Exhibit H

Expert Advisory Panel on Breast Implants
Record of Proceedings
(September 29-30[1], 2005)

Note: This Record of Proceedings has been edited for confidential information in accordance with the Treasury Board Manual - Policy & Guidelines on Security; the relevant Sections of the Access to Information Act are indicated in [ ] where information has been removed.

The Expert Advisory Panel on Breast Implants was mandated to provide scientific, medical and clinical advice on current and emerging issues related to safety and effectiveness of breast implants.

Health Canada took a phased approach to reviewing and assessing license applications to sell silicone gel-filled breast implants in Canada, with public input being an integral part of the decision making process. In the first phase, a Scientific Advisory Panel (SAP) was convened on March 22-23, 2005 to consider questions posed to them by Health Canada on emerging issues related to the safety and effectiveness of silicone gel-filled breast implants. The second phase of the assessment was a combined Expert Advisory Panel (EAP) meeting and public forum on September 29-30, 2005. The EAP heard presentations from stakeholders, patient groups, consumers and members of the public. The public also made their views known to the EAP by providing their input online, or by mail or facsimile. Health Canada will consider the advice received from the EAP, which includes many of the original members of the SAP, during its regulatory review of these medical device license applications.

The EAP (Panel) members were provided with:

- evidence submitted to the Therapeutic Products Directorate (TPD) by the manufacturers (Inamed and Mentor) in support of specific breast implant license applications
- copies of the September 29th presentations of the manufacturers
- public briefing documents from the manufacturers posted on the Health Canada website
- copies of the presentations and/or background documents from the public presenters who provided this material
- public views provided online, or by mail or facsimile

The Panel had the opportunity to hear presentations from both companies and the public presenters on September 29th and ask questions for clarification purposes.

[1] The record reflects proceedings of the second day only

The Panel was requested to address the following areas for the standard gel-filled implants:

1. Preclinical Data:

   a. Has the extent of gel bleed been adequately investigated, and have questions regarding the potential health effects of any exposure to low molecular weight silicones been addressed?
   b. Have the potential mechanisms of rupture been adequately studied, to the extent that the lifetime of these devices *in vivo* can be sufficiently described in the patient labelling?

2. Clinical Data:

   a. Is the data provided sufficient to establish how the devices perform *in vivo*?
   b. Is the data adequately presented in the proposed product labelling?

3. Labelling:

   a. Should additional information be provided to patients and physicians with regard to proactive implant follow-up procedures specific to the Canadian context?
   b. Have issues pertaining to recent literature regarding women who undergo augmentation procedures and a potential association with suicide been adequately addressed?
   c. Are the reported second generation effects, such as lower birth weights adequately documented, and should they be discussed in the labelling?
   d. Should additional information or physician training be provided to surgeons, regarding implantation best practices to help minimize complications?

The Panel deliberated on the provided questions during the second day of the meeting on September 30th. This record reflects proceedings of the second day only.

Question 1.a

Has the extent of gel bleed been adequately investigated, and have questions regarding the potential health effects of any exposure to low molecular weight silicones been addressed?

Background

Gel bleed studies are used to determine how easily the oil in the gel migrates from the implant to the surrounding tissue and beyond. This is traditionally tested by placing the implant on a material that is absorbent for silicone, customarily another silicone, and measuring the rate at which the material leeches out ($g/week/cm^2$). This test lasts several

weeks, and the rate of bleed tends to decrease over time. These tests are designed to be a worst-case scenario, a gross overestimation of what would occur *in vivo*, and are accelerated to allow for a preclinical assessment of various device designs.

Inamed additionally used a variation of this test, with hydrocarbon-modified disks, to obtain data that has more relevance to hydrophobic hydrocarbon domains found *in vivo*. The rates of bleed measured in these tests were less than those measured into silicones, as expected.

Mentor developed a new test that measures diffusion into a physiological fluid (porcine serum) to better mimic live tissue. Very low rates of diffusion of silicone were measured into this predominantly aqueous environment.

Long-term clinical studies seem to indicate no significant loss of mass post-implantation, thereby substantiating the idea that the preclinical data, particularly into silicone or hydrocarbon discs, overestimates the situation *in vivo*.

Both companies fulfilled the requirements for gel bleed testing and completed additional testing as well. There are two aspects of preclinical gel bleed studies to be considered: how much material leaves the implant to the local biological environment (*e.g.*, capsular tissue); and what effect does gel bleed have on the physical properties of the shell.

In vivo results from the literature

In order to consider a real life, *in vivo* situation, the levels of silicones in explanted breast tissue must be assessed. A single small study from literature in the material provided found a higher silicone content in women with implants (3 patients, 8 - 1333 ng/g of low molecular weight cyclic silicones in tissue) than in non-implanted patients (3 patients, low molecular weight silicones not detected) but the significance of this single, very small study is unclear.

Materials Performance

It was stated that gel bleed has decreased in the newer generations of breast implants under consideration by the panel, including those with textured surfaces, and that gel bleed does not cause, nor is associated with, product rupture. The risks associated with the clinical consequence of gel bleed, new barrier shells, etc., seem to be similar to saline. There have been no studies to indicate that gel bleed is consequential.

[Section 20(1)(b)]

Low Molecular Weight Silicones

Silicones do not dissolve in water to a significant degree. Low molecular weight (LMW) silicones are only marginally soluble in water, and there is essentially no solubility for larger compounds/polymers. There is very little LMW silicone initially present in these implants. There have been no successful preclinical tests to demonstrate that high molecular weight silicone will migrate into an aqueous based solution.

The companies examined the amount of LMW silicones (D4, D5 and D6) that are free to migrate from the implant into systems *in vivo*. In a 1991 study using unrestrained gel, silicones (including LMW silicones) were carbon 14 tagged and it was found that less than 1% leaves the implant. Other studies have demonstrated that the biological half-life of D4 (10-50 days) is such that LMW silicones that do leach from the implant will be eliminated from the system fairly quickly. It was therefore concluded: i) that the amounts of LMW silicones leaching out of implants are not high, and ii) the quantities of silicone bleeding from the implant are far below the level at which toxic effects would be expected (see, however, the section below on immunotoxicology).

Care must be taken in selecting the controls used in testing, as there are many other forms of silicone exposure in the daily environment. For example silicones are found in shampoo conditioners, in deodorant, in beer *etc*. In the case of diabetics it has been calculated that after 15 years of using lubricated syringes, they would have been exposed to as much as 3 - 4 grams of silicone without, to date, any association between the silicone and clinical consequences. Exposure rates from the implants are comparable or lower, based on weight changes from retrieval studies. Ultimately to understand all the effects of silicone *in vivo*, further data is needed.

From the toxicological point of view, the immune system can be a target for toxic chemicals, therapeutic drugs, or any foreign substances called xenobiotics. The adverse effects of xenobiotics can be observed at different levels: organ, cells and molecules. Immunotoxicity has been defined as the adverse effects on the immune system of foreign substances. A chemical substance should be considered immunotoxic when undesired events of the chemical are: (i) a direct and/or indirect action of the xenobiotic (and/or its biotransformation product) on the immune system; or (ii) an immunologically-based host response to the compound and/or its metabolite(s), or host antigens are modified by the compound or its metabolite(s). These undesirable effects of xenobiotics were classified in two main categories; the alterations of normal immune responses through an immunodepression or an immunopotentiation which will consequently modify the host defense mechanisms, or the induction of abnormal immune responses such as allergy and autoimmunity.

For the immunotoxicology assessment, both companies provided appropriate information to show that they are not immunosuppressive materials by using the Tier I and II Assessment Protocols. However, peer-reviewed literature at least brings into question the potential of silicones and/or implant devices to induce autoimmune or hypersensitivity reactions.

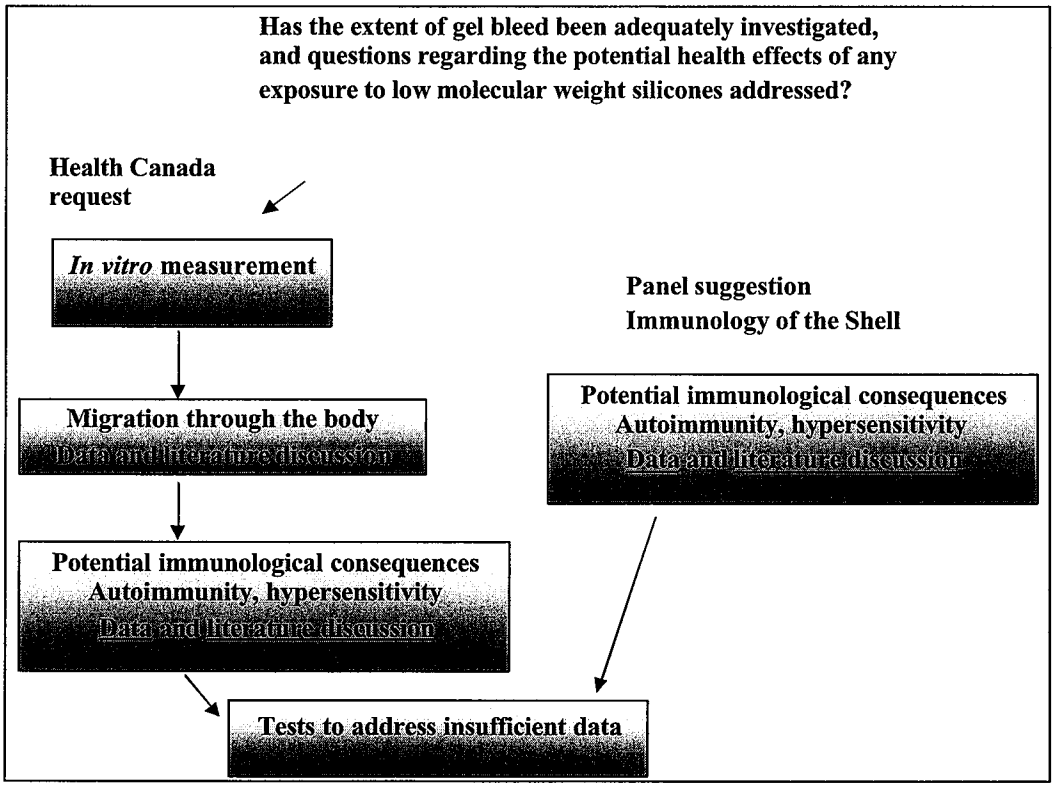
Therefore, Inamed and Mentor should consider the following (Figure 1):

1. There should be a complete review of the published literature on the potential of silicones and/or implant devices to induce autoimmune or hypersensitivity and an appropriate critical analysis.

2. Preclinical testing should address this point using animal models (according to peer-reviewed literature).

3. If possible include in clinical studies the monitoring of immunological endpoints to address this issue.

Figure 1: Flow chart to consider immunotoxicology; Items to be performed are underlined



Conclusion

Both companies have fulfilled the requirements for gel testing. The potential toxicities were identified and appropriately considered.

The updated three year Clinical Trial Data *in vitro* information is sufficient, but long-term data will be necessary to determine if there are any unidentified risks. Overall, no disease process was illustrated, bleed rates are well below toxicological thresholds.

Quantities of bleed reported are insufficient to cause concern with respect to health risks.

It was stated that a battery of tests has shown that the products are safe.

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Recommendation

i) **The Panel felt that the questions regarding the potential health effects of any exposure to low molecular weight silicones had not been sufficiently addressed.**
ii) **The Panel recommends to Health Canada that the manufacturers must demonstrate that migrated silicone provides acceptable risks of hypersensitivity and autoimmunity by a critical review of company and literature data and, if necessary, by undertaking studies in animal models.**

Voting on Recommendation: 10 of 12 Panel members agreed with the recommendation

Question 1.b

Have the potential mechanisms of rupture been adequately studied, to the extent that the lifetime of these devices *in vivo* can be sufficiently described in the patient labelling?

Background

There are American Society for Testing and Materials (ASTM) guidelines for determining the mechanical properties and structural integrity of the implant shell.

The following procedure is followed when evaluating an explanted device to determine the cause of failure:

1) visual inspection;
2) slightly squeeze product to see if there are any openings through which gel extrudes;
3) if a 'failed' region detected, that region is examined under a microscope (optical or scanning electron microscope); and
4) evaluate damage occurring from surgical incidences (primary cause of failure; suture needle or scalpel) identified by matching striations on implants to scalpel blade grind lines, and imprints due to needle tips.

Panel member agreed that the technique s used by the manufactures for testing these devices are appropriate and that potential failure mechanisms as well as the potential mechanisms of rupture have been adequately analyzed and addressed by both manufacturers.

The questions are: Why do we have failures *in vivo*? What is the lifetime of these devices *in vivo*?

Why do we have failures in vivo?

The known causes of implant rupture were reviewed by the panel:

1. Manufacturing defects
2. Improper implant handling prior to surgical procedure
3. Inadvertent needle sticks during suturing at implantation
4. Implantation surgery
5. Open capsulotomy
6. Closed capsulotomy
7. Needle biopsy or aspiration
8. Wrinkles or folds
9. Greater-than-necessary compression during mammography
10. Trauma
11. *In vivo* Processes
12. Explantation surgery

Although it was noted that the manufacturers have used state of the art techniques to prove durability and longevity of these implants, any device has to be used properly. In this regard, two issues were discussed. First, surgeons try to make small incisions so that there is very little scar tissue. The silicone gel implants are already full when implanted, and in some cases incisions are made to insert these implants are too small such that the surgeon has to force the implant through. There must be proper education and training for clinicians that use these devices. Second, it was noted that rupture is a breaking of the device and a fracture is permanent deformation of the device. The latter is more likely to occur in cohesive implants, and best practices indicate that incisions should be larger for cohesive implants to reduce the likelihood of gel fractures.

There was a comment on the phenomenon of swelling of the shell. After the implant is made, and even after being placed in the body, swelling of the implant shell may continue. The effect of swelling may decrease the mechanical properties of the shell. To evaluate this phenomenon, mechanical testing with explants and relevant controls would have to be conducted. Neither manufacturer has measured swelling as a function of implantation time. However, literature studies on implants suggest that the changes in mechanical properties as a function of shell swelling do not significantly hamper performance.

[Section 20(1)(b)]

What is the lifetime of these devices in vivo?

There are certain limitations on the data and prediction methods that are used for evaluating the lifetime of these devices.

Due to the fact that some of the data presented has been extrapolated over time it was recommended that a range on the lifespan of the device be included in the labelling in place of the statement 'This is not a lifetime device'. The suggested phrasing of this addition is 'We anticipate that you will require another implant by time X'. The re-operation rates generally fall into the range of 12 - 15 years. It may be difficult for a manufacturer to identify a specific value for the lifetime of the device; therefore, a broader range may be more appropriate.

Although patients should be made aware of the eventual failure of the device, there was not a clear consensus of whether the patients needed to be informed of the potential causes of failure.

[Section 20(1)(b)]

It was explained that the advantage of textured implants is that they develop a thinner, softer, more pliable capsule around the implanted device. A clinician generally uses a textured device with a contoured or anatomical shape (teardrop shape implant) in order to limit any change in its anatomical positioning. It was noted that there are texturing differences between manufacturers. Inamed's Biocell textured implants form an excellent, almost Velcro like, adherence to the capsule. ***[Section 20(1)(b)]***

Panel members felt that the informational brochures that are provided to patients adequately address the necessary information regarding the lifetime of the device. The rupture rates are included in the patient consent forms, but are not differentiated by type. It was suggested that the information could be elaborated on by differentiating the types of rupture and perhaps the rates of rupture for different classifications of surgery.

Conclusion

Potential failure mechanisms as well as the potential mechanisms of rupture have been adequately analyzed and addressed by both manufacturers. Clinical significance should dictate whether a differentiation should be made in the types of rupture (symptomatic *vs.* asymptomatic, or silent *vs.* non-silent rupture) in the labelling. Manufacturers should continue retrieval and analysis studies.

Recommendation

i) **The potential mechanisms of rupture have been adequately studied. The manufacturers should provide details on the mode of failure due to local stress induced in the shell during implantation.**
ii) **The lifetimes of these devices *in vivo* have been adequately studied using good engineering practice. Due to the limited laboratory fatigue data, there is uncertainty associated with the predicted lifetime.**

iii) The patient labeling should acknowledge that the implant is not a lifetime device and that most likely the implant will need to be replaced with subs equent surgery.

Voting on Recommendation:
i) 12 of 12 Panel members agreed with the recommendation
ii) 12 of 12 Panel members agreed with the recommendation
iii) 11 of 12 Panel members agreed with the recommendation

Question 2.a

Is the data provided sufficient to establish how the devices perform *in vivo*?

Background

For their clinical data, both manufacturers have initiated 'core' and 'adjunct' studies. The panel views the core studies as being better designed, more controlled and resulting in data of better quality than the adjunct studies.

The Inamed clinical data on silicone-filled breast implants comes from three multi-center studies: (1) the prospective core studies: the Core responsive study (715 patients) and the Core cohesive study (941 patients); (2) the prospective adjunct study (about 40,000 patients); and (3) the European cross-sectional studies designed to obtain long-term rupture data using MRI screening for silent rupture: one for responsive gel implants (106 patients) and one for cohesive gel implants Style 410 (144 patients). In addition, two ongoing retrieval studies have been initiated providing insight into ruptures through analysis of devices explanted from the patients in the Core and Adjunct studies (266 responsive, 328 cohesive).

Complete four year data are available for the responsiveness study and complete two year data are available for the cohesive study. For the Core responsive study, the compliance rates were 83%, 89% and 83% for the augmentation, reconstruction and revision cohorts respectively. For the Core cohesive study, these rates were 90%, 89% and 90%.

Efficacy results: Patient satisfaction (two year) was high for the Core study patients: 94%, 94% and 87% for the augmentation, reconstruction and revision cohorts respectively for the Core responsive study; and 98%, 91% and 91% respectively for the Core cohesive study. There was some improvement in quality of life. For both Core studies, the augmentation cohort showed improvement in physical self-concept and body esteem related to sexual attractiveness at one year. All cohorts had improvement in quality of life measures for patient satisfaction related to breast size and shape. There was no change for general items such as overall self-esteem for augmentation and reconstruction patients in the Core responsive and cohesive studies.

Safety results: The rupture rate was very low. For the Core responsive study, the estimates at four years were 1.4%, 0% and 1.9% for the augmentation, reconstruction and revision cohorts respectively which includes suspected ruptures identified through MRI. For the Core cohesive study, there were no confirmed ruptures and one suspected rupture yielding rates 0.1%, 0% and 0% respectively at two years. The European studies found rupture rates based on MRI screening, and not confirmed by explantation, of 8% at a mean of 11 years in responsive study, and 1.0% at mean of six years in the cohesive study.

From retrieval studies, surgical damage was found to be the leading cause of rupture (75% of the 60 ruptured implants for responsive; 72% of 64 ruptured implants for cohesive). The surgical techniques associated with rupture were: use of sharp instruments, creation of a fold in the surface of the device during implantation, and straining the shell by forcing the implant through a small opening.

The Mentor clinical data on the safety and efficacy of gel silicone-filled breast implants comes from two multi-center studies: (1) the Core round study designed as a 10 - year prospective study (n=1007); (2) the Adjunct study designed as a five year open enrollment study for reconstruction and revision (80484 patients).

Data are available at three years post-implantation for 88% of eligible primary augmentation patients, 82% of eligible reconstruction patients and 87% of eligible revision patients. (Mentor also provided a three year report on the safety and efficacy of the Mentor round silicone gel breast implant (after enrollment, the 1007 patients were assessed at 10 weeks and 1, 2, and 3 years)).

Efficacy results: 97% of the augmentation, 98% of the reconstruction and 95% of the revision patients would have breast implant surgery again. For the augmentation cohort, self-esteem score, sexual attractiveness and chest score improved, the Medical Outcome Short Form 36 (SF-36) physical and mental component scores worsened but this disappeared after adjusting for age, and there was no change in self concept scale. For the reconstruction cohort, functioning improved, self esteem and self concept did not change, and chest score improved. For the revision cohort, there was no change in self concept and self esteem, no change in sexual attractiveness scale, and chest score improved.

Safety results: For the Core study, there were very few ruptures: 0.5% in the augmentation cohort, 0.9% reconstruction cohort, and 5.3% in the revision cohort (which included three patients with suspected rupture detected by MRI and one patient with confirmed rupture by explantation). Capsular contracture rates were 8.1%, 8.3% and 18.0% respectively for the augmentation, reconstruction and revision cohorts respectively, and reoperation rates were 15.2%, 26.6% and 27.9% respectively. The reasons for removal/replacement were patient request (31%, 15% and 14%) and capsular contracture (5%, 4% and 13%) for the augmentation, reconstruction and revision cohorts respectively. For the Adjunct study, 29% of the reconstruction and 21% of the revision patients returned for the five year visit. Very few ruptures occurred (0.5% in the

reconstruction cohort, 0.9% in the revision cohort) and removal and capsular contrature rates were, respectively, 14% and 14% for the reconstruction cohort, and 13% and 17% for the revision cohort.

There is no evidence in the data, submitted as part of the adjunct studies, of any apparent increase in autoimmune diseases with implants in the short term. The purpose of longer term data and a registry would be to continue to examine this issue as well as all issues of long term safety and efficacy.

The data from the Core studies were considered to be of higher quality. Several concerns were discussed regarding these studies:

(1) The study population consists of all patients receiving these devices from surgeons who have access to the devices and are in the study. These surgeons may not be representative of the larger community of practitioners that could be implanting these devices. If the study surgeons are the best skilled and trained then the safety and efficacy results may not be as good in the larger community. A profile of these surgeons should be provided in order to help assess the generalizability of the study results.
(2) The sample size is small but is based on an FDA guideline. No power calculations have been provided to indicate that the sample size is sufficiently large to detect safety and efficacy outcomes of importance.
(3) The core studies are ongoing and follow-up period is relatively short. In the public presentations, various presenters indicated that a time period of 5 to 10 years would be desirable.

Some members believe that the lack of a risk analysis on the exposure to general anaesthesia and surgery is a concern and is not well developed.

Recommendation

The data is sufficient to establish how the devices perform *in vivo*. However they do not address all aspects of long-term safety. Annual reports must be submitted that update on ongoing studies particularly up to 10 year follow-up and including an annual report from the Core Study. This annual report should also include a synthesis of clinical studies and feedback from the health care professionals (compiled either by manufacturer or Health Canada). This information should be provided by device and shell type. This information should be freely available.

Voting on Recommendation: 10 of 12 Panel members agreed with the recommendation

Question 2.b

Is the data adequately presented in the proposed product labelling?

Background

Panel members felt that the patient brochures lay out the information in a way that is accessible and understandable to patients. The data recorded in the report is the same as that of the labelling but is presented in different styles. There is a large quantity of information to convey in the labelling, and the tables are clear and concise but may not be as user friendly as the readable patient brochures. They inform the patient of how often she might expect to have more surgery in written as opposed to tabular form.

The primary focus is on labelling for the patient, but the information is also presented adequately to the surgeon, as they are the intermediary between the patient and the device manufacturer.

Under regulations, labelling is defined as everything that goes with the product. Currently labelling information is found in the sterile box that contains the implants. It was suggested that it made little sense that these materials be placed in the sterile box, as they should be given to patients for review and discussion before using the device. Most of these materials are provided to the physicians by the manufacturer at no extra cost.

Presently, identification cards with serial numbers, lot number, reference numbers, model numbers and other pertinent details are distributed to patients after their surgeries. This registration of devices by the manufacturer is voluntary at present but should become mandatory. It was noted that this presents advantages for patients who have to undergo re-operation and may have lost track of their original implants.

The information presented in the labelling information is a mixture of both core and adjunct data. Generally the core data will be better because it will have a higher follow up rate, whereas the adjunct studies have higher rates of loss or dropout, making their data more difficult to evaluate and less reliable. Inamed verbally presented three year data and Mentor presented two to three years of the standard gel implants. Due to lack of data provided it is difficult to determine rates and the manufacturers need to indicate where the data is coming from.

The panel had concerns regarding the mixing of core and adjunct data in the labelling. The recommendation is that the labelling information separate out the adjunct data, and clearly label data as core and adjunct. It was suggested that definitions of terms could be included in the labelling, since a layperson may not know the difference between a core and adjunct study.

More information should be included in the labelling on the following issues. Both manufacturers should revise the labelling on breast-feeding for breast reconstruction. The labelling should be clear that all breast tissue as well as the nipple is removed with breast reconstruction thus making it impossible for breast-feeding to occur. It was noted that

breast reconstruction may be performed for reasons other than mastectomy and therefore breast feeding is still a possible concern. The section for patients should include more information on mental health and body image.

It was noted that statements are included in some product labelling acknowledging that some women with breast implants believe that their implants have caused connective tissue disease, however, there is no scientific literature to support this at this time. Even so, it was suggested that all labels acknowledge that "some women with breast implants believe that their implants have caused connective tissue disease." Such an acknowledgement would promote informed decision-making and respect alternative sources of knowledge on this subject.

In general, the labeling should use more neutral language since this will avoid biased presentation of facts and coercive information and promote informed consent of patients.

Recommendation

Data is not adequately presented in the labelling. The information should not be enclosed in the sterile box with the product. It must be available for the patients to consider before surgery *via* both printed material and website. Identification cards with model and serial number provided to patient should be made mandatory. All of these recommendations should be equally applied to both companies.

Information in the product monograph should be thoroughly reviewed by Health Canada evaluators to ensure more neutral language in the patient and physician labelling.

The following contra-indications should be included in the labelling: clinical depression, eating disorders, desire to breast feed.

Patient Labeling:

Patients should understand that multiple surgical procedures on the breast may cause irreversible changes to the breast itself. Patients should discuss this issue carefully with their plastic surgeon if subsequent surgery is necessary.

Physician Labeling:

Patients undergoing multiple surgical procedures on their breast should be informed that subsequent procedures may cause irreversible changes to the breast and strong consideration should be given to implant removal.

Voting on Recommendation: 12 of 12 Panel members agreed with the recommendation

Question 3.a

Should additional information be provided to patients and physicians with regard to proactive implant follow-up procedures specific to the Canadian context?

Background

The usefulness of the article (Holmich, et al, EJR 2005) in the provided information package on Magnetic Resonance Imaging (MRI) detection of silicone breast implant rupture was questioned. For example, three MRI machines with different field strengths and inconsistent imaging protocols were used for the study, one machine lacked the ability to perform "silicone-specific sequences". In addition there was no breakdown provided of the types of implants that were evaluated by MRI study, *i.e.*, implant manufacturer, size of implants, type of implant (textured *vs.* smooth), *etc.* How applicable the findings of this article will be in reference to the new cohesive silicone implants was also questioned.

The results of this study yielded one false positive and nine false negatives for breast implant rupture.

The group discussed the perceived role of MRI for breast implant rupture. It was felt that the role of MRI was not certain based on the reference provided. Members were particularly concerned about the high frequency of false negative MRI examinations and felt that the false positive examination was worrisome as it resulted in the unnecessary removal of an intact implant. Members agreed that the scientific value of MRI screening must be determined prior to the manufacturers stating that MRI should be done to screen for implant rupture.

It was also noted that the implants that are being evaluated are different in that the silicone gel and the silicone outer membrane are more tightly bound to each other and the inner gel is much more solid in structure due to the cohesiveness that the manufacturers have created *via* new chemical properties of the gel.

It is possible that the silicone filled implants, particularly those filled with cohesive silicone, may have different MRI appearances compared to older silicone filled and saline filled implants. Further MRI analysis of these implants is warranted to better understand the imaging characteristics of these new devices.

How does MRI measure up as a diagnostic tool? When compared to the other imaging technologies such as ultrasound and mammography, MRI seems to be as good as, or may be better, for detecting certain abnormalities but the strength of evidence to support this is incomplete.

Studies have been performed comparing mammography *versus* MRI screening for breast cancer. MRI sensitivity and specificity, in recent publications, have been demonstrated to be as good as, or slightly superior to mammography, as a cancer detection tool, but accessibility and cost are definitely factors that will hinder MRI expansion in this area.

The panel members felt that all women should participate in screening for detection of breast malignancy. The presence of breast implants may require modification of the clinical examination and imaging regimens employed for malignancy screening, but this issue is not unique to silicone filled breast implants alone.

Members were particularly concerned about the current situation of very long waiting lists for patients requiring MRI examination. In reality, screening for implant integrity would probably not be deemed urgent and the individual would be required to wait quite a long time to access MRI in our current healthcare system. It may not be possible in some jurisdictions to insure an annual MRI for implant integrity. In addition, MRI is definitely more expensive than mammography or ultrasound, and the burden of cost may be transferred to the patient if imaging is deemed to not be medically warranted but rather be related to periodic, or scheduled surveillance of the implant integrity as suggested by the manufacturer.

Conclusion

Generally patients are encouraged to deal with their breast health as if they did not have implants. This is particularly relevant in reference to current established protocols for breast malignancy screening or diagnosis. All women with implants should adhere to these screening and diagnostic algorithms.

It was suggested that the process for determining implant integrity should be related to clinical signs and symptoms. The following represents a possible approach to suspected problems with implant integrity:

1 - patient self-examination
2 - new symptom or sign suspected,
3 - physician physical examination, related to a periodic review or new symptoms and signs, suggests findings that warrant further investigation,
4 - ultrasound, mammogram or both of the implant and the breast involved should be acquired,
5 - MRI if ultrasound is negative or inconclusive,
6 - explantation of suspected implant in consultation with the plastic surgeon.

Presently, the manufacturer's labelling indicates "MRI be done every 1 - 2 years or at a frequency determined by their plastic surgeon".

It was suggested that the recommendation for MRI screening for implant integrity be removed from labelling primarily due to lack of scientific evidence supporting its use, uncertainty about imaging appearances of cohesive silicone filled implants and issues related to timely access to MRI resources in our health care system. Certainly, the cost of MRI must also be considered as the patient may be required to bear the cost of implant integrity screening if it is not deemed to be an indication that warrants expedited access to MRI or funding from the public health care system.

Members felt that MRI should be used to investigate breast implant signs and symptoms and not be used for scheduled, or periodic, screening for breast implant integrity. The members expressed concerns about the possibility of facilitating a psychosomatic condition, in an otherwise healthy person, if one were to continuously check for implant failure not associated with breast signs or symptoms.

The manufacturers should be strenuously encouraged to meet the requirements of long-term (10 year) patient surveillance. In particular, further data should be gathered about the MRI features of the new cohesive silicone breast implants.

Recommendation

There is no current scientific evidence to reliably support repeated (every 1 - 2 years) breast MRI for patients with breast implants. Assessment of silicone filled breast implants should be at the discretion of the plastic surgeon, in consultation with the patient, and preferably be based on new breast symptoms or signs.

It is expected that manufacturers will complete their mandate to accrue 10 year data, including MRI, for any patients enrolled in company supervised research protocols.

Women should follow generally recognized guidelines for breast health.

Voting on Recommendation: 11 of 12 Panel members agreed with the recommendation

Question 3.b

Have issues pertaining to recent literature regarding women who undergo augmentation procedures and a potential association with suicide been adequately addressed?

Background

Although there is a relatively higher percentage of suicide among patients having undergone breast implant surgery, many of these patients had pre-operative psychiatric disorders including depression, body dysmorphic disorder (BDD) or an eating disorder

causing body dissatisfaction. Any of these disorders could have led to suicidal ideation before surgery.

Although body dysmorphic disorder is a rare condition, when present it is very serious. Surgeons should readily be able to identify BDD patients, but it is those patients whose psychiatric state is difficult to detect (for example, those patients with low self esteem who may believe that this surgery will solve all their problems), that would benefit from psychological screening and treatment prior to implantation surgery. It was stated that it would be advantageous if patients could be screened and those with some psychiatric issues have treatment before undergoing this type of surgery.

Although not all suicides are caused by clinical depression, a patient who is clinically depressed should not be undergoing anything but life-saving surgery. It was suggested that the following statement to be included in patient labelling: "Although no causal link was established between breast augmentation surgery and suicide, patients experiencing a clinical depression and/or an eating disorder are urged to seek psychiatric treatment and to postpone surgery until the complete resolution of their clinical depression." It was suggested that the following statement to be included in physician labelling: "Patients experiencing clinical depression and/or an eating disorder should be referred to a psychiatrist and their surgery postponed until the complete resolution of their clinical depression." Suggestions concerning a softening of wording could be "encouraged to seek further specialized assessment and management" rather than need for psychiatric assessment as there may be a stigma attached to psychiatric consultation.

Both patients and physicians need to be informed that there is an unusual presence of suicide in this patient population. The purpose of labelling is to safeguard the patient and to help patients struggling with psychological issues to make informed decisions, and to obtain the proper psychological support and care before their surgery.

Since breast augmentation surgery is mainly an elective body altering procedure, the onus may be better placed on the surgeon to thoughtfully discuss with the patient the goals, motivations and realistic expectation of outcomes. Unrealistic expectations on the part of the patient may be an indication that a recommendation for psychological counseling is needed prior to surgery. A large part of a plastic surgeon's education includes the assessment of patients for this kind of surgery, which is mainly elective.

Conclusion

Although no causal association was established between breast augmentation surgery and suicide, patients experiencing depressive and/or eating disorders are urged to seek professional assessment.

Recommendation

Insert for the Physician

Contraindications:

Patients presenting with body dysmorphic disorder, or any other psychosis.

Precautions:

Patients presenting with depression and/or an eating disorder, if untreated, should be referred for treatment before considering breast augmentation surgery. If they are in treatment, communication between the plastic surgeon and the treating mental health professional is strongly recommended.

Labeling for the patient

Although no causal link was established between breast augmentation surgery and suicide, patients with psychiatric disorders such as depression and eating disorders, should postpone the decision for breast augmentation, until the complete resolution of the depression and/or the eating disorder.

Voting on Recommendation: 12 of 12 Panel members agreed with the recommendation

Question 3.c

Are the reported second generation effects, such as lower birth weights adequately documented, and should they be discussed in the labelling?

Background

A study evaluating 2200 offspring of women having had breast implants, and using 20 controls, found no statistical significant difference in birth weight between infants of implanted *versus* non-implanted women.

There was a trivial but statistically significant difference in the small subgroup of women with multiple births after implant surgery. Transfers to other hospitals also had a statistically significant difference but the importance of this finding could not be ascertained. These two differences were concluded to be clinically irrelevant.

They also studied the dose response (*i.e.*, the longer the mother was exposed to the implant the more likely an effect would be seen on the infant) and no effect was found.

The study results were considered not to be robust. There were no clearly stated *a priori* hypotheses and large quantities of data were 'mined' for a number of different associations. Logistic regression was used to compare two very different groups and nothing of significance could be found. Therefore, there is not enough information to support inclusion in the labelling.

Difference between implant patients and non-implant patients for breast-feeding and the presence of silicone in milk was determined to be negligible. There is sufficient information on breast-feeding in the labelling from both manufacturers and therefore second generation effects should not be added.

Conclusion

There is no other history of second generation effects and not enough information to support inclusion in the labelling. There is sufficient information on breast-feeding in the labelling from both manufacturers and therefore second generation effects should not be added.

Recommendation

This information does not need to go into the labelling. Further research is needed to establish a mechanism of action.

Voting on Recommendation: 12 of 12 Panel members agreed with the recommendation

Question 3.d

Should additional information or physician training be provided to surgeons, regarding implantation best practices to help minimize complications?

Background

Additional training to be provided by the manufacturers to surgeons can be suggested in the use of these devices as they are highly specialized. The general feeling is that there would be little if any resistance in providing specialized training to surgeons in the implantation of these devices as inadequate surgical technique, implant selection and intraoperative decision making would increase the likelihood of complications and reflect badly on the device.

Inamed considered a proportional hazards regression model assessing five clinical outcomes; re-operation, implant replacement or removal, implant rupture, capsular contracture and infection, in relation to eleven patient, device and surgical characteristics.

Those eleven characteristics were patients' age, device height, device projection, device size, anaesthesia, surgical facility, incision site, implant placement, pocket irrigation with antibiotic and pocket irrigation with steroid.

For augmentation, no association was found for the clinical outcomes re-operation, implant rupture, capsular contracture or infection. They did find an association between implant placement and removal in relation to device height; for example, moderate height implants had a 2.7 times greater risk of implant replacement or removal than low projection.

For reconstruction, no association was found for the clinical outcomes in implant replacement or removal, implant rupture or infection. Re-operation rates were related to implant placement; implants with subglandular placement were twice as likely to require re-implantation as those placed submuscularly. A relationship was also found between the clinical outcome of capsular contracture and patient's age; implants in patients over 45 years of age were eight times as likely to develop capsular contracture than those under the age of 45. Possibly a confounding variable exists, as with increasing patient age there is increased ptosis and therefore increased subglandular implantation. This information is recommended to be presented to physicians in additional training.

Conclusion

There should be specialized training for physicians to ensure proper placement of these devices and to minimize the likelihood of suboptimal outcomes.

Recommendation

Strongly suggest that these specialized devices require additional education for the surgeon, since proper use is critical.

For patient labelling:

The data suggests that in order to obtain the best outcome it is recommended that surgery be performed by a plastic surgeon who received specialized training to perform the procedure.

The committee very strongly recommends that Health Canada only permit provision of these devices to Royal College certified plastic surgeons who have been specifically trained on the use and technique of these devices.

Voting on Recommendation: 12 of 12 Panel members agreed with the recommendation

Additional Recommendations

Establishment of a National Breast Implant Registry

The importance of a patient registry was discussed several times by the Panel during its deliberations. In particular, during the public presentations the concept of a registry was raised by the British Columbia Centre of Excellence for Women's Health. They provided a draft of a document on a breast implant registry and reviewed the international experiences with breast implant registries. The Panel concurs that a comprehensive breast implant registry would enhance our understanding of the safety and efficacy of these devices, improve our understanding of experiences with these devices, increase our ability for conducting research on a large representative sample of women, and increase our knowledge of the health care utilization implications.

Concerns were expressed about the number of devices that will be implanted outside the hospital system and the associated lack of accreditation and review compared to that in hospital.

A registry could be implemented and coordinated by a national organization such as the Canadian Institute of Health Information (CIHI), possibly in partnership with interested academic organizations.

Recommendation

The committee recommends that Health Canada establish a national breast implant registry.

Development of a Decision Aid for Making an Informed Decision

In the material provided by the manufacturers, there is information provided to the women on making their decision regarding silicone breast implants. However, the material provided is not a scientifically developed decision aid.

Some Panel members felt that the desire for augmentation as an indication for use of these devices could reinforce the concepts that some body shapes and sizes are better and more valued than others. This may contribute to body image and weight preoccupation, eating disorders and exercise excesses as a public health issue. Other members view the improvement of quality of life to be highly beneficial. It is in this setting of balancing harms and benefits that a decision aid is most useful.

An understanding of the benefits and harms of silicone breast implants is essential in making an informed decision. This decision can be very difficult and a properly designed decision aid is needed. This decision aid should be developed within a decision making framework taking into consideration decisional conflict, realistic expectations and knowledge. In particular, the decision aid will need to adequately reflect the information

that will be part of labelling including quality of life, the lifetime of these devices and issues related to body image and mental health.

Recommendation

The committee recommends that Health Canada develop a decision aid in helping women to make an informed decision regarding silicone breast implants.