

Memo to the FDA/CDRH

Re. Comments on Breast Implants (Docket No. 2004D-0002), Draft Guidance Document #1239

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This memo is to offer comments on the Draft Guidance Document on the title subject. First, I would like to commend the FDA for the thorough approach that they are taking on difficult, contentious, but very important matter. The draft document is very good but leaves out several areas which will be addressed as items below:

1. The toxicity of the degradation products of breast implants is not specifically considered.

In general, it is well known that low molecular weight materials are released through gel bleed (and rupture) and that they decompose under biological conditions. They are known to generate silanol-containing species, which frequently are biologically active but are not well characterized. Careful identification of the quantity and composition of such species should be carried out, and the toxicological properties measured if not already available (Batich, 1996; Birkefeld, 2004). A sufficiently long time should be allowed for the degradation (e.g., 5 year accelerated study). It is sometimes appropriate to use time-temperature superposition to carry out accelerated studies (e.g., McLinn, 1994)

2. Not all materials used in construction have been identified.

For instance, coupling agents are likely to be present as free species (uncoupled) in the silicone elastomer, but are not generally mentioned. This may reflect the view that they react and are no longer available, but there is no evidence for this. All materials used should be identified, and their fate quantified for the most part. The barrier material is sometimes not clearly identified as to composition.

3. Manufacture date should be included for all devices on the packaging.
4. For item 4.3 (Extractables), a minimum time and temperature should be suggested for the extraction steps (e.g., 3 hours at 37 C). The FT-IR method may be inadequate to identify species, and GC/MS may also be needed (for instance, to distinguish D3 from D5).
5. Item 6.4 (Cohesivity Testing) does not include measurements on gel after mechanical manipulation (i.e., such manipulation would cause some fragmentation of the gel, and would reflect the actual use condition).
6. Articles referred to (e.g., note after section 7) in the Guidance document should be posted on the FDA web site if possible.

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7. Package sealing materials should be identified in case migrations of volatile glue constituents are able to enter the implant.

References:

Batich,C, DePalma, D. , Marotta,J, Latorre,G, Hardt, N, "Silicone Degradation Reactions," C. in "Immunology of Silicones," ed. M. Potter and N. Rose, Springer Verlag (Berlin), p. 13-23 (1996).

Birkefeld AB, Eckert H, Pfeleiderer B. "A study of the aging of silicone breast implants using (29)Si, (1)H relaxation and DSC measurements". *Biomaterials*. 2004 Aug;25(18):4405-13.

McLinn, J.; "Qualification Testing" in *Medical Device and Diagnostic Industry* May 1994 p. 224