APPENDIX 3

Chronology of regulatory, communication and other activities undertaken regarding PIP implants

Date	Event
13 September 1999	First application and approval for a PIP silicone gel implant for individual patient use under the Special Access Scheme (SAS).
22 September 1998	Precise Medical Supplies lodged application to register three types of breast implant manufactured by Poly Implant Prothèse (PIP): implants pre-filled with a polysaccharide solution; implants pre-filled with a silicone gel; and implants pre-filled with saline. Applications to register the polysaccharide-filled and silicone-filled implants were not pursued due to lack of data from PIP to support registration. The application for registration was supported by European Commission (EC) certification for each implant type issued by TÜV Rheinland in October 1997. Manufacturer was PIP at 337 Avenue de Bruxelles, La Seyne Cedex, France. EC certification was based on assessment for Class IIb products.
15 March 2000	PIP saline prefilled implants, sponsored by Precise Medical Supplies, registered on ARTG.
4 October 2002	New medical devices framework introduced in Australia - implantable mammary prostheses are classified as Class III medical devices.
16 October 2002	Transfer of sponsorship of all PIP-manufactured products from Precise Medical Products to Medical Vision Australia.
31 October 2002	First adverse event report for PIP silicone gel implant (arising from SAS use). Rupture of implant 2 years post-implantation.
14 November 2002	Medical Vision Australia applied to include PIP silicone gel implants on the ARTG. However, the application was not made under the provisions of the new regulatory framework and was not supported by the correct level of conformity assessment certification.
14 April 2003	Application for conformity assessment lodged by Medical Vision Australia for silicone gel breast implants manufactured by PIP.
28 May 2003	TGA accepted application for conformity assessment and notifies applicant.
28 May 2003	Evaluation of application for conformity assessment commences. Application referred within the TGA for the following evaluations of data provided in the dossier: a) microbiological assessment b) biocompatibility and biological safety assessment c) materials and manufacturing assessment d) clinical assessment.

Date	Event
May 2003	Arrangements for onsite audit of the PIP manufacturing facility commenced.
17-19 November 2003	TGA audit of PIP facilities at 337 Ave de Bruxelles, La Seyne Sur Mer, France.
15 December 2003	Manufacturer provided additional information relating to non-conformities identified during the audit.
March 2004	PIP obtained an EC Conformity Assessment Certificate (covering the necessary scope for PIP implants) from the European Notified Body, TÜV Rheinland.
23 August 2004	All non-conformities identified at the TGA onsite audit resolved and the TGA audit report closed out.
3 September 2004	Application considered by Medical Devices Evaluation Committee (MDEC) following referral by the TGA. The MDEC resolution was no objection to the inclusion of these implants on the ARTG subject to the provision of comprehensive annual post-market reports to the TGA for a period of 7 years from the date of inclusion.
18 October 2004	TGA issued Conformity Assessment Certificates (CAC) to PIP for the manufacture of a range of silicone gel-filled breast implants. CAC valid for five years.
3 November 2004	Application by the sponsor Medical Vision Australia for ARTG inclusion of the PIP implants covered by the TGA Conformity Assessment Certificate.
30 November 2004	PIP Implants included on ARTG (nine ARTG entries) for the sponsor Medical Vision Australia.
4 July 2006	First SAS approval for titanium dioxide coated silicone gel breast implants.
10 November 2006	First patient enrolled in a clinical trial sponsored by Medical Vision Australia using PIP titanium dioxide coated silicone gel breast implants.
4 June 2007	TGA acknowledged clinical trial notification for clinical trial using the PIP titanium dioxide coated implants.
31 August 2009	TGA contacted Medical Vision Australia regarding impending expiry of TGA CAC for PIP implants (expiry on 18 October 2009).
25 September 2009	Medical Vision Australia submitted an application to vary the manufacturer's evidence used to support their ARTG entries for PIP gel-filled implants. Variation was requested because the manufacturer was changing from TGA certification (due to expire on 18/10/2009) to European (CE) certification. CE certification was issued by EU Notified Body, TÜV Rheinland, and included Design Exam certification.
30 September 2009	TGA accepted the variation to the manufacturer's evidence with result that PIP implants were included in the ARTG on the basis of CE certification.
18 October 2009	PIP's TGA Conformity Assessment Certificate expired after 5 years.

Date	Event
31 March 2010	TGA notified by Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) of its decision to recall and suspend the marketing of silicone breast implants manufactured by PIP because it had "registered" an increase in reports regarding implant rupture and local complications and had discovered that the company had used an unauthorised silicone gel in the products.
31 March 2010	TGA contacted by Medical Vision Australia regarding the French recall of PIP implants.
1 April 2010	TGA wrote to Medical Vision Australia requesting details of the distribution of PIP implants in Australia.
2 April 2010	AFSSAPS advised the TGA that further information would be very difficult to obtain because PIP officially went into receivership on 30 March 2010 and was "currently dissolved".
3 April 2010	Medical Vision Australia advises TGA that it had ceased importation and supply of PIP implants, and had contacted medical practitioners requesting that the stock be returned and not used.
3 April 2010	TGA request sent to UK Medicines and Healthcare products Regulatory Authority (MHRA) asking for any further information on the reasons for the PIP recall in France.
6 April 2010	Request for information from MHRA for implant rupture rates. Request information from AFSSAPS for implant rupture rates that led to recall action. Medical Vision Australia confirmed that all importation and distribution of PIP products had been halted. It also advised that it will advise all implanting surgeons to stop any further operations and return stock to the sponsor. Note: the 7 customers known to have stock were contacted by email and phone. All customers acknowledged the email.
6 April 2010	Notice posted on the TGA website advising that Medical Vision Australia was undertaking the recall of all non-implanted silicone gel breast implants manufactured by PIP. A copy of the recall notice to customers, the web statement and notification to colleges is attached
6 April 2010	TGA sent a copy of the recall notice to the Australasian College of Cosmetic Surgery (ACCS) and the Australian Society of Plastic Surgeons (ASPS).
6 April 2010	TGA requested information about implant ruptures from AFSSAPS.
7 April 2010	TGA requested Medical Vision Australia to send a "Product Notification" to all surgeons who may have purchased PIP implants.
7 April 2010	Medical Vision Australia advised all surgeons who have implanted PIP implants sourced from that company about the recall.
7 April 2010	Response from MHRA with general outline of the issues as understood. MHRA advice that rupture rate for PIP implants in UK was "not unusual".

Date	Event
8 April 2010	State and territory health departments notified of recall of PIP implants
8 April 2010	"Product Notification" sent to surgeons by Medical Vision Australia advising that all unused PIP implants were being recalled due to concerns about their failure rate and that at this time, no action is required other than the normal follow-up procedures for patients implanted with this product.
13 April 2010	TGA follow up with AFSSAPS regarding email request of 6 April 2010, concerning rate of breast implant rupture.
14 April 2010	PIP implants cancelled from ARTG.
29 April 2010	AFSSAPS advised the TGA that, while true rates of rupture were not available, it had observed a relative increase in the rate of rupture of PIP implants over the period 2007 to 2009 and it was this apparent increase that led to the discovery of gel substitution and subsequent recall.
April – May – June 2010	TGA performed laboratory testing of samples of PIP implants.
19 May 2010	TGA website updated with information for consumers stating it was continuing its investigation into issues relating to overseas reports of increased rupture rates of PIP implants and that the TGA was awaiting the results of tests being conducted internationally on the implants.
10 June 2010	TGA requested AFSSAPS to provide information on the unauthorised gel composition used by PIP and their test results.
11 June 2010	Outline of tests to be performed provided by AFSSAPS. No formulation details provided for unapproved gel other than "the silicone included in PIP implants are issued from known European industrial suppliers".
12 June 2010	TGA requested AFSSAPS to provide production records to match with lots supplied in Australia.
22 June 2010	AFSSAPS unable to provide information on production records but advised that they believed that implants of the types with "MX and Asymmetric references produced after 2006" would have had the approved gel.
29 June 2010	Email from AFSSAPS indicating that test results "have been delayed".
2 July 2010	TGA website updated with laboratory test results indicating that PIP implants supplied in Australia conform to the relevant international standards for gel cytotoxicity and shell strength.
28 July 2010	Email from AFSSAPS providing information when test results would be available, and seeking information about the laboratory testing performed by the TGA.
4 September 2010	AFSSAPS email advising that they had seized implants and raw materials from PIP.
20 September 2010	Request from MHRA to share the results of the TGA's laboratory testing.
28 September 2010	AFSSAPS provided advice about their test results and a copy of the accompanying press statement.

Date	Event
29 September 2010	TGA provided advice to MHRA regarding the TGA laboratory test results.
30 September 2010	TGA requested additional information from AFSSAPS regarding their test results.
30 September 2010	MHRA requested permission to use information provided by TGA.
1 October 2010	TGA received advice from MHRA about its web statement.
1 October 2010	TGA website updated to reference AFSSAPS and MHRA websites for additional information and confirming TGA test results. TGA sent notification of update to TGA's website to the Australian Society of Plastic Surgeons and the Australasian College of Cosmetic Surgeons.
5 October 2010	TGA requested information from MHRA about their awareness of any testing being undertaken in other countries.
12 October 2010	Medical Vision Australia advises the TGA that all recalled stock, which had not been provided to the TGA for testing, had been destroyed.
12 October 2010	Request from AFSSAPS for information regarding batches of breast implants tested by TGA.
22 October 2010	TGA responded to AFSSAPS with requested test information.
25 October 2010	Request from AFSSAPS for further clarification of TGA's test results.
25 November 2010	Recall was closed on TGA database following confirmation from Medical Vision Australia that all returned product had been destroyed.
27 January 2011	TGA coordinated simultaneous release of web statement with FDA in the USA regarding the issue of lymphoma associated with breast implants. TGA continued to consult the FDA on this issue.
7 February 2011	TGA held teleconference with Australian Society of Plastic Surgeons to discuss enhancing the breast implant registry and providing an update regarding PIP and also regarding ALCL.
7 December 2011	TGA received information from AFSSAPS about a case of ALCL associated with a PIP implant and confirming its previous advice to patients. AFSSAPS requested specific information about breast implants and cases of ALCL in Australia
21 December 2011	TGA provided advice to AFSSAPS in response to their questions about breast implants and reported cases of ALCL in Australia.
21 December 2011	AFSSAPS advised the TGA that in France, media coverage states health authorities were considering recommending removal of PIP implants from 30,000 women in France.
21 December 2011	TGA web statement posted regarding media coverage in France linking PIP with ALCL.

Date	Event
22 December 2011	Updated web statement from MHRA regarding consultations with other European agencies and TGA. MHRA stated that there is no evidence of any increase in incidence of cancer associated with PIP breast implants and no evidence of any disproportionate rupture rates other than in France.
23 December 2011	Announcement by the French Minister of Health recommending that women in France have their PIP implants removed although there is no urgency to do this. Recommendation was due to the increased rupture rate not to do with any association with cancer.
3 January 2012	TGA contacted ASPS, ACCS and RACS and members of TGA's statutory expert advisory committees regarding PIP breast implants and establishment of an expert advisory panel.
3 January 2012	TGA contacted all state and territory CHOs regarding PIP implants and requested data from their jurisdictions.
3 January 2012	TGA contacted regulatory authorities in Switzerland, Canada, Singapore, USA, Brazil, European Commission and Japan seeking further information on PIP available in their jurisdictions.
3 January 2012	TGA contacted Private Health Insurance Administration Council seeking information on private health insurance data on PIP implants.
4 January 2012	First meeting of TGA expert advisory panel.
4 January 2012	TGA website updated with media release and "PIP implants – the Australian perspective".
4 January 2012	TGA contacted NSW Clinical Excellence Commission requesting PIP implant information.
4 January 2012	TGA sent letter to all current sponsors of breast implants requesting information about ruptures, other complaints and number of implants supplied.
6 January 2012	TGA requested ASPS, ACCS and RACS to instruct their members to assemble lists of their patients who have received a PIP implant.
6 January 2012	Telephone discussion with the offices of state and territory CHOs regarding any use of PIP implants in their jurisdictions.
6 January 2012	TGA sent further requests for information to regulatory authorities in Switzerland, USA, Japan, France, Singapore, Canada and EC.
7 January 2012	Breast Implant Information Line established at 6am.
7 January 2012	Media release by the Gillard Government announcing new hotline for women concerned about their breast implants.
7 January 2012	Further request from TGA To AFSSAPS and MHRA regarding testing requirements/results.
7 January 2012	TGA web statements on PIP implant Questions and Answers.

Date	Event
7 January 2012	TGA began contacting surgeons who were supplied with PIP implants.
7 January 2012	TGA contacted sponsors who may have supplied PIP implants under SAS.
8 January 2012	TGA discussed with ASPS and ACCS the information being conveyed to their members by the TGA.
9 January 2012	DoHA Chief Medical Officer convened a Clinical Advisory Committee to provide him with regular and frequent advice related to PIP breast implants.
9 January 2012	TGA requested from European Commission copies of TÜV Rheinland audit reports. Referred to AFSSAPS.
9 January 2012	TGA requested information from AFSSAPS on audits of breast implant manufacturers.
9 January 2012	TGA received response from AFSSAPS to regarding audit reports.
9 January 2012	TGA received response from AFSSAPS in response to email of 7 January 2012 requesting information regarding testing.
9 January 2012	TGA contacted Australian Commission on Safety and Quality in Health Care requesting data on PIP implants.
9 January 2012	TGA contacted CHOs of each state and territory advising them of the surgeons in their state who had used PIP implants.
10 January 2012	TGA sent registered letters to surgeons who may have supplied PIP implants. Letters also sent to ASPS and ACCS as part of mail out.
10 January 2012	TGA contacted Chair of Advisory Committee on Safety of Medicines to request advice on possible study designs that could be used to detect rupture rate of PIP compared to other prostheses.
10 January 2012	Letter to ASPS, ACCS and RACS requesting further data on PIP implants for analysis by TGA and to also request data from the Breast Implant Registry.
10 January 2012	TGA convened teleconference with state and territory CHOs.
11 January 2012	Communication with French Government seeking clarification of allegations of fraudulent activity by manufacturers of PIP implants.
11 January 2012	TGA convened teleconference of overseas regulators.
12 January 2012	TGA website updated with information regarding the TGA's testing of PIP implants, and an update to Questions and Answers.
12 January 2012	TGA contacted Medical Vision Australia requesting additional information regarding supply of PIP implants under SAS.
12 January 2012	TGA website updated to reflect changes to Questions and Answers on DoHA website and provide the latest results of laboratory testing.

Date	Event
12 January 2012	Email to AFSSAPS requesting information about breast implant samples and the introduction of the gel.
13 January 2012	TGA requested advice from the MHRA and the European Commission on European wide plans to ensure the safety of breast implants currently on the market.
13 January 2012	A summary of TGA's Laboratory testing results circulated to overseas regulators.
13 January 2012	Communication from French Government noting advice from the French Authorities has not been received regarding allegations of fraudulent activities by manufacturers of PIP implants, and seeking information on Australian implant rupture rates.
13 January 2012	Email from AFSSAPS in response email 12 January 2012, regarding tests carried out on PIP implants.
13 January 2012	Email to AFSSAPS requesting sample of implant containing each type of gel.
16 January 2012	Teleconference with state and territory CHOs to discuss available prostheses implant and removal data that could potentially be used to assess rupture rates.
17 January 2012	TGA sent letter to ASPS, ACCS and RACS requesting they send further information to their members in case some PIP implanting surgeons could not be contacted from the TGA mail-out on 10 January 2012.
19 January 2012	TGA convened International Laboratory Testing Panel for PIP breast implants to confer about laboratory testing for the scientific analysis of the quality and safety of PIP implants: this panel includes Australia, Brazil, the Czech Republic, European Commission, Germany, Ireland, UK and the Netherlands.
20 January 2012	Second meeting (teleconference) of TGA's expert advisory panel on PIP implants.
20 January 2012	TGA website updated
20 January 2012	Response from AFSSAPS to email of 13 Jan 2012 re providing samples of gel for testing.
27 January 2012	TGA website updated.
30 January 2012	Communication from French Government regarding the use of a different silicone gel and the outcome of criminal proceedings against PIP founder.
1 February 2012	AFSSAPS advised TGA of detailed reports (in French) of work undertaken by AFSSAPS.
3 February 2012	Communication with French Government responding to request for information on the number of cases of implant rupture rates in Australia, and seeking advice from AFSSAPS to assist Australian testing program.

Date	Event
3 February 2012	TGA website updated.
7 February 2012	Intra-dermal irritation testing on PIP gel and shell commenced.
9 February 2012	TGA hosted second teleconference of International Laboratory Testing Panel for PIP breast implants.
10 February 2012	Communication with European governments (Czech Republic, French, German and Netherlands) regarding respective policy decisions on PIP implants.
10 February 2012	TGA website updated.
17 February 2012	TGA website updated.
20 February 2012	Communication from Czech Ministry of Health regarding policy decisions on PIP implants.
23 February 2012	Third teleconference of TGA's expert advisory panel on PIP implants.
24 February 2012	TGA website updated.
1 March 2012	Questionnaires sent to surgeons who have reported ruptures of PIP implants, with the aim of gathering detailed information about the rupture, the gel, the actual or potential issues of the rupture and the contra-lateral implant if there is one.
2 March 2012	TGA website updated.
7 March 2012	DoHA received detailed reports of the AFSSAPS chemical, mechanical and biological testing.
8 March 2012	TGA hosted 3rd meeting of the International Laboratory Testing Panel for PIP breast implants (ITPP).
9 March 2012	TGA website updated.
10 March 2012	Media release by the Minister for Health, the Hon Tanya Plibersek MP, announcing access to subsidised MRI scans for women with PIP breast implants from 12 March 2012.
10 March 2012	TGA website updated with advice on subsidised MRI scans.
12 March 2012	Breast Implant Information Line script updated with information regarding subsidised MRI scans for women with PIP breast implants.
13 March 2012	Fourth teleconference of TGA's expert advisory panel on PIP implants.
16 March 2012	TGA website updated.
23 March 2012	TGA website updated.
30 March 2012	TGA website updated.

Date	Event
2 April 2012	TGA website updated.
5 April 2012	TGA website updated.
13 April 2012	TGA website updated.

Key

- Unshaded rows indicate regulatory and communication activities undertaken by the TGA.
- Shaded rows indicate activity undertaken by DoHA and media releases from the Health Minister and Parliamentary Secretary for Health and Ageing.