

CITIZEN PETITION 20 6  
April 6, 2006

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Dockets Management Branch  
Food and Drug Administration  
5630 Fishers Lane, Room 1061 (HFA-305)  
Rockville, MD 20852  
FAX 301/827-6870

The undersigned submits this petition under 21 C.F.R. 10.35 to request the Commissioner of the Food and Drug Administration (FDA) stay the current approvable letter with conditions of any and all Premarket Applications ("PMA's") for silicone gel-filled breast implants (SGFBIs) for an indefinite time due to the (2006) peer-reviewed published research finding significant levels of ionized platinum are released after implantation from second and third generation SGFBIs. The risks of this non-life saving device clearly outweigh any benefits and will cause women and their children born after implantation irreparable injury. We request that in accordance to 21 C.F.R. 14.7, the Commissioner expedite the review of this petition and make a reasonable effort to render a decision before any final action is taken regarding the approval of SGFBIs.

#### Statement of grounds

- Peer-reviewed published research by Maharaj 2004 "Platinum concentration in silicone breast implant material and capsular tissue by ICP-MS" (Exhibit A) found significant platinum levels in the connective tissue of breast implanted women. In conclusion the author states "Platinum (Pt) concentration in each group of breast implant material (gel, elastomer, double lumen, or foam) varied considerably. All materials contained much higher levels of Pt than has been reported by manufacturers... Platinum most likely occurs in implant material as hexavalent platinum (Pt) compounds, along with other ionized forms of Pt, and organoplatinum or silicon-Pt complexes. Although the concentration of Pt+6 is unknown, given the high toxicity and biological reactivity of ionized forms of Pt, any amount may be too much. A major toxicologic issue is immunogenicity, where absolute amounts have little significance in the development of allergic and immune disorders. As Pt in the form of soluble salts is a potent allergic sensitizer, a "safe" dose is unknown."
- Peer-reviewed published research (2006) by Analytical Chemistry titled "Total Platinum Concentration and Platinum Oxidation States in Body Fluids, Tissue, and Explants From Women Exposed to Silicone and Saline Breast Implants by IC-ICP-MS." (Exhibit B) came to the conclusion "Women exposed to silicone breast implants had higher Pt levels by approximately 60 to >1700 x for urine, 14 x for hair, 3 x for nails, and 100 x for breast milk samples, than individuals with no known Pt exposure. Pt in explanted silicone breast implant gel, whole blood, urine, brain tissue, and breast milk samples from women exposed to silicone breast implants occurred mainly in reactive forms...Silicone breast implants are

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the most likely source of the elevated total Pt levels, and the reactive forms of Pt in women exposed to these devices.”

- The abstract “Total platinum in urine of women exposed to silicone breast implants and in their children conceived after implantation by ICP-MS” was presented to the American Chemical Society Meeting 2005 by S.V.M. Maharaj, Ph.D. The abstract (Exhibit C) states “Inductively coupled plasma-mass spectrometry (ICP-MS) was used to determine the total platinum (pt) concentration in urine samples of women exposed to silicone and saline breast implants. Total Pt concentration was also determined in urine samples of children conceived before and after their mothers were implanted with silicone breast implants. Mean Pt concentration in urine samples of women exposed to silicone breast implants was higher [48.50 ug/L (range n.d. – 219.00); n=41] than in the general population. Mean Pt concentration in urine samples of children conceived after their mothers were implanted with silicone breast implants was higher [88.63 ug/L (range, 15.30 – 382.00); n=7] than in children conceived before their mothers were implanted [12.60 ug/L (range, 0.10 – 23.30); n= 4].” CANDO has now tested over twenty children born prior to and after their mothers were implanted with silicone gel-filled breast implants.
- A recent 2006 review by Inamed consultant Michael A. Brook titled “Platinum in silicone breast implants” produces no new peer-reviewed research but simply critiques any published research finding significant platinum levels in breast implanted women or their explants and any connection to disease by a treating physician. Brook states “Implanted women are reported to have platinum urine concentrations similar to those of unimplanted women...the half-life of platinum in vivo is relatively short (<3 days), although there is some evidence that workers with these very high exposures take considerably longer to rid the Pt from their system than the average population.” It should be noted that these statements are based on a letter to the editor of a journal and not peer-reviewed research. Brook further notes “Non-peer-reviewed data provided by Mentor to the FDA as part of their submission for approval of a new implant design is available. Platinum release profiles into the biological medium porcine serum, a system that may approximate the constitution of the human breast cavity, showed Pt loss over 120 days of 4.1. ug of a total 529 ug in a 125 cm<sup>3</sup> implant silicone. The oxidation state of the platinum was shown by X-ray absorption to be Pt(0).” At the April 2005 FDA advisory panel, one of the panel members Stephen Li, PhD, president of Medical Device Testing and Innovations stated “My own experience with X-Ray absorption is that it can’t tell you the valence state.” Brook concludes “The experimental evidence supports the conclusion that there are no clinical consequences of the platinum in silicone breast implants, which is to be expected based on the known toxicity of this metal in this oxidation state (zero).” To support this conclusion Brook uses the 1999 IOM Report and the 2002 FDA article. Both reports merely reviewed the published literature on platinum in breast implants and non-peer-reviewed statements by the manufacturer’s of breast implants and their paid consultants. The large studies to date looked only for

cancer rates and autoimmune or connective tissue diseases among breast implanted women. No questions were asked regarding neurological disease or known symptoms to toxic and hyper-sensitizing platinum exposure. If no independent research is conducted, then a "review" of the literature finds no "clinical consequences". Ernest Lykissa, Ph.D., forensic toxicologist states the following "Brook has made certain statements that clearly demonstrate his primary interests which are not the advancement of science, and definitely he is not driven for the public welfare. He is a hired consultant by the manufacturers of silicone breast implants. He puts no scientific evidence forth, as to how old aged silicone explants have sickened thousands of women in the USA and the rest of the world, but rather he continues in restating whatever evidence is declassified that applies only to brand new devices never implanted in the human body. He criticizes peer reviewed scientific data that has been published in some of the most important scientific journals in the world, but his challenges are mere opinions propagated by his employers. Our current publication in Analytical Chemistry (2006) finally arrives with ample evidence for the cause of ill health effects from these devices. The platinum catalyst that has been incorporated into the silicone gel component of the implants is being released from the depolymerized silicone gel and in the ionized form it is free to attack the human tissues, including the nervous system. I hope that this new research will alert the women and their physicians in evaluating very carefully their options, and it will shed some light to the dilemma that has been plaguing the women that were left uninformed by the manufacturers of these devices, as to the dangers that were hiding behind these prosthetic devices that were purported to offer aesthetic enhancements of their appearance."

- At the 2005 FDA advisory meeting Inamed stated that their implants did not leak platinum. Their methodology was determined to be irrelevant. Both Inamed and Mentor submitted unpublished data on brand new implants never implanted in the human body. Lykissa and Maharaj (2006) comes to the conclusion "the platinates utilized in the manufacture of the silicone gels of silicone breast implants were neutralized with vinyl binding that detached in the reactive, hot organosilicone oil mixture...all heavily crosslinked organosilicone envelopes (used in silicone- and saline breast implants, and in testicular implants) catalyzed with ionized Pt would be expected to undergo degradation and depolymerization with aging. Depending on the amount of ionized Pt that is liberated by the degradation process, proteins may become vulnerable to denaturation."
- Subject #3 in the Lykissa and Maharaj (2006) research had 1993 Mentor H.S. Siltex, Lot #65789, Catalog #354-4007 low bleed gel-filled third-generation implants which document the release of ionized platinum. Additional subjects who had third generation implants and their children born after implantation have been tested and found to have ionized platinum in their urine or breast secretions. They include the following: Exhibit D  
Subject #47 Still implanted with 1997 Mentor H.S. Siltex Low Bleed gel 450 cc breast implants Cat. No. 354-4507, Style 7000 Round, Lot 147384

Platinum urine results by ICP-MS 6.2 ug/l (speciation zero (0) 57%, +4 = 43%)  
 Subject #47a Son born 7/5/01 after implantation

Platinum urine results by ICP-MS 81.2 ug/l (speciation zero (0) 59%, +4 = 41%)  
 Exhibit E

Subject #53 Explanted 2/2/06 of 1990 Third-generation gel-filled breast implants

Platinum urine results by ICP-MS <0.01 ug/l

Platinum results from right breast secretion by ICP-MS 32.5 ug/l

Platinum results from left breast secretions by ICP-MS 7.5 ug/l

Platinum ionization by IC-ICP-MS of breast secretions (speciation zero (0)  
 34.4%, +2 =61.2%, +4 =4.4%

Platinum results from breast fat tissue taken at time of explantation 1.7 ug/l

- Michael Harbut, M.D., MPH, FCCP with the Center for Occupational and Environmental Medicine states "I have treated over 1,000 women with breast implants and have regularly seen the diseases caused by platinum salt exposures. As I published in 1999, women with exposure to platinum salts via their implants commonly present with shortness of breath, asthma, itching, rhinitis, memory loss, gastrointestinal disturbances, sometimes pulmonary fibrosis and sometimes COPD, among other, less common presentations."
- Claudia S. Miller, M.D., M.S., a board certified internist, allergist, and immunologist published research (1999) using a validated screening questionnaire for Toxicant-induced Loss of Tolerance (TILT) called the Quick Environmental Exposure and Sensitivity Inventory (QEESI) to study 87 people with surgical implants, three-quarters of whom had received breast implants. Miller found that compared to controls, implant recipients reported many more, and more severe, adverse responses to everyday chemical exposures. Further, implant recipients reported far more severe reactions to a wide variety of foods, medications, and other common exposures than did controls (Exhibit F). For more than a decade, Dr. Miller research has focused on people who report developing chronic, multi-system symptoms – headaches, memory and concentration difficulties, depression, fatigue, fibromyalgia, gastrointestinal problems, etc. – following an identifiable environmental exposure.

## **B. Conclusion**

In light of new peer-reviewed published research discussed above and the known association between Pt salt exposure with positive skin patch tests, contact dermatitis, asthma, immunogenicity, inhibitory effects on brain enzymes, neurotoxicity, mutagenicity, carcinogenicity, and anaphylactic reactions as well as the high failure and gel bleed factor of silicone breast implants, it would be in the public interest for the Commissioner to stay the current approvable letter with conditions of all PMA's for SGFBIs using platinum as a catalyst.

**C. Environmental Impact**

This petition qualifies for categorical exemption under 21 C.F.R. 25, 15, 25.30-32 from the preparation of an environmental assessment.

**D. Economic Impact**

A statement of the economic effect of the petition will be submitted if deemed necessary by the Commissioner.

**E. Certification**

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the petition.

Marlene Keeling, President  
Chemically Associated Neurological Disorders  
P.O. Box 682633  
Houston, Tx. 77268-2633  
281/444-0662 (281/444-5468 FAX) e-mail keeling.m@worldnet.att.net

**Exhibits****Exhibit A:**

Maharaj, SVM. Platinum concentration in silicone breast implant material and capsular tissue by IVP-MS. Anal Bioanal Chem (2004) 380: 84-89

**Exhibit B:**

Lykissa, ED, Maharaj, SVM. Total Platinum Concentration and Platinum Oxidation States in Body Fluids, Tissue, and Explants from Women Exposed to Silicone and Saline Breast Implants by IC-ICP-MS. Analytical Chemistry (published on-line April 1, 2006)

**Exhibit C:**

Maharaj, SVM, Lykissa, ED. Total platinum in urine of women exposed to silicone breast implants and in their children conceived after implantation by ICP-MS. Abstract presented to the American Chemical Society Meeting 2005

**Exhibit D:**

Lab reports for Subject #47 and 47a (son born 7/5/01 – four years after Mother's implantation and tested for urine platinum on 5/4/05)

**Exhibit E:**

Lab reports for Subject #53

**Exhibit F:**

Miller, CS, Prihoda, TJ. A controlled comparison of symptoms and chemical intolerances reported by Gulf War veterans, implant recipients and persons with multiple chemical sensitivity. Toxicology and Industrial Health (1999) 15, 386-397

**C. Environmental Impact**

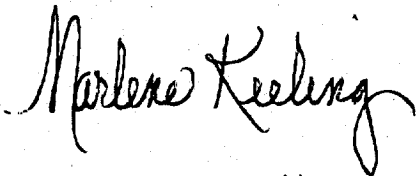
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**Exhibit C:**

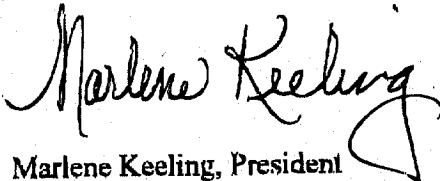
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Food and Drug Administration  
Department of Health and Human Services, Rm 1060  
5630 Fishers Lane  
Rockville, MD. 20870  
FAX 301/827-6870

Attn: Lyle Jaffe

This letter confirms my authorization to release test results stamped confidential with names and identifying markers removed as part of the citizen petition filed 4/6/06.



Marlene Keeling, President  
Chemically Associated Neurological Disorders  
P. O. Box 682633  
Houston, Tx. 77268-2633  
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keeling.m@worldnet.att.net

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