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Comment on Docket # 02N-0500

General and Plastic Surgery Devices
Classification of Silicone Sheeting

By
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This comment of the National Center for Policy Research for Women & Families is to express our strong concerns about the FDA proposal to classify silicone sheeting as Class I, the lowest level of regulation, and exempt silicone sheeting from premarket notification requirements.[1] The FDA proposal is in direct conflict with the recommendation of its Advisory Panel, convened on July 8, 2002, to require premarket notification.

Disregarding its own Panels' findings, the FDA proposes that 21 CFR § 878.4025 silicone sheeting read as follows:

(a) Identification. Silicone sheeting is intended to manage hyperproliferative (hypertrophic and keloid) scars on intact skin

(b) Classification. Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to the limitations in §878.9

There is a dearth of reliable evidence from prospective randomized clinical trials in the peer-reviewed published medical literature on the effectiveness of silicone sheeting products in either alleviating the symptoms or improving the appearance of hypertrophic scars and keloids. On the

contrary, according to Dr. Mimi Kokoska of Indiana University School of Medicine, "the general opinion on silicone sheeting does not support significant reduction in the dimensions or pigment characteristics of keloids..."[2] Studies have failed to demonstrate long-term effectiveness of silicone sheeting for the topical treatment of hypertrophic scars and have failed to investigate the effectiveness of silicone sheeting on representative numbers of individuals across racial, sexual or age categories. [3] [4] [5] This is especially important since keloids are more common among African Americans and Asian Americans compared to Whites.

In one of the few reported studies that was prospective and randomized, no differences were detected among patients with hypertrophic scars treated with silicone gel sheeting when compared to patients treated with a laser.[6] Moreover, a physician member of the FDA Advisory Panel reported on the observance of folliculitis and irritant reactions in his patient population to the use of silicone sheeting. [7]

There is no valid scientific information and therefore no consensus on the mechanism of action of silicone sheeting. The FDA Advisory Panel discussed the inexact science and queried whether silicone leaches out of the polymers into the wound, thus affecting CD36 cells. The Advisory Committee also examined the controversy over the effect of temperature

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[1] Memorandum to General and Plastic Surgery Devices Panel on "Classification of the Scar Management Device", June 11, 2002, author Sam R. Arepalli, Ph.D.

[2] Kokoska, M et al Hypertrophic Scarring and Keloids, available at http://www.emedicine.com/ent/topic37.htm

[3] Ricketts, CH et al. "Cytokine mRNA Changes During the Treatment of Hypertrophic Scars With Silicones and Nonsilicone Gel Dressings" *Dermatol Surg* 1996 Nov; 22(11):955-9.

[4] Suarez,M et al "A Novel Occlusive Dressing for Skin Resurfacing" *Dermatolog Surg* 1998 May;24(5):567-70

[5] Berman, B et al. "Comparison of a Silicone Gel Filled Cushion and Silicon Gel Sheeting for the Treatment of Hypertrophic or Keloid Scars", *Dermatol Surg* 1999 June; 25(6):484-6

9 Wittenberg, GP et al. "Prospective, single blind, randomized controlled study to assess the efficacy of the 585-nm flashlamp pumped pulsed dye-laser and silicone gel sheeting in hypertrophic scar treatment", *Arch Dermatol* 1999 Sept: 135(9):1049-55

[7] Department of Health and Human Services, FDA Center for Devices and Radiological Health, General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee, July 8, 2002, available at http://www.fda.gov/ohrms/dockets/as/02/transcripts/3876t1.doc

are concerned that the FDA's proposals to identify silicone sheeting as a device for the management of hyperproliferative scars on intact skin runs contrary to the scientific testimony presented to its own Advisory Panel, wherein hypertrophic scars were defined as compromised (not intact) skin. Indeed the scientific testimony identified three separate ways that hypertrophic scars acted as compromised skin.

In addition to the above concerns, there are reasons for the FDA to consider the risks of off label uses of silicone sheeting. The device is marketed to surgeons as intended for use in the repair of fractured orbital floors, nasal septums and perforated eardrums as well as in the pediatric population for surgical treatment of neonatal omphalocele. Silicone sheeting is marketed for all of these uses, as well as many others, and yet there is no reliable basis for assuring its safety and effectiveness for permanent or temporary use. Please note that the previously popular use of silicone sheeting for TMJ problems was found to cause permanent and debilitating injury.

There is a reasonable likelihood that silicone sheeting will be used in ways that have not been adequately tested, and without adequate warnings to patients, and such use could cause harm. According to the package insert for Silmax Sheeting, manufactured by Silmax Implants, "The patient must be told that silicone sheeting may cause autoimmune diseases...before they consent to surgery for the use of this and other silicone products." [8] If manufacturers are permitted to market silicone sheeting for any use, without any proof of safety, then the public's health is at risk. The labeling requirements in a premarket

[8] Silmax Implants. Available at http://www.silmaximplants.com/pdf_files/Silmaxsheet.pdf

notification provide some measure of assurance.[9] If silicone sheeting is classified as Class I, there will be fewer safeguards to protect patients.

Given the uncertain mechanism of silicone sheeting action, the anecdotal and limited nature of studies, the controversy over the physiology of scar tissue vis a vis its identification as "intact" skin, the unknown effect of on individuals from various racial groups, and the well-known off label uses of silicone sheeting, the FDA should conclude that silicone sheeting needs more FDA scrutiny and regulatory oversight, not less. Although the FDA Advisory Panel recommended Class I classification of silicone sheeting, they nonetheless overwhelmingly voted to recommend premarket notification requirements under 510(k) of the Federal Food Drug and Cosmetic Act. It seems that the Advisory Panel did not believe that general controls would provide a reasonable assurance of the safety and effectiveness of silicone sheeting across the spectrum of likely uses.

There is no scientific justification for the FDA to disregard the expert opinion of its Advisory Panel requiring 510 (k) controls on silicone sheeting. This comment supports the concerns of the Advisory Panel and urges the FDA to adopt premarket notification requirements for silicone sheeting. We also share the concerns of Advisory Committee member Dr. Robert McCauley about the long-term safety of silicone sheeting, and strongly urge that as an implanted product, this device should be classified as Class III.

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[9] Confer CDRH "Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff", issued December 3, 2002; available at http://wwwlfda.gov/cdrh/ode/guidance/857.html