they need to provide evidence of chemical equivalence. Saying → Haven't shown this chemically – they reiterated that it's only 2-3% of envelope. Told them this is not enough, they need to show its chem. equiv. – explained Part 18 in 10993. ↳ & do tox. risk assessment to determine if it's the same or they need to do test.

Prepared by [redacted]

Discrepancy of identity of closure patch in documentation **Q: Is it MED 2245, as appears in some of the materials and manufacturing data or is it MED6 6400?**	MED6 6400 – IS patch MED 2245 – IS glue.
There were fatigue tests conducted in 1996 of 3 samples from each of the sample sizes, 2 million cycles was conducted. This appears a bit low to me, and know EN12180 is not good in this respect– have you considered fatigue testing to failure and recording the number of cycles? – also this testing was done pre 1,1,1 trichloroethane change in Feb 2001.	P.I.P. did some tests for FDA (at 10 mill. cycles) as requested for saline implant. Conceded that 2 mill cycles is low. Are currently engaged in starting the fatigue testing for the gel implant again, they are tendering (??) for the fatigue testers so that they can either have them on site or lease long term off-site. Some intending to test to failure & work out force involved. Their justification is that all the mechanical parameters have not changed at all from the old env. to the new envelope – all specs are same (showed us the Design change folder on this – all same or tighter specs.)
Biological safety testing There are two issues from the biological safety data: 1 the dosage used in the reproductive toxicity testing is equivalent to 2 500cc implants and yet you intend to market up to 800cc implants **Q how can you justify the applicability of data that relates to the lower dosage?** 2 The genotoxicity regime you have used does not fully comply to ISO 10993-3. What is the scientific justification for not complying? ISO 10993-3 " ...a series of in vitro tests shall be used. This series shall include at least 3 assays. At least 2 of these should preferably use mammalian cells as a target	– Still not able to justify this – the Reg. Officer said she wanted time to discuss it testing home & and will get back to TGA – the Reg. Officer requested that she will get back to us in letter, tried to explain 10993-3 – got imp. Reg. officer relying on testing home's explanation – told her there really was none.

Prepared by [redacted]