

CITIZEN PETITION

November 18, 2003

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services, Rm 1061
5630 Fishers Lane
Rockville, MD. 20852
FAX 301/827-6870

Re: Silicone Gel-filled Breast Implants

The undersigned submits this petition under 21 C.F.R. 10.35 to request that the Commissioner of the Food and Drug Administration (FDA) delay approval of any and all Premarket Applications ("PMAs") for silicone gel-filled breast implants (SGFBIs) until additional valid long-term scientific data is collected. 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 the action concerned in the petition is finalized. In addition to the conditions agreed upon by Inamed, we request that the following conditions be met:

A. Action Requested

1. We request that the FDA require long-term research (age-matched to core study participants in a control group) regarding symptoms including, but not limited to, the following: muscle, joint, neurological (including depression), muscle pain, joint pain, morning stiffness, fatigue, and generalized pain. This study should be funded by Inamed but conducted and reviewed by an independent third party. The third party must be independent of plastic surgeons as well as all companies manufacturing breast implants.
2. We request that platinum (including valence) testing and measurements be conducted in connective tissue (scar capsule tissue) and explants in a retrieval study. Included in this platinum study would be chemical and metal sensitization studies of women who have reported leaking or ruptured implants where platinum has been used as the catalyst in the manufacturing process.
3. We request that the FDA require a breast-milk study using appropriate measurements of low molecular weight silicone, particulate debris, heavy metals, and cytokine levels to determine safety of breast milk from implanted mothers versus controls. This study should be funded by Inamed but conducted and reviewed by an independent third party.

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4. We request *in-vivo and in-vitro* testing for biological responses to silicone elastomer particles, less than 10 micrometers in size. This testing is needed to determine a cellular response to particulate debris in a retrieval study, which should include monocyte, macrophage and fibroblast responses.
5. We request that blood be drawn on an annual basis from all women in the Inamed core study. This blood should be tested for natural killer cell counts and for inflammatory and anti-inflammatory cytokine levels. This blood should then be stored for future research.
6. We request that the expected serviceable life of the implant while in the human body be determined and stated in the informed consent along with the expected shelf life.

B. Statement of Grounds

- The General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee voted 9-6 to approve Inamed's SGFBIs, with conditions. This panel included four plastic surgeons – one with a stated conflict of interest – and two breast surgeons. While plastic surgeons should be included on the panel for their expertise, they should be excluded from voting, as they or their colleagues will financially benefit if the device is approved.
- One member of the panel stated she decided to vote for approval after she heard Inamed's summation, proposal of conditions for approval, and commitment to follow-up. Unfortunately, the best predictor of future behavior is past behavior. In Inamed's "Adjunct" study of reconstruction patients barely half stayed in the study for one year and even fewer (27%) stayed for three years. The revision patients were even less likely to stay in the study. Less than half (44%) stayed in the study for one year and only one in five (20%) stayed for three years. Inamed had only a 57% rate of follow-up for reconstruction patients after approval of their saline-filled breast implants was obtained. Their follow-up for augmentation patients was only 62%. Neither is high enough to assure adequate follow-up at ten years, as the FDA has required. Manufacturers have shown time and again that they have no incentive or motivation on follow-up.
- Some members of the panel voiced "shock" that only one, two and three years of data were provided for consideration. Inamed stated on October 14, 2003 that the implants under review had been used for ten years in the U.S. and for twenty-five years in Europe. Even after this amount of time Inamed still has not been able to provide studies showing long-term implant safety. This is a red flag and raises questions of caution and concern.

- In 1992, the FDA announced its decision to allow SGFBIs on the market only under controlled clinical studies for reconstruction after mastectomy, correction of congenital deformities, or replacement of ruptured SGFBIs due to medical or surgical reasons. Until these clinical studies could be submitted and reviewed, the FDA authorized temporary and limited distribution of silicone gel-filled implants for reconstructive patients on an urgent need basis, with a very detailed informed consent form.
- The FDA denied applications for using SGFBIs for augmentation but planned that the manufacturers would later conduct clinical trials that would include a limited number of augmentation patients (the core studies).
- On July 24, 1992, the FDA approved Mentor Corporation's Stage 2, Adjunct Study protocol for silicone gel-filled implants for reconstruction and revision only. A memo (attached as Exhibit A) dated 9/25/92 from St. John's Regional Health Center, Springfield, Missouri to the Institutional Review Committee (IRC) members regarding the "Mentor Adjunct Study of Silicone Gel Breast Implants" makes the following statements:

"Our subcommittee had a number of concerns about the design of this study and the consent form. The protocol did not appear to us to be a 'research study' in any familiar sense of that term.

- a) There is no accrual goal. The study is simply open for five years to any women who qualify. Participants are to be followed for five years.*
- b) There are few exclusion criteria...*
- c) Inclusion criteria are very subjective and general.*

The consent form omitted a good deal of information that we believed should be revealed. In one section we found an outright error (when compared to information given in the protocol itself). Tobias Meeker called Dr. Grant Bagley of the FDA...Dr. Bagley represented 'the clinical point of view' for the FDA team...A National Advisory Commission (NAC) was formed to review the status of silicone breast implants. The NAC recommended that a PMA should be required for marketing of silicone gel-filled breast implants. But the NAC also states that these devices should continue to be widely available to persons in unusual circumstances who would have medical need for them. To this end, the commission recommended that there be a limited core study that would be quite controlled and an adjunct study that would make the devices widely available (since not everyone with

medical need – due to location or whatever – would be able to qualify for a traditional clinical trial.) The Mentor 'study' is designed to serve this latter purposes. Dr. Bagley said of this protocol: 'It is an administrative device to continue to make these devices widely available to those who have such need that the lack of established safety can be over- looked if there is a good informed consent process and the oversight of an IRC... One of the surgeons who hopes to do these procedures met with us... His understanding that this protocol was designed 'to give the illusion of a study' so that the devices could remain on the market... We feel that we are being asked to rubber-stamp a political solution to this highly politicized issue. This 'study' will recklessly put many women at risk. Asking IRCs to behave in this manner violates their mandate and calls into question their integrity. It appears to us that the FDA has lost its objectivity."

- On 11/4/92, Tobias Meeker, Director, Ethics Program at St. John's sent a letter (Exhibit B) to David Kessler, M.D., Director, FDA expressing his concerns regarding Mentor's adjunct study. He reiterates many of his grave concerns expressed in the above memo including the following:

"A woman could simply report to a surgeon that she didn't like the appearance of her breasts due to say – ptosis – and medically 'qualify' to have reconstruction with silicone gel... We realize that many plastic surgeons have firm convictions that the silicone poses no health risk. We respect their convictions, but point out that strong convictions do not constitute scientific evidence... FDA has concluded that women who desire breast augmentation are at higher risk than patients with breast cancer who have had a mastectomy

Unlike patients who have undergone mastectomy, they still have breast tissue and the presence of an implant complicates the use of mammography for the detection of breast cancer. In the end, it comes down to this: In our opinion the risk-benefit ratio does not at this time favor the unrestricted use of silicone breast implants in healthy women. The design of the Mentor adjunct study belies the concerns you (Dr. Kessler) expressed. This study makes these devices widely available to women who have not had mastectomies. If women are to be offered these implants outside of scientifically valid studies, we believe this offer should be restricted to the present 'urgent need' population... To assume that a good consent process (with IRC oversight) will protect subjects from unjustified risks strikes us as a faulty assumption. This implant is a product with unproven safety and demonstrated (but unproven) risks. Further, we are concerned that misrepresenting this 'administrative device' as a legitimate scientific study misleads potential recipients, making it more difficult for them to assess risk."

- We believe the same agreement was made with McGhan (now Inamed Corporation). Many plastic surgeons have built their own outpatient surgical facilities to circumvent the concerns expressed by the Institutional Review Committee in the above memo and letter. We request, as consumers, a more detailed explanation of the FDA's design and approval of the AR-90 and adjunct study to determine long term risk in light of the above memo and letter. We request, as consumers, to know why we do not have ten or more years of data from a well designed clinical study to determine long term risk for reconstruction and revision patients. According to Inamed's documents, their 5-year adjunct study for reconstruction patients started on 11/25/97 and ended 8/22/02 with a follow-up compliance of 27% at 3 years. We request, as consumers, to know why the follow-up of the adjunct study by Inamed had such low compliance rates to thereby, render the data useless. Consumers can only have true informed consent when they know the risks they can expect and are willing to accept. Two or three years of data are inadequate to determine risk for a device that will be implanted and not removed until suspected of being ruptured.
- When silicone gel-filled devices are implanted into young woman of childbearing age, they can possibly pass chemicals such as low-molecular weight silicone, degradation particles, and ionized platinum to children born after implantation either through the placental barrier or in breast-milk. Research by Holten et al., 1995 documents a case report (attached as Exhibit C) in which silicone accumulated in the lactiferous ductal system of the breast with the underlying prostheses being intact. It demonstrated the disconcerting potential of silicone to migrate through tissue planes that were not disrupted. Inamed currently states on their website regarding breast-feeding and children "*A woman with breast implants who has questions about risks while pregnant or breast feeding should consult her physician.*" Until the proper testing is conducted on breast-milk from implanted women and the long-term clinical studies are completed, it is impossible for a physician to advise a pregnant woman with implants on risks.
- Some members of the panel expressed "alarm" that all symptoms including muscle, joint, neurological, muscle pain, joint pain, morning stiffness, fatigue, and generalized pain increased after only two years of implantation. The panel did not have a control group of age-matched women (other plastic surgery patients without any type of implant) and in the general population to determine the significance of this data. Therefore before these devices are approved, we request a study control group to be evaluated yearly. We request that this study be funded by Inamed but conducted and reviewed by an independent third party. Depression should be added to this list of symptoms in light of three studies indicating a three-fold increased rate of suicide by breast implanted women – Brinton et al., 2001 (Exhibit D), Koot et al., 2003 (Exhibit E), and Pukkala et al., 2003 (Exhibit F).
- At the hearings the FDA admitted the issue regarding systemic disease and mixed connective tissue disease in implanted patients has still not been resolved.

- In U. S. patent number 6,251,137 (Exhibit G) filed 6/26/01 by McGhan (now Inamed) it states: "Silicone filled implants typically comprise about 10-20% cross-linked silicone which forms an interconnected 'sponge' in the implant with the remainder of the filler material being low molecular weight silicone oil... adverse medical consequences have recently become associated with the use of silicone gel filled implants because it has been discovered that the silicone oil can migrate through the implant shell and the silicone oil is not biocompatible with other human tissues". This information presents grave unknown safety risks.
- In 1999, research from Teuber, et al., (Exhibit H) states: "Silicone gel once it leaves the implant is not biologically inert and in some persons can elicit profound pathogenic responses... an unexplained change in the chemical composition of the implanted silicone gel, rendering it more fluid-like, may have increased its propensity to migrate locally. Unfortunately, little research has been performed on biodegradation of silicone in the body, although there is evidence that this may occur... the implants and extractable gel/fluid were sent to the manufacturer (McGhan Medical Corporation, Santa Barbara, CA, USA) for analysis, but no information is available on the results of the analysis to determine if the ratio of polymer chain length had shifted... the relentless inflammatory response against widespread silicone has already resulted in the near total loss of function of the hand... no doubt can remain that silicone can induce severe, devastating local inflammation." Breast implant manufacturers have known since 1978 about potential migration of silicone gel when research reported by Capozzi et al., (Exhibit I) documented that thin gel had migrated through subcutaneous planes as far as the groin from a ruptured breast implant.
- Inamed reported 30 days after implantation, 0.06% of radio labeled gel left the implant site. At the hearing, one of the members of the panel made the observation that Inamed reported in their retrieval collections none of the implants lost more than 5 grams of material. The member of the panel stated: "In orthopedics, a half a gram would cause osteolysis in the same time period, so 5 grams is actually a 'whopping' amount of material." He further stated: "If you had 5 grams distributed kind of uniformly rather than in a lump, it possibly could be missed in visual observation by the explanting surgeon." In orthopedics and joint replacement, the most biologically active particles are ones that cannot be seen visually. Since 1995 the scope of wear-related problems in orthopedics has expanded to include not only the local effects of debris but also systemic distribution and effects, as reported in the book "*Implant Wear: in Total Joint Replacement*". According to the authors, both implants and the wear debris they generate are thought to release chemically active metal ions. The inflammatory response to metallic and polymeric debris in lymph nodes has been found to include immune activation of macrophages and associated production of cytokines. Before approval of this device, consumers need to know how much gel can be predicted to leave the implant site after ten or more years of implantation or after rupture. Sam Arepalli, PhD., FDA Chemist, stated that even with a barrier layer you could not completely eliminate bleed of the gel from an implant. There is

presently no way to remove the gel, particle debris, and platinum after it has spread to all parts of the body.

- One of the members of the panel expressed his concern that there seemed to be a disconnect between Inamed's testing showing how difficult it was to rupture a new implant and what actually happens in the body. This disconnect could be explained by 1998 research by Adams, et al, (Exhibit J) which found: "Ninety-eight percent of implants and other previously implanted silicone devices were found to have evidence of lipid infiltration... We conclude that lipids infiltrate the outer silicone shell and may be a factor related to breast implant aging and rupture due to progressive mechanical weakening of the outer silicone shell." This disconnect might also be explained by the 1995 research by Tang, et al., (Exhibit K) which made the following conclusion: "Chronic inflammatory processes, in many cases in response to fragments of implanted biomaterials, may cause implant failure... In some instances, material-mediated inflammatory responses may even cause degradation of the material itself (via oxidative products released by implant-associated inflammatory cells)." Before approval is given, Inamed should be required to conduct testing on explanted devices to determine if lipid infiltrates have weakened the shell strength, if chronic inflammatory processes have caused degradation of the material, or determine a logical explanation of rupture rates.
- We, as consumers, do not detect any real progress and request the FDA to inform us on the status of the research as recommended by the Institute Of Medicine (IOM) after a review of the safety of silicone breast implants in 1999. The IOM made the following recommendations:
 1. *"Reliable techniques for the measuring of silicone concentration in body fluids and tissues are needed to provide established, agreed-upon values and ranges of silicone concentrations in body fluids and tissues with or without exposure to silicone from an implanted medical device. Such developments could improve the study of silicones and silicone distribution in humans, could help with regulatory requirements, and might in some circumstances resolve questions by providing quantitative data on the presence or absence of silicones."*
 2. *Ongoing surveillance of recipients of silicone breast implants should be carried out for representative groups of women, including long-term outcomes and local complications, with attention to, or definition of the following:*
 - *Implant physical and chemical characteristics,*
 - *Tracking identified individual implants,*
 - *Using appropriate, standardized, and validated technologies for detecting and defining outcomes,*
 - *Carrying out associated toxicology studies by standards consistent with accepted toxicological standards for other devices; and*
 - *Ensuring representative samples, appropriate controls and randomization in any specific studies, as required by good experimental design.*

3. *The development of a national model of informed consent for women undergoing breast implantation should be encouraged, and the continuing effectiveness of such a model should be monitored*

- The FDA guidance document (Exhibit L) makes the following statement: "...for the metal used as the catalyst in the curing reaction, you should provide the valence state and the amount of residue of the catalyst." We request an explanation as to why the valence state of the platinum catalyst at the time of manufacture was not provided by Inamed. Dow notified the EPA (Exhibit M) on 12/27/96 of substantial risk to their 3-8015 Intermediate Platinum #2 used as a catalyst in making breast implants. This notification was the result of skin sensitization studies. Please advise if Inamed uses Dow 3-8015 Intermediate Platinum #2 as a catalyst in making the breast implants under current review. If not, please explain in detail the catalyst used and the safety data provided, as no published research is available.
- Recent German research by Flassbeck, et al, 2003 (Exhibit N) "*Determination of Siloxanes, Silicon, and Platinum in Tissues of Women with Silicone Gel-filled Implants*" demonstrates that for the first time in published research, platinum leaks from intact prostheses and accumulates in a lipid-rich medium analogous to fat tissue or fibrous tissue in humans. Further this research clearly demonstrates elevated levels of the siloxanes D4-D6 in fatty tissue of a woman with a "bleeding" implant. The data from this work clearly show that the use of elemental silicon as an indicator of migration from breast implants to the surrounding tissue is not appropriate. In the FDA's letter (Exhibit O) dated 3/30/01 in response to my petition (Docket Number OOP-16-7/CP-1 Exhibit P) it quoted from the IOM's review of the potential toxicity of silicon and stated: "...there is ample evidence that infants breast-fed by mothers with silicone breast implants receive no higher silicon intakes than infants breast-fed by mothers without breast implants. Infants receiving cow's milk or commercial infant formula feedings are likely to have higher silicon intakes than breast-fed infants." The independent research by Flassbeck demonstrates that the Dow funded, Semple, et al., 1998 (Exhibit Q) study of elemental silicon is not an appropriate measurement to determine safety of breast-milk from implanted mothers.
- In the FDA's letter to CANDO dated 3/30/01 it stated: "The supplier of the platinum catalyst used to manufacture breast implants, and scientist who have studied the chemistry of these catalyst, have recently assured the FDA that chloroplatinic acid is consumed during the formation of these catalysts and is not present in the materials used to produce the implants." Inamed's data of metal analysis found the following: Shell Pt (3.3 PPM), Patch Pt (2.6 PPM), and Gel (4 PPM). With the Flassbeck research (2003) data showing platinum accumulating in human tissues, with the Maharaj research data showing significant platinum found in connective tissue of implanted women, and with the data presented to the FDA (Exhibit R) from Ernest Lykissa, Ph.D. suggestive that ionic platinum in various oxidation states may be present in explanted devices, it becomes imperative that the FDA require Inamed to quantify the amount of platinum and the valence state in explants, fluids, and tissues

in a retrieval study. Platinum is listed as a suspected respiratory, neurological, immune, and organ toxicant. Chloroplatinic acid is one of the most hypersensitizing agents known to man. Before approval is given for implantation of young women of childbearing age, Inamed and the FDA should determine if the platinum used in breast implants reverts back to its original form, at any time, after implantation.

- Naidu, et al., (Exhibit S) in 1996 research concluded that an acute in vivo inflammatory response to silicone elastomer particulate debris is particle-type specific and that silicone elastomer particles are acutely inflammatory. Because of concern over well documented "particle disease or chronic inflammatory syndrome" the following questions need to be answered before approval is given:
 1. How does silicone elastomer and gel age and degrade inside the body?
 2. How does the chemical composition of the shell or gel change during any stage of the degradation process?
 3. What size and how many elastomer particles can be generated inside the body in five or ten years?
 4. Does absorption of silicone fluid and body fats by the elastomer shell weaken and accelerate degradation and breakdown of the elastomer shell?
 5. Can these particles further physically degrade into smaller and more reactive particles inside the body?
 6. Can monocytes, macrophages and fibroblasts become activated, inside the body, when they ingest silicone elastomer particles and/or silicone fluid or gel droplets from silicone gel-filled breast implant and their shells?
 7. Can macrophages synthesize and release inflammatory and anti-inflammatory cytokines, inside the body, after they ingest silicone elastomer from the implant shell?
- The FDA stated that the finding of excesses of cancer including lung (or respiratory), cervical, vulvar, and leukemia in implanted women have been reported in more than one study. Inamed currently states on their website under cancer risks "At this time, there is no scientific evidence that women with silicone breast implants are more susceptible to cancer than other women." We believe this is inaccurate and misleading.
- Inamed reported a diagnosed rupture rate of 4.7% for breast cancer reconstruction patients, 2.2% for revision patients, and 1% for augmentation patients. The FDA assumed the rupture rate was higher than reported, since most of the data was based on the first MRI screening at 1 year and only 29% of the core group had an MRI. Augmentation and revision patients may lose all of their natural breast tissue if silicone from ruptured implants has to be scraped out of the tissues as reported by Vanessa Rose Ferrelli (Exhibit T) at the hearings. This presents an unacceptable outcome with high patient dissatisfaction.

C. Conclusion

For the above stated reasons, the Commissioner should delay the approval of any and all PMA's for SGFBIs until rupture rates and long-term risk has been ascertained and the conditions stated above have been met.

D. Environmental Impact

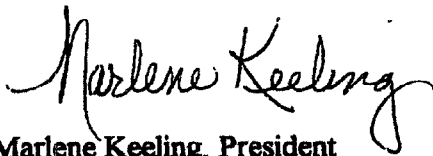
This petition qualifies for categorical exemption under 21 C.F.R. 25.15, 25.30-32 from the preparation of an environmental assessment.

E. Economic Impact

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

F. 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.



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Exhibits

Exhibit A:

Memo from St. John's Regional Health Center, Springfield, Missouri to the Institutional Review Committee (IRC) members regarding the "Mentor Adjunct Study of Silicone Gel Breast Implants".

Exhibit B:

Letter dated 11-4-92 to David Kessler, M.D. Director, FDA from Tobias Meeker, Director, Ethics Program at St. John's Regional Health Center, Springfield, Missouri

Exhibit C:

Holten, IW, Barnett, RA. Intraductal Migration of Silicone from Intact Gel Breast Prostheses. *Plast Reconstr Surg* 1995 Mar; 95 (3): 563-6 PMID 7870784

Exhibit D:

Brinton, LA, Lubin, JH, Burich, MC, Colton, T, Hoover, RN. Mortality among Augmentation Mammoplasty Patients. *Epidemiology* 2001;12: 321-326

Exhibit E:

Koot, VCM, Peeters, PHM, Granath, DE, Nyren, O. Total and cause specific mortality among Swedish women with cosmetic breast implants: prospective study. *BMJ* 2993; 326: 527-8

Exhibit F:

Pukkala, E, Kulmala, I, Hovi, SL, Hemminki, E, Keskimaki, I, Lipworth, L, Buice, JD, McLaughlin, JK. Causes of Death Among Finnish Women with Cosmetic Breast Implants, 1971-2001. *Ann Plast Surg* 2003;51: 339-342

Exhibit G:

U. S. Patent number 6,251,137 filed 6/26/01 by McGhan (now Inamed Corporation)

Exhibit H:

Teuber, SS, Reilly, DA, Howell, L, Oide, C, Gershwin, ME. Severe Migratory Granulomatous Reactions to Silicone Gel in 3 Patients. *J Rheumatol* 1999;26: 699-704

Exhibit I:

Capozzi, A, Dubou, R, Pennisi, VR. Distant Migration of Silicone Gel from a Ruptured Breast Implant. *Plast Reconstr Surg* 1978 Aug; 62 (2) 302-3 PMID 353852

Exhibit J:

Adams, WP Jr, Robinson JB jr, Rohrich RJ. Lipid Infiltrations as a Possible Biologic Cause of Silicone Gel Breast Implant Aging. *Plast Reconstr Surg* 1998 Jan; 101 (1): 64-8 PMID 9427917

Exhibit K:

Tang, L, Eaton, JW. Inflammatory Responses to Biomaterials. *Am J Clin Pathol* 1995 Apr; 103-4 PMID 7726145

Exhibit L:

Guidance for Saline, Silicone Gel, and Alternative Breast Implants; Guidance for Industry and FDA.

Exhibit M:

Dow Corning letter dated 12/27/96 to U. S. Environmental Protection Agency. Dow Corning letter to FDA dated 1/28/97 in compliance with the Toxic Substances and Control Act. Agenda for Dow Corning/ FDA meeting 3/18/97. Dow Corning Mammary Implant Material Formulation (includes chloroplatinic acid 3-8015 INT PLATNM2).

Exhibit N:

Flassbeck, D, Pfeleiderer, B, Klemens, P, Heumann, KG, Eltze, E, Hirner, AV. Determination of siloxanes, silicon, and platinum in tissues of women with silicone gel-filled implants. *Anal Bioanal Chem* 2003;375: 356-362

Exhibit O:

FDA letter dated 3/30/01 in response to Chemically Associated Neurological Disorders (CANDO) petition Docket Number OOP-1607/CP-1 filed 11/7/00

Exhibit P:

CANDO petition Docket Number OOP-1607/CP-1 filed 11/7/00

Exhibit Q:

Semple, JL, Lugowski, SJ, Baines, CJ, Smith, DC, McHugh, A. Breast Milk Contamination and Silicone Implants: Preliminary Results Using Silicon as a Proxy Measurement for Silicone. *Plast Reconstr Surg* 1998;102: 528-532

Exhibit R:

Lykissa, E. Speciation of Platinum in Whole Blood Samples Compared to Speciation of Platinum Released From Subject's Implant. Platinum in Samples of Women with Silicone Gel-filled or Silicone Saline Implants and Their Children.

Exhibit S:

Naidu, SH, Beredjicklain, P, Adler, L, Bord, FW Jr, Baker, DG. In Vivo Inflammatory Response to Silicone Elastomer Particulate Debris. J Hand Surg (Am) 1996 May; 21 (3): 496-500 PMID 8724486

Exhibit T:

Statement at 10/14/03 FDA hearing by Vanessa Rose Ferrelli

Other References

Maharaj, SVM, Platinum Concentration in Silicone Breast Implant Material and Corresponding Connective Tissue by Inductively Coupled Plasma-mass Spectrometry. 2003., pers. comm..

Wright, TM, Goodman, SB (eds). Implant Wear: In Total Joint Replacement. American Academy of Orthopaedic Surgeons, Rosemont, IL. 2000

Ojo-Amaize, EA, Lawless, OJ, Peter, JB. Elevated Concentrations of Interleukin-1beta and Interleukin-1 Receptor Antagonist in Plasma of Women with Silicone Breast Implants. Clinical and Diagnostic Laboratory Immunology 1996; 3: 257-259

Empl, M, Renaud, S, Erne, B, Fuhr, P, Straube, A, Schaeren-Wiemers, N, Steck, AJ. TNF-alpha Expression in Painful and Nonpainful Neuropathies. Neurology 2001 May 22; 56 (10): 1371-7 PMID 11376190

Deprez, M, Lubke, U, Verlaet, M, Debrus, S, Delvenne, P, Martin, JJ. Detection of Cytokines in Human Sural Nerve Biopsies; an Immunohistochemical and Molecular Study. Acta Neuropathol (Berl) 2001 Apr; 101 (4): 393-404 PMID 11355311

Lindenlaub, T, Sommer, C. Cytokines in Sural Nerve Biopsies from Inflammatory and Non-inflammatory Neuropathies. Acta Neuropathol (Berl) 2003 Jun; 105 (6): 593-602 PMID 12734666

The following organizations support this petition:

Toxic Discovery Network - Missouri
United Silicone Survivors of the World – Houston Chapter
The Breast Implant Information Exchange - Illinois
Silicone Solutions Outreach - Louisiana
United Silicone Survivors of the World – New Mexico Chapter
National Silicone Implant Foundation - Texas
United Silicone Survivors of the World – Florida Chapter
Implant Veterans of Toxic Exposure - Idaho
Coalition of Silicone Survivors - Colorado
Silicone, Saline Information Support System – Nevada
Cen-Tex Silicone Implant Support – Texas
Toxic2KIDS - Missouri
Members of Saline Support Internet Support Groups (Yahoo)
In The Know – California
United Silicone Survivors of the World – Ohio Chapter
Children Afflicted by Toxic Substances – New York
Command Trust - California
Humantics Foundation for Women
United Silicone Survivors of the World – Oregon Chapter

TO: Dockets Management Branch

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**I am sending this petition by FAX and by mail (which includes all of the exhibits.)
Please confirm your receipt of this information.**
