Poly implant Prothese (Pip) Breast Implants: Final report of the Expert Group

Sir Bruce Keogh, NHS Medical Director

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POLY IMPLANT PROTHESE (PIP) BREAST IMPLANTS: FINAL REPORT OF THE EXPERT GROUP

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SUMMARY AND RECOMMENDATIONS

We have carefully reviewed the available evidence on breast implants from the company Poly Implant Prothèse (PIP), including the results of additional studies commissioned since our interim report in January. We have concluded that

- rigorous world-wide chemical and toxicological analyses of a wide variety of PIP implants have not shown any evidence of significant risk to human health;
- there is no reason to believe that further testing will change this conclusion, given the results of the chemical analysis and the number of batches that have now been tested world-wide, which have all reached a similar conclusion;
- PIP implants are significantly more likely to rupture or leak silicone than other implants, by a factor of around 2-6, and this difference is detectable within 5 years of implantation;
- in a proportion of cases, failure of the PIP implant results in local reactions but these are readily detected by outward clinical signs – "silent" ruptures (ruptures which come to light only on explantation) are not generally associated with these local reactions.

In sum, PIP implants are clearly substandard although there is no evidence of a significant increased risk of clinical problems in the absence of rupture.

In the light of these conclusions we reiterate and amplify our previous advice that:

- all providers of breast implant surgery should contact any women who have or may have PIP implants– if they have not already done so – and offer them a specialist consultation and any appropriate investigation to determine if the implants are still intact;
- if the original provider is unable or unwilling to do this, a woman should seek referral through her GP to an appropriate specialist;
- if there is any sign of rupture, she should be offered an explantation;
- if the implants still appear to be intact she should be offered the opportunity to discuss with her specialist the best way forward, taking into account the factors listed in paragraph 33 of this report;
- if in the light of this advice a woman decides with her specialist that, in her individual circumstances, she wishes to have her implants removed her healthcare provider should support her in carrying out this surgery. Where her original provider is unable or unwilling to help, the NHS will remove but not normally replace the implant;
- if a woman decides not to seek early explantation, she should be offered annual follow up in line with the advice issued by the specialty surgical associations in January 2012 (see para 4). Women who make this choice should be encouraged to consult their doctor if they notice any signs of tenderness or pain, or swollen lymph glands in or around their breasts or armpits, which may indicate a rupture. At the first signs of rupture, they should be offered removal of the implants.

What we knew at the time of our interim report (January 2012)

- PIP implants are not associated with a higher risk of breast cancer or other forms of cancer than other breast implants – indeed, the incidence of breast cancer for women with PIP implants is *lower* than that in the general female population.
- Standard toxicological tests carried out in the UK, France and Australia showed no evidence of cytotoxicity (damage to cells) or genotoxicity (genetic mutations).
- One test carried out by the French authorities suggested that PIP implants could cause skin irritation in rabbits.

What was still inconsistent or uncertain

- Tests on the mechanical strength of the shells of PIP implants showed inconsistent evidence on whether they met standard international tests.
- Evidence on spontaneously reported rupture rates was inconsistent – most countries had reported rupture rates well below the rupture rates estimated from careful follow-up in the "core studies" for the leading brands of silicone breast implants, but the French regulator AFSSAPS had reported a large increase in rupture rates from March 2010 onwards and a further acceleration in 2012.
- Apart from one study, available only in an unpublished manuscript at the time of our January report, there was no available data which made it possible to compare rupture rates between PIP and other brands of silicone breast implants, even approximately, on a like for like basis.

What this report adds

- Chemical analyses of further batches of the silicone used in PIP implants and other silicone breast implants shows that there are higher levels of siloxanes in the former, and that these vary between batches. The presence of these siloxanes is not considered to constitute a significant risk to health, even in the event of a complete rupture of a PIP implant. Apart from this, there is no significant variation between batches, and no significant differences between PIP and other implants.
- In particular, there are no other organic impurities in PIP implants.
- There were no significant inorganic impurities in any batch. The levels of platinum in the silicone of PIP implants are lower than in medical grade silicone. A very low level of caesium was found (not considered to be of significance to health).
- Further toxicological testing in Australia confirms that the silicone gel in PIP implants does not cause cytotoxicity.
- Tests commissioned by the Australian authorities, and carried out to international standards in laboratories in France and Australia, found no

evidence of a potential to cause skin irritation (contradicting the earlier findings from the French regulator).

- Analysis of retrospective data on explantation of PIP and other breast implants during the period 2001-2011 provides evidence that PIP implants have a higher rupture rate, and that patients with PIP implants are at greater risk of associated clinical signs at explantation (local reaction and lymph node enlargement).
- Adjusting for likely sources of bias the rate of implant failure for PIP implants is estimated at around 6-12% at 5 years, and 15-30% at 10 years. This can be broadly compared with the reported rupture rates of 10% at 10 years for Allergan implants and 14% at 8 years for Mentor implants. All these estimates are subject to considerable uncertainty, in part because of poor follow-up.
- Analysis of prospective data on explantations carried out since January 2012, many of them for purely prophylactic reasons, suggests that where there were already signs of a problem before explantation, local reactions were more likely to be found at explantation. Thus external signs of problems should be taken seriously. Conversely, “silent” ruptures (ruptures which come to light only on explantation) are not generally associated with these local reactions.

POLY IMPLANT PROTHESE (PIP) BREAST IMPLANTS: FINAL REPORT OF THE EXPERT GROUP

Introduction

This is the final report of the expert group set up under my chairmanship to review evidence of the potential risks to health of the silicone gel breast implants made by the French company Poly Implant Prothèse (PIP), and to advise the Department of Health in England[a] on policy in relation to women who received these implants. The members of the group are listed at the Annex.

2. In our interim report[1], published in January 2012, we reviewed the data then available on the toxicity of the non-medical grade silicone illegally used by PIP and on the rates of rupture of the implants. We

i endorsed the advice from the French cancer institute[2] that PIP implants were not associated with a higher risk of cancer than other breast implants[b]

ii noted that there was no evidence from the toxicological studies to date that the gel filler used in PIP implants was intrinsically harmful

iii considered that the available statistical evidence was insufficient to form a view on the rate of rupture of PIP implants compared to other implants

iv noted that there were risks associated with the policy of routine, preventative explantation adopted in some European countries

v concluded on the basis of these considerations that there was no clear evidence at that time that patients with a PIP implant were at greater risk of harm than those with other implants

vi endorsed the advice issued by the Medicines and Healthcare Products Regulatory Agency (MHRA) in December 2011, that there was no specific safety concern which required a recommendation of routine removal of PIP implants

vii recognised however the anxiety of many women who received PIP implants in good faith on the assumption that they were manufactured in accordance with EC standards

viii endorsed therefore the decision of DH ministers that women who had received PIP implants as part of NHS treatment should be contacted, given relevant information and advice, and offered a consultation on the best way forward in their individual circumstances. This could include removal and replacement of the implant if, informed by an assessment of clinical need, risk or the impact of unresolved concerns, a woman with her doctor decided that it was right to do so

[a] The devolved administrations (Scotland, Wales and Northern Ireland) have separate responsibility for healthcare policy in their territories but sent observers to the expert group.

[b] The incidence of breast cancer in this (generally healthy) population is less than for women generally. All breast implants are associated with a slight excess risk of one rare form of cancer (anaplastic large cell lymphoma) but there is no evidence of an additional risk for PIP implants compared with other breast implants.

ix called on private providers to offer similar care to their patients

x endorsed the decision of ministers that, where a private provider was no longer in business or was unwilling or unable to meet their moral and legal obligations towards their patients, the NHS should offer a consultation, a scan where appropriate, and removal (but not normally replacement) of the implants where a woman and her doctor decided this was the right thing to do.

3. Underlying all our considerations were three key principles:

i the final decision should be based on a personal discussion between each woman and her doctor based on her individual circumstances;

ii decisions should be informed by the emerging scientific and clinical evidence;

iii all those advising women should show compassion for their particular circumstances and should recognise that anxiety is in itself a real risk to health.

4. Consequently, the NHS Chief Executive Sir David Nicholson wrote to all NHS organisations[3], and the Chief Medical Officer Dame Sally Davies to GPs and specialists[4], summarising the available evidence and setting out the model of care which the NHS was expected to offer. This guidance was subsequently reinforced and clarified in two further letters from the CMO[5]. In addition, the Royal College of Surgeons and its affiliated specialty associations – the Association of Breast Surgery (ABS), the British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS), the British Association of Aesthetic Plastic Surgeons (BAAPS) and the Federation of Surgical Specialist Associations – issued more detailed clinical guidance for GPs and specialists, including advising annual follow-up for women who decided not to have their implants removed[6].

5. Following our interim report, the European Union's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) also reviewed the available data and published a report[7]. Their conclusions were similar to ours:

> "The limited clinical data, along with the absence of epidemiologic data on PIP silicone breast implants provide insufficient evidence to warrant a conclusion that women with PIP silicone breast implants have a greater risk to their health than women with breast implants from other manufacturers. In regard to breast implants in general there is a reasonable number of large, good-quality studies showing no increase in any cancer type or connective tissue disease among women with standard silicone breast implants (including women with ruptured implants). However, in the case of PIP implants, when the limited available clinical information is taken together with the findings from tests of the physical and chemical properties of the shell and silicone, and of the *in vivo* irritancy test, some concerns are raised about the safety of PIP breast implants as the possibility for health effects cannot be ruled out."

6. Both the SCENIHR report and our interim report emphasised the limitations of the available data. Particular issues were

i the suspicion that there could be significant variation in the chemical composition of different batches of the silicone gel used among PIP implants[8], implying that it would be necessary to test for possible toxicity in a large number of samples of PIP implants to be reasonably confident about the possible risks to health;

ii the lack of robust data on comparative rates of ruptures and other adverse events, which made it difficult to achieve a fair comparison between PIP and other implants.

We therefore decided to commission further work to address both these issues. The results of this additional work are summarised in the following sections, and in more detail at Appendices I and II.

Chemical and toxicological analysis

Chemical analysis

7. Samples of silicone gel from five batches of PIP breast implants, manufactured between about 2005 and 2010, were compared with gel samples from six batches of medical grade breast implants from other manufacturers. The samples were analysed by the research laboratory LGC for both organic and inorganic impurities, using a variety of standard analytical methods. When this new information is combined with analyses carried out by the French regulator Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS, now the Agence Nationale de Sécurité du Medicament, ANSM) and the Australian regulator Therapeutic Goods Administration (TGA), the following conclusions can be drawn (see Appendix I for further detail):

i in general, there is little variation in chemical composition from batch to batch and little difference between PIP and medical grade silicone. In particular, no inorganic or organic impurities were detected other than those listed below;

ii the PIP batches showed higher levels of low molecular weight cyclic silicones (the siloxanes including octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5), and dodecamethylcyclohexasiloxane (D6)) as compared with medical grade silicone, with some variation between batches. Work to measure the concentration of the siloxanes is still in progress and will be published as soon as the data are available, but some idea of the possible range of levels is shown in the results from TGA quoted in Appendix I;

iii levels of platinum (used as a catalyst in the polymerisation process) were lower for the PIP implants compared with the medical grade silicone

iv a very low level of caesium (0.3 parts per million) was found in the PIP implants, but not in medical grade silicone. This is not considered to be of biological relevance.

8. Siloxanes are used in a variety of applications and we are all exposed to low levels through consumer products, such as hair and skin care products, antiperspirants and deodorants. The possible implications for human health have been studied in a 2004 review by the Scientific Committee on Consumer Products (SCCP)[9] and, in the specific context of PIP breast implants, in recent work by the TGA's expert panel[10]. The conclusion drawn is that even in the event of a complete rupture of a PIP implant there would be no significant risk to human health.

9. It has been frequently suggested[11] that testing of intact PIP implants should be supplemented by tests on prostheses that have been explanted, for instance after rupture. The TGA have analysed the "milky fluid" described by some surgeons on explantation of PIP implants[12] and concluded that it consisted essentially of a suspension of silicones in water, rather than the product of some inflammatory reaction.

10. Silicone polymers of high molecular weight are considered highly unlikely to cross the barrier into breast milk and current advice from the MHRA[13] is that women with PIP breast implants should continue to breast feed their infants. In theory it is possible that the lower molecular weight siloxanes could migrate into breast milk; the MHRA have therefore arranged for chemical analysis of a sample of breast milk from a patient with ruptured PIP implants and we will publish the results as soon as they are available. In the meanwhile, in the light of the advice in the SCCP review, we consider that there is no reason to depart from the current MHRA advice.

Toxicity testing

11. Information about the potential toxicity of the silicone gel used in PIP implants is available from a variety of tests reported by the MHRA in 2010[14], by the French regulator (AFSSAPS) in 2011[15], and by the Australian regulator (TGA) in 2010 and 2012[16]. The conclusions drawn from these investigations are:

i all tests to date for cytotoxicity (damage to cells) and genotoxicity (genetic mutations) have been negative;

ii the most recent tests for skin irritation, carried out to recognised international protocols, were negative. An earlier test reported in the 2011 paper from AFSSAPS showed positive results for skin irritation in rabbits. TGA have more recently attempted to replicate this finding, commissioning tests at a laboratory in France (the laboratory that did the original work for AFSSAPS) and a laboratory in Australia. The results were negative for all the batches tested.

The interpretation of these findings is that, judged by the most relevant internationally accepted standards, the gel filler material used in PIP implants is not irritant and does not pose a threat to human health.

12. To give additional assurance, and guided by the results of the chemical analyses, the MHRA have commissioned a further series of toxicity tests on additional samples of PIP silicone gel, using standard methods to assess the potential of the gel to cause cytotoxicity, genotoxicity, or skin irritation. The results of these tests will be published as soon as they are available.

13. In the light of the findings from the chemical analysis, that there is little variation in chemical composition between batches of PIP implants made over a period of 5 years, it seems increasingly unlikely that testing of further samples will reveal any cause for concern. However, work is continuing both in the UK and internationally to provide as complete a picture as possible of the chemical and toxicological profile of PIP silicone.

Data on ruptures and other clinical problems

Retrospective data collection

14. In February 2012, at the request of the expert group, MHRA contacted all the major providers of breast implants, both in the NHS and in the private sector, and asked them to complete a questionnaire seeking information for both PIP and other brands on

i the total number of women who received implants each year over the period 2001-2011

ii the reasons for explantation[c], and the clinical findings at explantation, of all explantations carried out over the same period.

In response to this request we received information on some 240,000 implants given to 130,000 women and detailed findings from 5,600 explant operations. Although this does not represent a complete return we are confident that the data collected is sufficiently representative to give a robust picture of the relative performance of PIP compared to other implants. However, the observed rates of adverse events will inevitably be underestimates of the true underlying absolute risks, partly because some patients may have been explanted at centres other than those that returned data, but mainly because many cosmetic surgery providers were unable to maintain complete follow-up of their patients and so many symptoms will have gone undetected.

15. In addition, evidence from the long-term studies of other brands of implants required by the US Food and Drug Administration (FDA)[17] suggest that many ruptures have no clinical consequences ("silent ruptures") and can be detected only by scanning. For primary augmentation, rupture rates of 10% (95% confidence interval 7-14%) at 10 years have been reported for the Allergan implants and of 14% (7-24%) at 8 years for the Mentor implants, using a subgroup being followed up by MRI. In contrast, the same Mentor study gave rupture rates of only 1.1% at 6 years based on spontaneous reporting[18]. This illustrates the difficulty in ensuring that rupture rates for different implants are compared on a truly comparable basis.

16. Despite these limitations, the data we have collected constitute a very rich data source which lends itself to a large number of possible analyses (see again Appendix II for further details). For simplicity, we have concentrated on two main composite outcomes:

[c] Possible reasons for explantation could include suspected rupture, signs of local reaction without apparent rupture, problems with the contralateral implant, aesthetic appearance, or other reasons.

i "implant failure", defined as any one of rupture (confirmed at explantation), significant silicone leakage from either implant (confirmed at explantation), or clinical evidence of local reaction to silicone leakage (seen before explantation);

ii "local clinical signs", defined as any one of local tissue reaction or lymph node involvement (whether seen before explantation or at explantation).

17. The main findings from this analysis are:

i PIP implants are more likely to fail than other implants, by a factor of around 2-6, and the divergence between PIP and other implants is already apparent after 5 years;

ii the failure rate for PIP implants is estimated on the basis of these reported adverse events at 1.2% at 5 years, rising to 3.1% at 10 years. This compares with a failure rate for other brands of silicone gel implant of 0.2 - 0.4% at 5 years and 0.5 - 1.1% at 10 years. However the true underlying failure rate, including "silent" ruptures, will be greater than this for the reasons set out above;

iii PIP implants are more likely than other implants, by a factor of around 3-5, to result in local clinical signs. The rate of explants with local clinical signs is 0.8% at 5 years rising to 2.1% at 10 years . In absolute terms, these complication rates appear quite low although again the true underlying rates may be rather higher[d];

iv PIP implants are not associated with higher risks of other clinical problems such as capsular contraction, haematoma or cancer.

These results are all statistically significant according to standard tests. The quoted ranges are wider than the classic statistical confidence intervals, with an additional judgemental contribution due to data limitations. Detailed tables are at Appendix II.

18. We carried out a large number of additional analyses to test the robustness of these findings. Details are in Appendix II, but some key points are:

i the excess problems for PIP implants may be partially the result of reporting bias (the greater tendency for women to seek explantation or for clinicians to report problems) after the discovery of the fraud in March 2010, but this accounts only for some of the excess – excluding data from 2010 onwards still results in a clear and statistically significant excess risk on all measures for PIP implants;

ii relatively few PIP implants were used for NHS breast reconstructions, but an excess risk was still observed in this group;

iii the largest use of PIP implants was in non-NHS augmentation: restricting analysis to this group, and explantations before 2010, reveals low absolute failure rates but a significant 5-fold excess in PIP implants.

[d] The discrepancy between observed and true rates for clinical signs is likely to be smaller than that for implant failure since, by their nature, clinically observable signs are more likely to result in a decision to explant.

Prospective data collection

19. Since January 2012, surgeons have carried out a substantial number of explantations of PIP implants. Through the three surgical associations referred to in para 4 (ABS, BAPRAS and BAAPS) we asked surgeons carrying out these operations to complete a questionnaire listing the reasons for explantation and the clinical findings. To date, 761 questionnaires have been returned. The results (see Appendix II) complement and in some cases confirm those from the retrospective analysis; in particular

i about two thirds of the explantations have been carried out for purely prophylactic reasons (described in the questionnaire as "for anxiety only") rather than because of cosmetic reasons or clinically apparent signs;

ii in the group of patients who underwent implant removal for prophylactic reasons, evidence of implant failure (rupture or severe gel bleed) was apparent in 23% of explantations, and clinical signs associated with this implant failure in 2.2%. This compares to a rate of implant failure of 64%, and a rate of finding of clinical signs of 35%, for explantations carried out for other reasons;

iii not surprisingly, in most cases where clinical problems were detected at explantation, these were already apparent to the patient or clinician before the operation – few women who had explantation for prophylactic reasons had these more significant problems.

In sum, although clinically undetected ruptures of PIP implants are quite common, such "silent" ruptures were infrequently associated with severe clinical problems.

Other available data

20. Berry and Stanek[19] recently reported the results of a follow-up study of 457 patients who received PIP implants between 2000 and 2005. All patients were invited for a follow-up and those who responded were assessed by ultrasound and, if appropriate, by surgical explantation. We have re-analysed these results by kind permission of the authors. 37% of patients could not be contacted and a further 9% declined the invitation to follow-up. Of the remainder, a rupture was found in one or more implants in 35% of cases. We estimate that the rupture rate at 10 years after implantation could lie between 18% (if we assume that those not followed up were all free from rupture) and, more plausibly, 31% (assuming that these unobserved patients were similar to those with follow up).

21. Data from the French regulator ANSM (formerly AFSSAPS) show a very sharp increase in the number of ruptures reported after March 2010, and a further upturn after December 2011. By the end of April 2012 ANSM had received reports of 2,702 ruptures in 2,252 women – 7.5% of the estimated 30,000 French women with PIP implants – with a median time to rupture of 5½ years. ANSM also report that 5,257 preventative explantations have been carried out in France, of which 80% showed intact implants with no clinical symptoms.

22. One of the major UK providers of cosmetic treatments have kindly shared with the group their own analyses of rupture rates for PIP implants, by quarter of implantation. These show a very rapid increase in the number of reported ruptures after December 2011, in common with the AFSSAPS data. The data also show that for some individual implantation cohorts the rupture rate is already 10% or more, in some cases after less than 5 years.

23. The MHRA's own monitoring of adverse events shows that, between 2007 and 2009, 201 ruptures of PIP implants had been reported, representing a rupture rate of about 0.6% based on an estimated 35,000 women with PIP implants; over the same period 70 ruptures were reported from other brands who had a larger share of the market. Since then the rate of adverse incident reports has increased rapidly and the cumulative total now stands at 679 from spontaneous adverse incident reports, and a further 241 from the prospective data collection, giving an overall rupture rate of 2.2%. Comparison with the retrospective data collected from implanting centres suggests that only about 1 in 6 ruptures have been reported through the adverse incident system.

Conclusions

24. The wide range of results from different sources shows the difficulty of making firm estimates, due to the paucity of directly comparable data, poor follow-up, and lack of consistency in definitions of clinical findings.

25. Nevertheless the available data show convincingly that PIP implants are associated with higher rates of rupture and higher rates of clinical problems compared with other implants. Estimating the <u>absolute</u> risks associated with PIP implants is more difficult: drawing the evidence together suggests

i the failure rate of 1.2% at 5 years and 3.1% at 10 years found in our retrospective study (para 17) is a substantial under-estimate due to incomplete follow-up without imaging, perhaps by a factor of 5-10

ii the study by Berry and Stanek (para 20) suggests a failure rate of around 30% at 10 years with good follow-up

iii recent PIP explant activity suggests 5-year rupture rates of at least 7% (para 21) and 10% (para 22)

iv FDA data suggests a rupture rate of around 10-14% at 8-10 years for non-PIP implants, to which the excess risk of PIP could be applied.

Based on these findings we estimate that the rate of implant failure (rupture or significant silicone bleed) for PIP implants could be 6-12% after 5 years rising to 15-30% after 10 years, in line with the study by Berry and Stanek referred to at para 20.

26. However, a proportion of these ruptures will be of little clinical consequence. From our retrospective analysis we estimated that the risk of significant clinical problems for PIP implants was around 0.8% after 5 years, rising to 2.1% after 10 years (para 17), and although these figures will be underestimates for the reasons already given the degree of underestimation will be less than for the rupture rate. A large proportion of these clinical problems – up to 90%, according to our prospective analysis – will already have been apparent through clinical examination before

explantation. In contrast, where explantations are carried out purely for preventative reasons, the risk of finding clinical problems is low (1-2%).

Other reported symptoms

27. There have been widespread reports of systemic symptoms associated with PIP implants – generalised pain, respiratory problems, anxiety, fatigue – and calls for the Department of Health to collect information to assess the frequency with which such symptoms occur. We have considered this carefully but did not feel that such a data collection would be helpful, for three main reasons:

i the symptoms described are common in the general population. A systematic study would therefore need to establish some kind of control group as well as addressing the various forms of unconscious bias which might influence the results – for instance, the possibility that women with PIP implants might be more likely to report symptoms than a matched sample from the general population;

ii similar symptoms have been ascribed to other breast implants in the past, and a number of very careful epidemiological studies have been carried out[20]. These studies have uniformly failed to demonstrate any convincing causal link between implants and symptom prevalence. One study[21] specifically addressed the problem of reporting bias and showed that, when self-reported symptoms suggestive of connected disease disorders including rheumatoid arthritis were reassessed by a clinician blind to whether the patient was in the implant group or the control group, the apparently significant association disappeared;

iii despite extensive toxicology testing, no evidence has yet been found that any of the chemical constituents of silicone gel are potentially harmful and no biologically plausible mechanisms have been suggested to link silicone gel with the symptoms described. In this respect, as noted in para 7 above, PIP silicone gel is no different from the gels used in other implants.

28. This is not in any way to dismiss the reality or clinical importance of the symptoms reported. As we noted in our interim report[22], anxiety is in itself a genuine health issue and may well increase the risk of other health problems. These symptoms may therefore be very relevant to the decision which an individual woman takes, after discussion with her clinician, about the possible removal of her implants. But we do not believe that a further research study at this stage is likely to yield any useful information on whether, in general, PIP implants are likely to pose a risk to health as compared to other implants.

Ethical considerations

29. In our interim report, we noted that women who received PIP implants would have assumed in good faith that their implants contained medical grade silicone, in line with the CE mark. We argued as a consequence that there was a duty of care on the part of the providers of breast implant surgery to look after their patients and, with due regard to their wishes, to offer whatever was reasonably needed to ensure

their longer-term health. We noted in this context that anxiety is in itself a form of health risk.

30. All this remain true – indeed, it is even more relevant now that we have robust evidence that PIP implants are more likely to rupture and more likely to cause local reactions than other implants. In particular, we believe that all providers who have implanted PIP implants have a responsibility to take all reasonable proactive steps to contact their former patients, and to share with them the best available objective information about the possible risks to their health – including the evidence summarised in this report – so that they can reach an informed decision on whether they want their implants removed.

Discussion and conclusions

31. The key points which we draw out of the available information are as follows:

i rigorous world-wide chemical and toxicological analyses of a wide variety of PIP implants have not shown any evidence of significant risk to human health;

ii there is no reason to believe that further testing will change this conclusion, given the results of the chemical analysis and the number of batches that have now been tested world-wide, which have all reached a similar conclusion;

iii PIP implants are significantly more likely to rupture or leak silicone than other implants, by a factor of around 2-6, and this difference is detectable within 5 years of implantation;

iv in a proportion of cases, failure of the PIP implant results in local reactions but these are readily detected by outward clinical signs – "silent" ruptures (ruptures which came to light only on explantation) are not generally associated with these local reactions.

In sum, PIP implants are clearly substandard although there is no evidence of a significant increased risk of clinical problems in the absence of rupture.

32. In the light of these findings, we are reiterating and amplifying our earlier advice that:

i **all providers of breast implant surgery should contact any woman who has or may have PIP implants**– if they have not already done so – **and offer her a specialist consultation and any appropriate investigation to determine if the implants are still intact**;

ii **if the original provider is unable or unwilling to do this, a woman should seek referral through her GP to an appropriate specialist**;

iii **if there is any sign of rupture, she should be offered an explantation**;

iv **if the implants still appear to be intact she should be offered the opportunity to discuss with her specialist the best way forward**.

33. In approaching this discussion, **we recommend that the following factors should be taken into consideration**:

i there is a risk of morbidity and mortality associated with any surgery, even for this generally healthy population;

ii the available evidence from the Allergan and Mentor core studies[23] suggests that the risks of complications are greater for subsequent breast augmentation procedures than for a primary breast augmentation;

iii all breast implants have a finite risk of failure; if a woman decides not to seek early removal of her PIP implants there is still a 15-30% chance that she will develop a rupture which may need surgery at some stage within 10 years of implantation; the available data suggests that the risk of failure of PIP implants in any 12-month period is more or less constant from 3 years after implantation onwards;

iv the more significant adverse consequences of rupture or leakage of PIP implants appear to occur primarily in cases where the signs are already apparent on clinical examination, rather than for "silent" ruptures;

v breast cancer patients who develop enlarged axillary lymph nodes following implant-based breast reconstruction require full investigation by the multidisciplinary breast team with responsibility for their care. Other women with ruptured implants who develop enlarged axillary lymph nodes require appropriate investigation (which may include image-guided lymph node biopsy) to determine if the additional complications associated with axillary surgery at the time of explantation would be justified;

vi if the woman decides not to seek an explantation at this time, a policy of annual review with explantation at the earliest sign of rupture will forestall at least a proportion of the cases in which a rupture or leakage of silicone gel might result in significant clinical problems;

vii despite extensive testing in the UK and internationally, there is to date no evidence implicating PIP implants (or other silicone breast implants) in other forms of longer term damage to health.

34. If in the light of this advice a woman decides, with her doctor, that in her individual circumstances she wishes to have her implants removed **her healthcare provider should support her in carrying out this surgery.** Where her original provider is unable or unwilling to help, the NHS will remove but not normally replace the implant.

35. If a woman decides not to seek early explantation:

i **she should be offered annual follow up in line with the advice of the three specialty surgical associations** (see para 4);

ii **she should be encouraged to consult her doctor if she notices any signs of tenderness or pain, or swollen lymph glands in or around her breasts or armpits, which may indicate a rupture** (or could be the symptoms of another disease not related to breast implants);

iii **if there are signs of a possible rupture, she should be offered the removal of the implants** – as would be the case for any breast implant.

Equalities implications

36. In our interim report, we considered the implications of the public sector equality duty in s149 of the Equality Act 2010 and concluded that there was no evidence to suggest that anyone sharing a protected characteristic (including age, disability, gender, marriage etc status, pregnancy and maternity status, race, religion and sexual orientation) would be subject to special disadvantage as a result of our advice or of the policies adopted by the Department. We believe this is still true.

Further work

37. The expert group will disband following this, our final report. However, officials at the Department of Health and MHRA will continue to monitor developments in the available information, and in particular the results of the further toxicological work already commissioned (para 12), and will issue amended advice – or reconvene this group – as needed.

38. Wider issues over the regulation of cosmetic surgery and other cosmetic procedures will be considered in the review announced by ministers in January[24]. A further announcement about this review will be made in the near future, together with a call for interested parties to submit evidence to the review team.

Sir Bruce Keogh KBE, DSc, FRCS, FRCP
NHS Medical Director

18 June 2012

List of abbreviations

ABS	Association of Breast Surgery
AFSSAPS	Agence Française de Sécurité Sanitaire des Produits de Santé (now Agence Nationale de Sécurité du Medicament, ANSM)
BAAPS	British Association of Aesthetic Plastic Surgeons
BAPRAS	British Association of Plastic, Reconstructive and Aesthetic Surgeons
D4, D5, D6	Low molecular weight cyclic silicones
FDA	Federal Drugs Administration (USA)
INCa	Institut National du Cancer (France)
LGC	A chemical research consultancy, formerly the Laboratory of the Government Chemist
MHRA	Medicines and Healthcare products Regulatory Agency
PIP	Poly Implant Prothèse
SCCP	Scientific Committee on Consumer Products (European Commission)
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks (European Commission)
TGA	Therapeutic Goods Administration (Australian Federal Government)

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ANNEX: MEMBERSHIP OF THE EXPERT GROUP

Sir Bruce Keogh (NHS Medical Director) – Chairman

Mr Simon Edwards (Head of Policy Royal College of Surgeons of England)

Mr Fazel Fatah (Consultant plastic surgeon, President British Association of Aesthetic Plastic Surgeons)

Mr Tim Goodacre (Consultant plastic surgeon, Past President British Association of Plastic Reconstructive and Aesthetic Surgeons)

Dame Deirdre Hine

Sir Ian Kennedy

Professor Ian Kimber (Professor of Toxicology, Manchester University, Toxicology member of the Committee on the Safety of Devices)

Mr Ian Martin (President of the Federation of Surgical Specialist Associations)

Mr Richard Milner (Consultant plastic surgeon, President British Association of Plastic Reconstructive and Aesthetic Surgeons)

Mr Richard Rainsbury (Consultant Surgeon, President of the Association of Breast Surgery) *[alternate: Miss Julie Doughty]*

Dr Anne-Marie Slowther (Associate Professor of Clinical Ethics, Warwick Medical School, Consultant Clinical Ethicist, University Hospitals, Coventry and Warwickshire NHS Trust)

Professor David Spiegelhalter (Professor of Bio Statistics and Winton, Professor of the Public Understanding of Risk, University of Cambridge)

Dr Andrew Vallance-Owen (former Group Medical Director, BUPA; chairman, Cosmetic Surgery Group of the Independent Healthcare Advisory Service (IHAS))

Professor Norman Williams (Professor of Surgery and Director of Surgical Innovation at Barts and The London School of Medicine and Dentistry, President of the Royal College of Surgeons of England)

Mr Simon Withey (Consultant plastic surgeon, Member of Council of British Association of Aesthetic Plastic Surgeons, Member of the Steering Committee looking at Standards in Aesthetic Plastic Surgery)