

Poly Implant Prothèse (PIP) Breast Implants:
Report of the Chief Medical Officer

April 2012

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Preface

Chief Medical Officer, Professor Chris Baggoley

I understand that this has been, and will continue to be, a difficult time for many women who have PIP breast implants. Some women may be worried about their implants and the harm that they may cause, and they may still have unanswered questions.

This report aims to present the information we have at the moment, to provide answers to common questions and to assist women who have to make choices about their own PIP breast implants.

So far, scientific tests have identified some differences between the PIP breast implants and other brands of silicone breast implants, but these differences are small and do not indicate that there is an increased safety risk associated with PIP implants.

I have talked to a variety of experts about what these test results mean. In particular, I would like to thank the members of the Chief Medical Officer's Clinical Advisory Committee, who have helped me understand what these tests mean for both clinicians and consumers.

As the Therapeutic Goods Administration and international bodies continue to accumulate evidence as part of their ongoing activities, we expect there will be more information to review. Where the information is different from that already known I would like to reassure you that we will discuss it with experts and provide updated public advice.

1. Key Information

Key Information: Silicone gel filled Breast Implants

Health consequences

All silicone gel filled breast implants are considered high risk medical devices

- They have a limited lifespan - the risk of rupture increases with time, with an estimate of 10-15% by 10 years.
- A rupture may not present with any clinical signs or symptoms.
- Magnetic Resonance Imaging (MRI) is the best imaging method to detect rupture. No imaging test currently can predict rupture.
- Silicone from ruptured breast implants may migrate, resulting in swollen and sometimes sore lymph nodes.
- There is no evidence of increased risk of breast cancer or connective tissue diseases.
- There is a possible link between all silicone breast implants and a specific but rare cancer called Anaplastic Large Cell Lymphoma (ALCL), but any risk appears very small.

PIP breast implants

- Testing by the Therapeutic Goods Administration (TGA) has not identified a specific serious safety concern with PIP breast implants.
- It has been suggested that PIP breast implants may be more likely to rupture than other silicone gel-filled breast implants. The information we have cannot confirm or exclude this possibility but the number of reported ruptures in Australia to date is within an expected range.
- There is no evidence that the risk of ALCL in the breast for PIP breast implants is greater than for all silicone gel filled breast implants. No cases of ALCL in the breast in women with PIP breast implants have been reported in Australia.

Removing breast implants (explantation surgery)

All silicone gel filled breast implants

- Surgery for ruptured breast implants is not urgent, unless there are signs of breast tissue reaction.
- As with all surgery, there are risks associated with anaesthesia. In healthy people, as expected in the majority of women with breast implants, the risk of death associated with anaesthesia is approximately 1/100,000.
- Local complications are common.
- If replacement with new implants is undertaken, there is a likely increased risk of delayed local complications such as contracture, rupture, implant removal and reoperation associated with the second and subsequent surgeries compared with the primary or initial surgery. If necessary, reoperation may be required earlier following revision surgery than primary augmentation surgery.

Medicare rebate

- Medicare rebates are available for the cost of medical services related to managing PIP breast implants concerns including GP and surgeon consultations, diagnostic tests and surgery and related anaesthetic services to remove and replace implants when clinically indicated.
- A Medicare rebate is available for MRI to assess the structural integrity of known or suspected PIP breast implants for a 12-month period, until 12 March 2013.

2. Executive Summary

The manufacturer of PIP breast implants was authorised to use a medical grade silicone but has used non-approved silicone in its production processes.

A specific serious safety concern for PIP breast implants has not been identified from the mechanical, toxicology or chemical tests carried out by the TGA to date. Specifically:

- Testing in Australia, the UK and France did not show any chemical toxicity to either living cells (cytotoxicity) or DNA within the genetic machinery of the cell (genotoxicity).
- Although the Agence Francaise de Securite Sanitaire des Produits de Sante (AFSSAPS) reported that intra-dermal irritation tests showed an irritant potential, intra-dermal irritation studies commissioned by the TGA in both Australian and French laboratories showed no evidence of irritation.
- The AFSSAPS reported that there are differences in the physical and chemical properties of different batches of PIP breast implants that relate to the use of authorised and unauthorised silicone filler gels. Testing by the TGA has also found such differences, particularly the presence of low molecular weight siloxanes, but these are not regarded as being of clinical significance.
- Although AFSSAPS reported failures related to the tensile elongation test, repeated tests conducted by the TGA (including tensile elongation) have met all relevant international standards for shell integrity.

Silicone gel filled breast implants have a limited lifespan, with the risk of rupture increasing over time. It is estimated that 10-15% of any brand of silicone breast implant will be ruptured at 10 years.

Rupture can be asymptomatic, and the best imaging method of detecting rupture is MRI. Women who know they have a PIP breast implant, or where clinical advice is that they might have, can access a Medicare rebate for a MRI to assess the integrity of their implant/s (available for MRIs performed from Monday, 12 March 2012, for a 12-month period).

There is no evidence that silicone gel filled breast implants cause breast cancer. There is a possible (but very low risk) link between all silicone breast implants and anaplastic large cell lymphoma occurring in the breast. There is no evidence of an increased risk for PIP breast implants compared with other silicone breast implants.

Some consumers with PIP breast implants have reported experiencing systemic symptoms such as fatigue, hair loss and headaches. While there is no published evidence that silicone gel filled breast implants cause connective tissue disease, the TGA is attempting to collect further information on these individual reports. As systemic or general symptoms can be experienced as part of many different health conditions, it is important that women experiencing these symptoms visit their medical practitioners to have these symptoms evaluated.

Local complications associated with explantation surgery (surgery to remove implants) are common. If replacement with new implants is undertaken, there is a likely increased risk of delayed complications such as contracture, rupture, implant removal and reoperation associated with the second and subsequent surgeries compared with the primary surgery.

Medicare rebates are available for the cost of medical services related to managing PIP breast implants concerns including GP and surgeon consultations, diagnostic tests and surgery and related anaesthetic services to remove and replace implants when clinically indicated.

Overall, there is not enough evidence to conclude that women with PIP silicone breast implants have a greater health risk than women with other brands. Australian tests to date have all been conducted in accordance with international standards and the results show the implants have met the standards required. Therefore, in light of the risks of surgery there is insufficient evidence to recommend routine removal of PIP implants without a medical indication such as rupture or significant symptoms.

Women are encouraged to discuss their individual situation with their doctor to assess the risks and benefits relevant to their own circumstances. Important information is provided in the Key Information box, section 1, to assist women and doctors in balancing these risks and benefits.

This report presents the information available to April 2012. Importantly, it comprises results from key tests conducted by the TGA and other regulators, and published scientific literature. Evidence continues to be accumulated by the TGA, and will be integrated into an ongoing risk assessment communicated via the TGA website and to consumer groups and clinician organisations, especially where this may be different from current advice.

3. Background

In late December 2011, the French Government recommended that women with breast implants manufactured by the French company Poly Implant Prothèse should consider having them removed as a non-emergency precautionary measure. This was on advice from the French regulator, AFSSAPS, which was concerned about a possible increased risk of rupture and leaks of gel with these implants, and an irritant effect found at laboratory testing not seen with silicone gels from other prostheses. Overseas governments have responded to this issue in different ways: some, such as the UK, advising that there is not enough evidence to recommend routine removal⁽¹⁾ and encouraging women and clinicians to discuss the relative risks and benefits; with others, including the German, Dutch and Czech Republic governments, recommending that the implants be removed. It is noteworthy, however, that the European Commission, through the report of its Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), has adopted a cautious approach and has not recommended routine explantation. They concluded that PIP implants may need to be exchanged for most women with a timeframe of the next 10-15 years⁽²⁾.

3.1. Silicone gel filled Breast Implants

Breast implants are used to augment breast size, or to reconstruct the breast following mastectomy or to correct an abnormality. In Australia, breast implants are either saline or silicone gel filled. A silicone gel filled breast implant is a silicone elastomer shell (sac) that has been filled with cohesive silicone gel.

3.2. PIP breast implants

Non-implanted PIP implants were recalled in Australia in April 2010 after the French regulatory authority (AFSSAPS) expressed concerns that there may have been an increased incidence of ruptures of this product associated with the use of an unauthorised silicone gel. The results of tests on gel cytotoxicity and shell strength conducted in 2010 on samples of PIP breast implants by the TGA, Australia's regulatory authority for therapeutic goods, were all in accordance with international standards⁽³⁾.

3.3. Australia

Following the expression of further concerns in relation to PIP breast implants by the French government in December 2011, including a recommendation to women to have them removed as a non-urgent precautionary measure, the TGA initiated an expanded laboratory testing program to further assess the quality and safety of the PIP breast implants. The testing plan and results are presented in section 4: Testing PIP Breast Implants.

An Expert Panel was convened by the TGA (4 January 2012) to provide specialist input into the review of evidence and further investigation of the safety of PIP implants. This panel is composed of clinical, scientific and epidemiological experts from TGA statutory medicine and medical device advisory committees, and experts from the Royal Australasian College of Surgeons, the Australian Society of Plastic Surgeons and the Australasian College of Cosmetic Surgery.

A Clinical Advisory Committee was convened by the Chief Medical Officer (9 January 2012) to provide him with regular and frequent advice on clinical measures, risks and benefits, and communication strategies in response to health concerns related to PIP breast implants. The committee includes senior representatives of relevant clinical and consumer groups (see Appendix A for membership). The issues considered by this committee have greatly informed this CMO Report, focusing on the clinical issues and impact.

The aim of this report is to provide a source of information on the relevant scientific literature, testing results and clinical management support available on PIP silicone gel filled breast implants. It presents the current situation in Australia as at April 2012.

3.4. Breast implants in Australia

The TGA estimates that approximately 13,000 silicone gel breast implants manufactured by PIP have been supplied to the Australian market between 1999 and 2010. It is not known how many of these are currently implanted in women, nor how many women currently have this brand of implant, but an estimate of 5,000 women would appear reasonable as most women will have these for cosmetic breast augmentation reasons and have bilateral implants.

It is not known how many women, if any, received PIP breast implants from breast surgery performed overseas.

4. Testing PIP Breast Implants

4.1. Production of Silicone gel filled breast implants

The thickness of the silicone elastomer shell (sac) of a breast implant varies, but is typically between 0.5 and 1.0 mm thick. There is a hole at the back of the shell through which the silicones that are later cured to form the gel material are introduced. The hole is sealed using a silicone patch after the shell has been filled.

The raw material silicones that are used to make the silicone gel are a mixture of chemically reactive and un-reactive silicone oils. The gel is produced by curing the silicone raw materials inside the sealed (patched) shell. During the curing process, the reactive silicones form a matrix of lightly cross-linked polydimethyl siloxanes (silicones) swollen by the viscous silicone fluid (oil), which is not chemically bonded to the gel and can constitute around 90% of the gel. The cured gel is highly cohesive and has the consistency of a well set jelly.

4.2. Formulations of filler gel and shell used in PIP breast implants

AFSSAPS report that there are at least three different formulations of the filler gel used in PIP breast implants⁽⁴⁾. The authorised gel was manufactured using oils supplied and manufactured by the Nusil Corporation. The gel produced using these oils (Nusil MED 3 6300) has been extensively tested to demonstrate that it is biologically safe and suitable for use in medical applications. The unauthorised gels were manufactured using a combination of other brands of silicone raw materials, with two different formulations identified as PIP1 and PIP2. The PIP1 and PIP2 formulations do not appear to have been subjected to the sorts of biological safety tests that the Nusil MED 3 6300 gel has passed. Apparently, PIP1 was manufactured prior to 2008 and PIP2 from the beginning of 2008. It is not clear if or when the Nusil silicones were being used to manufacture the gel used in PIP breast implants.

4.3. Test Results – AFSSAPS, France

AFSSAPS reports indicate that studies investigating the integrity of the PIP shell found that the tensile set and fatigue resistance tests complied with the requirements of the international standard (ISO 14607:2007), while the tensile elongation of textured PIP breast implants did not comply⁽⁴⁾. AFSSAPS also commissioned cytotoxicity tests, a variety of genotoxicity tests and an intradermal irritation test. The tests concluded that the materials used in PIP implants are not cytotoxic or genotoxic, but the intradermal irritation test showed an irritant potential in the PIP gel. Testing of PIP breast implants by AFSSAPS was carried out on samples with an expiry date of 2011 or later.

Physico-chemical analysis has confirmed that different formulations of filler gel had been used and that there was variability in physical and chemical characteristics of the filler gels used in different batches of PIP breast implants. In particular, the different filler gels can be identified by the presence of low molecular weight silicones.

4.4. Testing Program – TGA, Australia

The TGA testing program has focused on four key areas:

- toxicity
- physical and mechanical properties
- chemical analysis
- explanted PIP implants.

4.4.1 Samples available for testing

The TGA testing plan is using the broadest cross-section of samples of PIP breast implants available to the TGA, and includes both PIP1 and PIP 2 formulations of the filler gel. To date, samples of the product with an expiry date before 2011 have not been available to the TGA.

The TGA has tested 19 different batches (29 samples) of PIP breast implants available in Australia plus batches of other brands of breast implant for comparison. The TGA has obtained a further five batches (23 samples) of PIP breast implants from overseas for the on-going testing program.

The TGA is investigating explanted PIP breast implants to complement testing being carried out on unused sterile PIP breast implants and to provide further evidence that will assist with determining the overall quality and safety of the product.

4.4.2 Testing regime

The tests conducted as part of the program are summarised in Table 1 below.

Table 1: TGA Testing Regime

Study	Test
Toxicology	<ul style="list-style-type: none">• Intra-dermal irritation - ISO 10993-10: 2010• Cytotoxicity - ISO 10993-5:2009
Chemical analysis	<ul style="list-style-type: none">• Chemically fingerprinting using Fourier transform infrared spectroscopy (FTIR)• Chemically profiling using gas chromatography–mass spectrometry (GC-MS), thermogravimetric analysis (TGA) and gel permeation chromatography (GPC)• Presence and quantification of D4-D6 siloxanes using headspace and direct injection GCMS• Presence of metals using inductively coupled plasma mass spectrometry (ICP-MS)
Physico-mechanical tests	<ul style="list-style-type: none">• Tensile Elongation - ISO 14607:2007 Annex B Section 1.2• Tensile Set - ISO 14607:2007 Annex B Section 1.3• Strength of joints, seams and seals - ISO 14607:2007 Annex B Section 2• Silicone Gel Cohesion - ISO 14607:2007 Annex D Section 4&5
Testing on explanted PIP implants	<ul style="list-style-type: none">• Visual examination with photography and microscopy, as well as chemical and mechanical analysis as appropriate.

The assessment conducted by TGA of explanted prostheses is focussed on evaluating any unusual features identified by the explanting surgeon. The TGA is documenting findings from visual inspections of the explanted PIP breast implants to determine if there are any observable trends in the quality of the shell and gel of the implants.

Implanted breast implants are not sterile and contain matter derived from the woman's tissues, as well as chemicals and materials from the surgical procedure that may confound chemical and toxicological tests. For example, the implant can be contaminated by chemicals from latex gloves and contact with various instruments, as well as cleaning and sterilising fluids used during or after surgery. Furthermore, containers and bags, which are used to store the explants, as well as microbiological organisms from the environment, can contaminate the implants during storage. This means that tests to determine the presence of chemicals that may be toxic could be invalid. Such tests should be carried out on unused sterile breast implants.

4.4.3 Limitations to testing

Testing provides a measure of the compliance of a particular sample with specified quality criteria. The quality of the sample is taken to be reflective of the batch from which the sample is drawn. However, the samples of PIP implants tested may not be representative of other batches of the product due to uncertainty relating to manufacturing quality. Nevertheless, it does provide a very useful support to other measures by providing an immediate assessment of quality of the portion or the sample of the batch tested.

Interpretation of testing results must be made with caution as there are limitations to the testing program, especially relating to a lack of unambiguous controls, presence of multiple gel formulations, lack of manufacturing batch documentation and a lack of samples manufactured prior to 2008.

4.5. Testing results and findings

A specific serious safety concern for PIP breast implants has not been identified from the particular mechanical, toxicology or chemical tests carried out by the TGA to date.

While the AFSSAPS reported a 'potential irritant' finding for the filler silicone gel, this is not consistent with testing results from studies commissioned by the TGA. Two different laboratories, one in Australia and one in France (the same laboratory used by AFSSAPS to conduct its dermal irritation tests), carried out tests on behalf of the TGA in accordance with those described in the designated international standard and results from both laboratories showed that the gel and the shell of tested PIP breast implants were non-irritant.

To date, repeated cytotoxicity testing by TGA has confirmed previous findings (from 2010) that the tested PIP gels do not contain chemicals that are toxic to living cells. Similar findings have been reported by AFSSAPS and the regulatory authority in the UK (MHRA)⁽⁶⁾. Both those authorities also reported that tests for genotoxicity indicated that the gel was not genotoxic (damaging to DNA).

Questions were raised about the amount of low molecular weight silicones (D4-D6 siloxanes) that may be present in unauthorised gels. To date, chemical testing indicates that the amount of these siloxanes (especially D4) in PIP breast implants is not a safety concern but is a useful test for identifying implants containing unauthorised gel. Further, testing has not identified any metals in the tested PIP breast implants that are at a level of concern.

While testing has not identified a serious quality concern, the TGA has noted that there is variability in the physical and chemical characteristics of different batches of PIP breast implants. The significance of this variability is still being investigated. The TGA testing has not identified problems regarding shell integrity, although AFSSAPS reported failures related to the tensile elongation test. Testing the tensile elongation of further samples of PIP breast implants confirmed the findings of 2010 that all tested samples comply with the requirements of the designated international standard.

To date, the TGA has observed that most filler gels from either unused or explanted PIP breast implants appear to be firm. However, the TGA has noticed that the occasional gel, which was from an implant that has been either explanted or removed from packaging and exposed to the environment over a long period of time, appears relatively less firm and oily. The significance of this observation is being further investigated.

Explanted PIP breast implants with ruptures were found to be associated with a ‘milky’ fluid, which testing showed to be predominantly an emulsion of water and silicone.

The TGA website contains details for the on-going TGA laboratory testing program at <http://www.tga.gov.au/safety/alerts-device-breast-implants-pip.htm>.

4.6. International cooperation

The TGA established an international testing panel for PIP breast implants (ITPP), which includes representatives from Brazil, Czech Republic, European Commission, Germany, Ireland, Netherlands and the United Kingdom. France has been invited to join in discussions, but has not been available. The role of the ITPP is to discuss laboratory testing of PIP breast implants through teleconferences and on-going email exchange. To date, the TGA has hosted three teleconferences (19 January, 9 February and 8 March 2012). No other country reported, at these meetings, that they have recent laboratory testing results.

5. Breast Implants and Cancer

5.1. Breast Cancer

Women who have silicone breast implants do not appear to be at an increased risk of developing breast cancer⁽⁶⁾. This evidence comes from several large cohort studies in Scandinavia⁽⁷⁻⁹⁾ and Canada⁽¹⁰⁾ which found the incidence of breast cancer in women with breast implants was not higher than that in women without implants.

The French National Institute for Cancer (INCa) advises that the risk of breast cancer in women with PIP implants is not greater than the risk of breast cancer in the general population⁽¹¹⁾. The UK Expert Group agrees that on the available evidence PIP implants are not associated with a higher risk of breast cancer than other silicone gel implants⁽¹⁾.

5.2. Anaplastic Large Cell Lymphoma (ALCL)

Anaplastic large cell lymphoma (ALCL) is a rare cancer of the immune system that can occur anywhere in the body. A U.S. Food and Drug Administration (FDA) review of the scientific literature published from 1997 through May 2010 identified 34 unique cases of ALCL in women with breast implants throughout the world⁽¹²⁾. Four of these cases were from Australia. The 34 cases of ALCL in women with breast implants identified by the FDA is an extremely small number compared with the estimated 5 to 10 million women who have received breast implants worldwide. Nevertheless, based on these data, it is possible that women with breast implants may have a very small but increased risk of ALCL⁽¹²⁻¹³⁾. Importantly, however, this is associated with breast implants in general, including ones filled with saline solution. Currently the TGA has received reports of six cases of ALCL in Australian women with breast implants. It appears that none of the women has had PIP implants.

6. Breast Implants and Health Consequences

6.1. Risk of rupture

Rupture is a recognised complication of all breast implants. Ruptures of breast implants can be either intra-capsular, where the gel is confined within the fibrous capsule that the body forms around the implant, or extra-capsular, where the gel has extended into the breast or other localised tissues⁽¹⁴⁾.

The risk of rupture of a breast implant increases over time, which means that the longer a woman has breast implants the more likely she is to experience a rupture.

Estimates of the frequency of breast implant rupture are variable. A report published by the FDA in June 2011⁽¹⁵⁾ provides an updated analysis of ongoing pre and post market studies being conducted by the two sponsors of silicone gel filled breast implants in the USA (Allergan and Mentor). For Allergan implants, the cumulative MRI-diagnosed rupture rates were 0.5% after two years rising to 10.1% (primary augmentation) after 10 years, and for Mentor implants a rate of 1% at three years rose to 13.6% at eight years (primary augmentation).

Holmich et al prospectively followed up a group of women who had an intact breast implant confirmed on a baseline MRI⁽¹⁶⁾. At the end of two years, there were definite ruptures in 10% of implants giving an overall rupture incidence rate of 5.3 ruptures/100 implants per year. Using this data they estimated that approximately 2% of implants would be ruptured by five years and 15-17% by 10 years.

There are no complete registry data available to provide information on the rate of rupture for PIP implants.

As of 12 April 2012, the TGA had received 288 reports of rupture of PIP breast implants of which 250 were confirmed, 38 were unconfirmed due to insufficient information to uniquely identify the patient, the implant used or to verify that a rupture has occurred.*

6.2. Diagnosis and investigation

Rupture of a silicone breast implant, or leaks of gel, can be associated with lumpiness or swelling in the breast or axilla (armpit), a change in the size, shape or feel of the breast, or redness, pain or tenderness.

About 50% of women who have a rupture may not experience any signs or symptoms that this has occurred⁽¹⁷⁾.

Different imaging methods can identify the integrity of breast implants and also the extent of possible silicone leakage into adjacent tissues. MRI is regarded as the imaging study of choice for the assessment of silicone implant rupture as it has been shown to have the highest sensitivity and specificity compared with other imaging methods such as ultrasound⁽¹⁸⁾. MRI has the ability to image the entire surface of the implant and surrounding tissue, however its diagnostic performance is far better when used in patients who have symptoms of rupture than in patients who do not⁽¹⁹⁾.

Breast MRI is generally regarded as a safe procedure but not all patients are able to undergo MRI because of cardiac pacemakers, aneurysm clips or other metallic foreign bodies not compatible with MRI. Some patients are very claustrophobic and cannot complete a MRI examination. The risk of claustrophobia is less with breast MRI than with conventional MRI, however, because a dedicated breast coil is used. The use of intravenous contrast is not required for breast MRI when used for the assessment of breast implant rupture.

*This data was amended on 10 May 2012 and updated in this document.

Ultrasound can be a useful technique for the evaluation of implant integrity in those who cannot have a MRI. Ultrasound is not as accurate as MRI in identifying rupture and is heavily dependent on the experience of the technician performing and interpreting the ultrasound⁽¹⁸⁾. While ultrasound is good in identifying ruptures originating from the front wall of an implant, it is poor at visualising rupture originating from the back wall of the implant.

Women who know they have a PIP breast implant, or where clinical advice is that they might have, can access a Medicare rebate for a MRI to assess the integrity of their implant/s. The listing of this Medicare item follows independent expert advice from the Medical Services Advisory Committee. The rebate is available for MRIs performed from Monday, 12 March 2012, for a 12-month period. Further details for patients, health care practitioners and diagnostic imaging providers can be found at <http://www.health.gov.au/internet/main/publishing.nsf/Content/di-mri-pip>.

6.3. Health consequences

Rupture of silicone gel filled breast implants, or leaks of gel, may result in the formation of lumps in the breast around the implant, or the gel may migrate to nearby tissues such as the chest wall or through the lymphatic system causing swollen lymph nodes (lymphadenopathy), most commonly of the axilla (armpit)⁽²⁰⁻²¹⁾. These lumps may cause swelling and discomfort or pain. The formation of silicone inflammatory reactions (granulomata) has been reported, and which in rare cases has required surgical removal of large amounts of tissue⁽²²⁾.

One study has attempted to look at the possible health implications over time of ruptured silicone breast implants that remained untreated⁽²³⁾. This Danish study followed 64 women with 96 MRI diagnosed ruptured implants who did not have symptoms that warranted surgical removal (explantation). A repeat MRI at two years identified that 11 implants (11%) in 10 women had signs of progression (moving from intra to extra capsular rupture or increasing extracapsular silicone spread), but all changes were considered minor.

It has previously been hypothesized that an increased exposure to silicone from ruptured implants may lead to more general ill health with systemic symptoms, such as those that occur with connective tissue disease (for example, systemic lupus erythematosus and rheumatoid arthritis). There is consistent epidemiological evidence from published large-scale studies as well as meta-analyses which conclude there is no evidence of an association between silicone breast implants and connective tissue diseases. This assessment is supported by the FDA⁽¹⁵⁾ and the recently released report on the safety of PIP Silicone Breast Implants by the European Commission's Scientific Committee⁽²⁾.

There is a small number of case reports of PIP breast implant rupture in the literature. These describe local breast inflammatory and fibrotic changes, and in one case silicone migration causing swollen lymph nodes (lymphadenopathy) and skin changes⁽²⁴⁻²⁶⁾. From the information available there appears to have been no long-term effects on health in these cases⁽¹⁾.

6.4. Explantation (surgical removal)

The risk of explantation can be considered in two groups: the risk associated with the anaesthesia, and the risk of complications from the breast surgery.

Many women with breast implants are healthy with no or few other health problems (co-morbidity)⁽²⁾. For a healthy patient undergoing general anaesthesia, the risk of death and serious complications is very low, with the Australian and New Zealand College of Anaesthetists advising that the risk of death is approximately 1 in 100,000⁽²⁷⁾. Further, all women with breast implants will have previously undergone at least one general anaesthetic which improves the ability to individualise an assessment of risk based on this past experience⁽²⁾.

Local complications are more common and can occur immediately after surgery or appear months or years later. Immediate complications include infection and bleeding. More delayed complications include capsular contracture, unequal breast shape (asymmetry), wrinkling, scarring, rupture and reoperation. Complications are higher in women who have implantations for reconstructive surgery after mastectomy than augmentation (enlargement)⁽²⁸⁻²⁹⁾. This is due to multiple factors including prior tissue damage from chemotherapy and/or radiotherapy, related surgical trauma of mastectomy and amount of tissue available⁽²⁾.

The risk of delayed complications appears to be greater in revision (second or subsequent) surgeries compared with the primary or initial surgery⁽²⁾. Table 2 shows some of the findings from an FDA analysis of cumulative incidence rates of complications for those undergoing a primary augmentation and a secondary (revision) augmentation procedure for two types of silicone breast implants in the US. The tables listing all complications from the FDA analysis are included at appendix B.

Table 2: Core Study complications over 10 and 8 years for Allergan and Mentor silicone gel-filled breast implant patients. Table shows cumulative incidence rates over time.

Complication	Allergan brand (cumulative incidence over 10 years)		Mentor brand (cumulative incidence over 8 years)	
	Primary Augmentation	Revision Augmentation	Primary Augmentation	Revision Augmentation
Reoperation	36.1%	46.0%	20.1%	37.8%
Implant removal	20.8%	32.4%	7.3%	21.1%
Implant rupture	10.1%	6.3%	13.6%	15.5%
Capsular contracture (Baker III/IV)	19.1%	27.5%	10.9%	24.1%

Handel et al followed up approximately 825 augmentation patients (1601 implants) and 695 implant revision patients (1534 implants) for up to 23 years (mean follow up per implants was 37.4 months). They found for breast augmentation patients that 15.5% of primary implants required subsequent reoperation compared with 21.9% of implants used for revision surgery⁽³⁰⁾. They also found that the average time between implantation and when reoperation was performed was shorter for revision surgeries compared with primary augmentation surgeries (mean of 39 vs 49 months). This means that women who have their breast implants removed and replaced are more likely to have complications than those having breast implants for the first time.

The surgical removal of breast implants may be more difficult if they are ruptured, and if there is associated inflammation surrounding the implant. In the longer term, inflammation may lead to the formation of fibrous or scar tissue. Most surgeons recommend removal of ruptured breast implants⁽²⁾, particularly for extra-capsular rupture, but do not regard the need for this surgery as urgent.

An important consideration for women considering explantation surgery is whether they should have their implants replaced. Women who do not have them replaced may have cosmetically undesirable dimpling, puckering, or sagging of the natural breast following implant removal. As discussed above, if replacement with new implants is undertaken there is a likely increased risk of delayed complications such as contracture, rupture, implant removal and reoperation associated with revision (or subsequent) surgeries when compared with the primary surgery.

6.5. Surgeon Experience

Some surgeons in Australia have raised concerns about higher rupture rates in PIP silicone breast implants. British surgeons, in their joint surgical guidance statement, state that “reports have suggested that in cases of PIP implant rupture/leak the inflammatory reaction may be more intense than usual...⁽³¹⁾. Similar anecdotal reports have been raised during discussions with Australian surgeons, and include the appearance of the implant at the time of removal (such as loss of integrity of the shell, the silicone appearing clumped) and evidence of fluid around the implant.

The TGA is attempting to collect this important information by sending a questionnaire to all surgeons who report a rupture of a PIP breast implant to the TGA. By 5 April 2012 the TGA had forwarded 102 surgeon questionnaires, with 27 completed forms returned (26.4%). The level of detail provided in the returned questionnaires has been variable, and combined with the current low rate of return, it is not possible to determine the extent of these implant changes or experiences in the Australian population at this stage.

6.6. Consumer Experience

Consumers have provided reports to the TGA on their experience with PIP breast implants. These reports are on local breast implant complications such as rupture and contractures, and anxiety and distress. A number of the consumer reports also described the consumer experiencing systemic symptom/s, such as fatigue, general malaise, hair loss and headaches, which are reported to be associated with their implant. The TGA is seeking consent from these individuals to contact their treating doctor to gain further information on the nature of their symptoms, and the results of any investigations.

Systemic or general symptoms, such as fatigue and headache, may be experienced as part of many different health conditions. It is important that women experiencing these symptoms visit their medical practitioner so that a personalised review can be carried out to exclude other underlying conditions.

6.7. Medicare Rebate

Normal Medicare arrangements apply to reimbursing patients for the usual cost of medical services related to managing health concerns about their PIP implants.

This includes Medicare rebates related to:

- consultations with their GP or surgeon
- imaging via ultrasound or MRI (as per section 6.2, for 12 months from March 12th 2012)
- surgery—the removal and replacement of breast implants under certain conditions.

Women are eligible for Medicare rebates for the surgical removal and replacement of breast implants where the treating clinician (surgeon) believes the surgery is indicated for physical reasons such as a rupture of the implant, and/or psychological reasons such as significant anxiety. These rebates contribute to the fees charged by doctors, including those of the surgeon, anaesthetist and any surgical assistants.

These rebates do not cover private hospital accommodation, private hospital theatre costs, or the cost of replacement breast implants. Private health insurance may contribute to accommodation and theatre costs in private hospitals, and the replacement implant under some policies.

Women may elect to be treated through the public hospital system. Subject to local arrangements, their medical practitioner can refer them to the nearest appropriate public hospital or to a surgeon who provides public hospital services, who will then be able to assess and advise on the best course of action in consultation with the patient.

7. Ongoing Work

The TGA is continuing to carry out laboratory testing in accordance with the testing program described in Section 4, and collecting information from surgeons and consumers as outlined in section 6. As more information becomes available it will be integrated into the ongoing risk assessment. Where new information may be different from existing information the public and clinical groups will be advised.

8. Key Source Documents (for full details see References)

European Commission: Scientific Committee on Emerging and Newly Identified Health Risks
Safety of PIP Silicone Breast Implant

Agence Francaise de Securite Sanitaire des Produits de Sante (AFSSAPS)
Record of Checks Carried Out by the Health Authorities on the Company Poly Implant Prothèse (PIP)

Joint surgical statement on clinical guidance for patients, GPs and surgeons
Poly Implant Prothèse (PIP) breast implants

Sir Bruce Keogh, NHS Medical Director, UK
Poly Implant Prostheses (PIP) Breast Implants: Interim Report of the Expert Group

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Appendix A:

Membership of the Chief Medical Officer's Clinical Advisory Committee

Core members	
Professor Chris Baggoley	Chief Medical Officer (Chair)
Ms Karen Carey	Consumers Health Forum of Australia
The Hon Maxine Morand	CEO Breast Cancer Network of Australia
Assoc Prof. Rodney Cooter	President, Australian Society of Plastic Surgeons
Dr Daniel Fleming	former President, Australasian College of Cosmetic Surgery
Professor John Horvath	Principal Medical Consultant, Department of Health and Ageing
Professor Claire Jackson	President, Royal Australian College of General Practitioners
Professor Richard Murray	President, Australian College of Rural and Remote Medicine
Dr Chris Pyke	President, Breast Surgeons Society of Australia and NZ
Professor Elizabeth Wylie	Royal Australian and New Zealand College of Radiologists
Dr Helen Zorbas	Chief Executive Officer, Cancer Australia
Dr Steven Hambleton	President, Australian Medical Association
Department of Health and Ageing (including TGA) Advisers	
Dr Brian Richards	Acting National Manager, Therapeutic Goods Administration
Mr Richard Bartlett	First Assistant Secretary, Medical Benefits Division

Appendix B:

Core Study complications and adverse outcomes as reported in the FDA Update on the Safety of Silicone Gel-Filled Breast Implants, p.45-48 (15).

TABLE 3. Core Study complications and adverse outcomes over 10 years post-implantation for Allergan Natrelle silicone gel-filled breast implant patients. Table shows cumulative incidence rates over time and 95% confidence intervals calculated using Kaplan-Meier analysis*.

Complication or Outcome	Primary Augmentation (N=455)	Revision Augmentation (N=147)	Primary Reconstruction (N=98)	Revision Reconstruction (N=15)
Asymmetry	3.3% (2.0-5.1)	6.5% (3.2-12.8)	23.2% (15.4-33.9)	6.7% (0.2-31.9)
Breast pain	10.9% (8.2-14.3)	11.7% (7.1-18.9)	6.8% (2.8-16.1)	0%
Breast/skin sensation changes	1.6% (0.8-3.3)	2.2% (0.7-6.6)	0%	0%
Bruising	0.4% (0.1-1.8)	3.0% (1.1-7.8)	1.0% (0.1-7.1)	6.7% (0.2-31.9)
Capsular contracture (Baker III/IV)	19.1% (15.6-23.3)	27.5% (20.3-36.6)	24.6% (16.2-36.2)	6.7% (0.2-31.9)
Delayed wound healing	1.1% (0.5-2.7)	0.7% (0.1-4.8)	1.0% (0.1-7.2)	0%
Hematoma	1.6% (0.7-3.2)	2.1% (0.7-6.3)	1.5% (0.2-10.4)	0%
Implant malposition	6.3% (3.9-8.4)	6.0% (3.1-11.7)	2.3% (0.6-8.9)	13.3% (1.7-40.5)
Implant palpability/visibility	1.9% (1.0-3.8)	6.0% (3.0-11.6)	6.5% (0.4-17.0)	6.7% (0.2-31.9)
Implant removal with or without replacement	20.8% (17.2-25.2-)	32.4% (25.0-41.3)	53.8% (43.65.3)	20% (4.3-48.1)
Implant rupture	10.1% (7.4-13.7)	6.3% (2.8-13.7)	27.2% (17.3-41.3)	6.7% (.2-31.9)
Infection	0.5% (0.1-2.1)	1.4% (0.3-5.4)	3.2% (1.0-9.5)	0%
Irritation	0%	0.7% (0.1-5.0)	0%	0%
Necrosis	0.2% (0-1.6%)	0%	2.3% (0.6-8.8)	0%
Nipple complications	6.3% (4.3-9.1)	1.4% (0.3-5.4)	3.3% (1.1-9.8)	0%
Ptosis	2.0% (1.0-3.9)	4.9% (2.2-10.5)	0%	0%
Redness	0.7% (0.2-2.0)	0.8% (0.1-5.2)	2.1% (0.5-8.3)	0%

Table 3 (continued).

Complication or Outcome	Primary Augmentation (N=455)	Revision Augmentation (N=147)	Primary Reconstruction (N=98)	Revision Reconstruction (N=15)
Reoperation	36.1% (31.6-40.9)	46.0% (38.0-54.9)	71.9% (61.5-81.4)	46.7% (21.3-73.4)
Scarring/hypertrophic scarring	4.2% (2.6-6.5)	6.6% (3.5-12.4)	5.5% (2.3-12.7)	0%
Seroma/fluid accumulation	1.8% (0.9-3.5)	6.0% (3.0-11.7)	2.4% (0.3-15.7)	6.7% (0.2-31.9)
Skin rash	0.9% (0.3-2.3)	0.7% (0.1-4.9)	2.1% (0.5-7.9)	6.7% (0.2-31.9)
Swelling	9.2% (6.8-15.0)	8.3% (4.6-14.5)	7.1% (3.5-14.4)	0%
Wrinkling	1.8% (0.8-3.7)	5.4% (2.6-11.0)	10.2% (5.2-19.6)	0%

* The number of patients evaluated at the 10 year follow-up were: 269 (primary augmentation), 74 (revision augmentation), 44 (primary reconstruction), and 8 (revision reconstruction).

TABLE 4. Core Study complications and adverse outcomes over 8 years post-implantation for Mentor MemoryGel silicone gel-filled breasts implant patients. Table shows cumulative incidence rates over time and 95% confidence intervals calculated using Kaplan-Meier analysis*.

Complication or Outcome	Primary Augmentation (N=552)	Revision Augmentation (N=145)	Primary Reconstruction (N=251)	Revision Reconstruction (N=60)
Breast mass	5.4% (3.7-7.8)	6.5% (3.4-12.0)	5.2% (2.9-9.3)	7.2% (2.8-18.2)
Breast pain	2.5% (1.5-4.3)	3.4% (1.3-8.8)	2.8% (1.2-6.2)	5.2% (1.7-15.3)
Breast/skin sensation changes	2.8% (1.7-4.5)	1.4% (0.4-5.4)	0%	1.8% (0.3-12.0)
Capsular contracture (Baker II)	2.0% (1.1-3.7)	6.2% (3.1-12.1)	4.4% (2.3-8.3)	4.0% (1.0-15.2)
Capsular contracture (Baker III/IV)	10.9% (8.5-13.9)	24.1% (17.7-32.3)	15.3% (11.1-20.9)	23.1% (14.1-36.6)
Delayed wound healing	0%	2.1% (0.7-6.3)	0%	1.7% (0.2-11.3)
Dog ear scars from mastectomy	0%	0%	1.6% (0.6-4.3)	3.4% (0.9-12.8)
Granuloma	0%	2.4% (0.8-7.4)	0%	5.0% (1.6-14.7)

Table 4 (continued).

Complication or Outcome	Primary Augmentation (N=552)	Revision Augmentation (N=145)	Primary Reconstruction (N=251)	Revision Reconstruction (N=60)
Hematoma	2.9% (1.8-4.8)	2.8% (1.1-7.2)	1.3% (0.4-3.9)	3.4% (0.9-13.0)
Implant extrusion	0%	1.4% (0.4-5.5)	1.2% (0.4-3.7)	1.7% (0.2-11.3)
Implant malposition	0%	2.5% (0.8-7.9)	2.6% (1.2-5.8)	6.7% (2.6-16.9)
Implant removal with or without replacement	7.3% (5.3-9.9)	21.1% (15.0-29.2)	23.3% (18.2-29.4)	29.0% (19.1-42.5)
Implant rupture **	13.6% (7.6-23.6)	15.5% (6.5-34.6)	14.0% (7.6-25.0)	21.3% (7.3-53.3)
Infection	1.6% (0.9-3.1)	1.4% (0.4-5.5)	6.2% (3.8-10.2)	0%
Inflammation of breast	0%	1.4% (0.4-5.5)	0%	1.7% (0.2-11.4)
Lactation difficulties	2.0% (1.1-3.8)	1.6% (0.4-6.1)	0%	0%
Metastatic disease	0%	0%	5.7% (3.3-9.6)	4.0% (1.0-15.2)
Miscarriage	2.9% (1.8-4.8)	2.5% (0.8-7.6)	2.3% (1.0-5.6)	0%
New diagnosis of breast cancer	0%	1.8% (0.5-7.2)	1.9% (0.7-5.1)	1.7% (0.2-11.4)
New diagnosis of rheumatic disease	1.8% (1.0-3.5)	1.7% (0.4-6.5)	2.6% (1.1-6.2)	3.4% (0.9-12.9)
Nipple complications	0%	0%	1.3% (0.4-4.1)	0%
Nipple sensation changes	11.8% (9.3-14.8)	14.6% (9.7-21.8)	2.1% (0.9-5.0)	1.7% (0.2-11.3)
Pre-eclampsia at 36 weeks pregnant	0%	1.1% (0.2-7.4)	0%	0%
Reoperation	20.1% (17.0-23.8)	37.8% (30.2-46.6)	38.8% (32.9-45.5)	40.8% (29.5-54.5)
Seroma	1.1% (0.5-2.5)	2.1% (0.7-6.3)	4.8% (2.8-8.4)	1.7% (0.2-11.3)

* The number of patients evaluated at the 10 year follow-up were: 291 (primary augmentation), 77 (revision augmentation), 151 (primary reconstruction), and 36 (revision reconstruction).

** Rupture rates were estimated in MRI cohort at 8 years post-implantation.