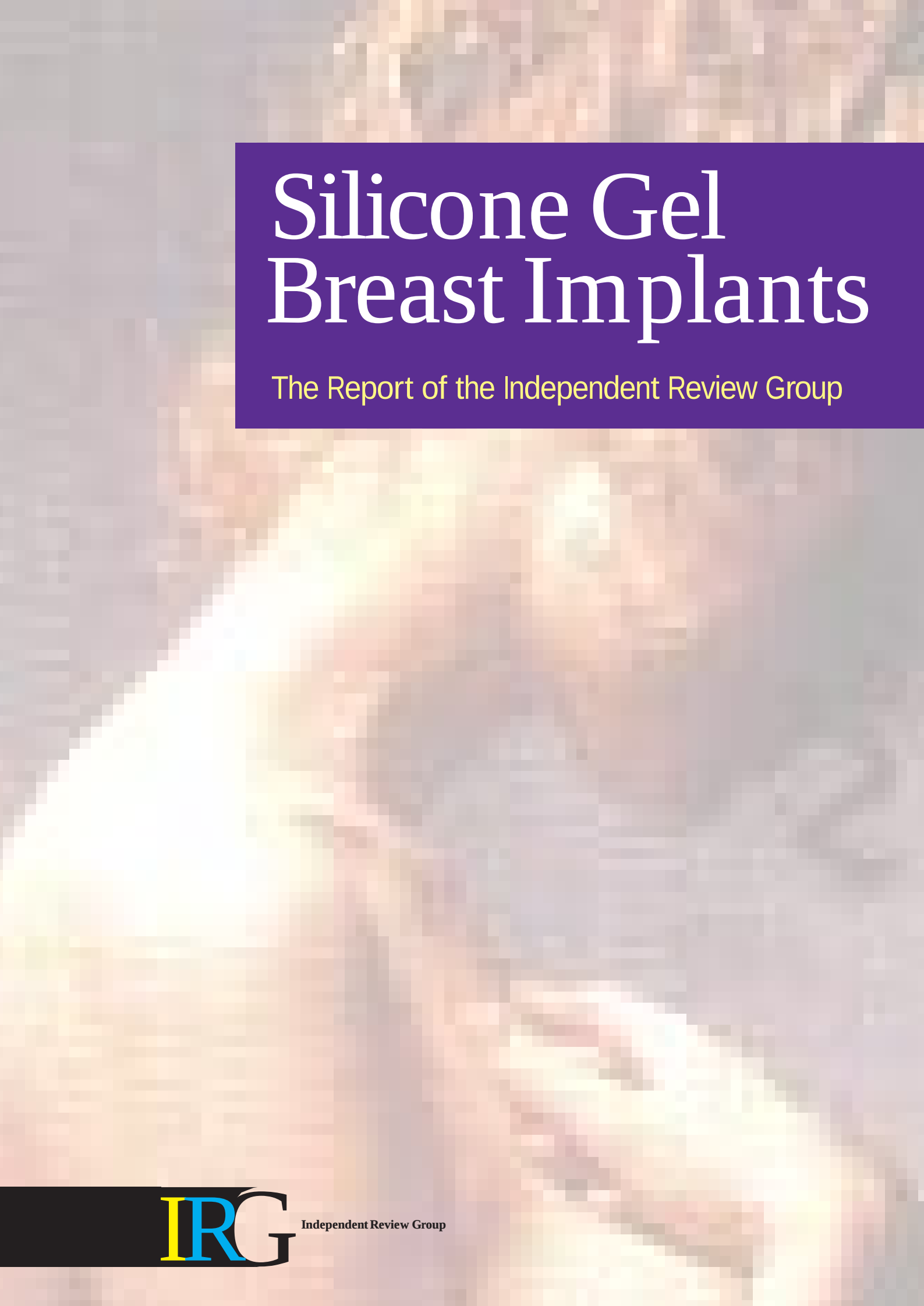

Silicone Gel Breast Implants

The Report of the Independent Review Group

IRG

Independent Review Group

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July 1998, web version 2011

Silicone Gel Breast Implants, The Report of the Independent Review Group has been prepared for publication by Jill Rogers Associates, Cambridge

Design by Information Design Workshop, London

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Foreword

To the Chief Medical Officer

I am pleased to present the report of the Independent Review Group. We were charged by you with the responsibility to *'review the evidence relating to the possible health risks associated with silicone gel breast implants, to examine the issues relating to pre-operative patient information and to report to you on our conclusions'.*

We are aware of the importance of the outcomes of our task for women who have had, and who will have, silicone gel breast implants, for their families, for health care professionals involved in their care, for manufacturers, lawyers, and others who are concerned with the issues surrounding the use of silicone gel breast implants.

Our members were selected for their independent views, their knowledge and understanding of the issues and lack of any vested interest in the conclusions reached. We have met frequently, have considered an extensive literature, and have taken evidence from expert witnesses, including patients, patient groups, clinicians, lawyers, manufacturers and scientists. This evidence has been gathered from experts both in the United Kingdom and overseas.

We have taken a fresh look at the existing and emerging scientific evidence for a link between silicone gel breast implants and effects on health. In the process of this, we have been conscious of the need to examine carefully the causes of ill health in a number of women with implants.

We have made recommendations which will address the concerns of women with silicone gel breast implants, encourage further research into important areas, and enable clinicians, manufacturers, scientists and the general public to work together to ensure the highest levels of confidence in the production, use and long term effects of silicone gel breast implants.

Professor Roger D Sturrock MD FRCP
Chairman of the Independent Review Group
The McLeod / Arthritis Research Campaign Professor of Rheumatology, University of Glasgow

Summary

The Independent Review Group (IRG) was established in response to concerns expressed by women in relation to silicone gel breast implants.

The Chief Medical Officer, at the request of the Minister of Health, Baroness Jay, set up the IRG with the remit:

> *'to review the evidence relating to the possible health risks associated with silicone gel breast implants, to examine the issues relating to pre-operative patient information, and to report to the Chief Medical Officer on its conclusions.'*

In fulfilling the remit, the IRG has taken a fresh look at the existing and emerging scientific evidence for a link between silicone gel breast implants and effects on health. Additionally, the IRG gathered evidence on the quality and quantity of information routinely provided to women about to undergo breast implantation. The IRG:

- reviewed the existing reports and evidence
- identified and considered new evidence
- considered the possible existence of a new, undefined syndrome
- considered the range of risks associated with silicone gel breast implants
- examined whether patient information is satisfactory
- considered how good clinical practice can be assured.

The IRG considered evidence from a number of sources, including:

- oral evidence from representatives / nominees of patient groups, lawyers, researchers, physicians, plastic surgeons, industry and the National Breast Implant Registry
- written evidence from interested parties, including women with breast implants, replies to requests for information, and additional information from those who gave oral evidence
- plaintiff and defence submissions to the scientific panel appointed to review the scientific merits of evidence presented in litigation in the United States
- unpublished scientific information, legal submissions, letters from women with silicone gel breast implants, Internet and press articles
- scientific publications
- data provided by manufacturers.

The IRG considered immense amounts of complex evidence and reached a number of conclusions.

1. There is no histopathological or conclusive immunological evidence for an abnormal immune response to silicone from breast implants in tissue.

2. There is no epidemiological evidence for any link between silicone gel breast implants and any established connective tissue disease. If there is a risk of connective tissue disease, it is too small to be quantified. The IRG cannot justify recommending further epidemiological studies to investigate this hypothesis.

3. Good evidence for the existence of atypical connective tissue disease or undefined conditions, such as 'silicone poisoning' is lacking. It is possible that other conditions such as low grade chronic infection may account for some of the non-specific illnesses noted in some women with silicone gel breast implants.

4. The overall biological response to silicone is consistent with conventional forms of response to foreign materials, rather than an unusual toxic reaction.

5. There is no evidence that children of women with breast implants are at increased risk of connective tissue disease.

6. The IRG recognised that there were issues such as the precise incidence of rupture where the scientific data were incomplete so that rigorous conclusions could not be drawn.

The IRG recognised that:

- there are physical and psychological benefits of breast implantation for many women
- there are a number of complications such as capsular contracture and gel bleed associated with breast implantation
- information provided to women to assist them in making informed decisions about whether to proceed with breast implant surgery is frequently inadequate, in terms of both quality and quantity
- there is a need to extend the principles of good clinical practice and clinical audit across some areas of the private sector
- there is a need to improve scientific quality in a number of areas of research relating to aspects of silicone gel breast implants.

To address these areas of concern, the IRG makes a number of recommendations.

Recommendation 1

The IRG recommends that all patients undergoing cosmetic breast augmentation surgery should be able to obtain, free of charge, from a designated body, comprehensive information about the benefits and risks of such surgery. This should be accompanied by a checklist of topics (see Figure 2) which should be covered when the possibility of an operation is discussed.

Recommendation 2

The IRG recommends that advertisements in all media promoting breast implant surgery should include a statement indicating that anyone contemplating this type of surgery can obtain information about the operation and its risks from a designated body.

Recommendation 3

The IRG recommends that all women undergoing or proposing to undergo cosmetic breast augmentation surgery should be offered the following:

1. an initial appointment with the surgeon carrying out the operation

2. an opportunity to discuss the checklist of issues with that surgeon. Figure 2 contains a list of issues that should be included in any checklist

3. information on the likely financial implications of breast implant surgery including the fact that further treatment and expenditure may be necessary at some time in the future. These costs may include not only initial consultations and operation but also regular follow-up, screening for rupture if this is thought to have occurred, explantation and reimplantation

4. a 'cooling off' period of several days between the initial consultation with the surgeon and the operation

5. a guarantee that any deposit or payment for the operation will be fully refunded if for any reason the woman changes her mind, even at the very last moment, and cancels the operation

6. an assurance that they will not come into direct contact with a representative of a particular manufacturer prior to agreeing to surgery.

Recommendation 4

The IRG recommends that a specific consent form be developed which incorporates, as an integral part, the checklist of issues (see Figure 2). The consent form should confirm that the different types of implant available have been discussed with the surgeon and the type agreed, and that all subjects on the checklist have been discussed to the woman's satisfaction along with any other concerns that the woman wishes to address. This consent form should be signed by the surgeon and the woman. One copy should be kept by the surgeon in the notes, and one copy kept by the woman.

Recommendation 5

The IRG recommends that measures should be introduced to ensure that proper standards of care are implemented in clinics carrying out breast implantation within the private sector. In particular, a quality assurance system, including the sending of a routine letter to the woman's GP, and clinical audit procedures should be standard practice within such clinics.

Recommendation 6

The IRG recommends that prospective registration of details of each breast implant and explant operation on the National Breast Implant Registry should be compulsory.

In addition all women should be given the opportunity to participate in long term follow-up projects with the full understanding that they may be contacted in the future to provide information to facilitate research.

It should be explained to the woman that the Registry will be used to gather accurate data on the outcomes associated with silicone gel breast implants, including the incidence of rupture.

Recommendation 7

The IRG recommends that all clinicians should report breast implant related adverse incidents to the Medical Devices Agency Adverse Incident Centre. The MDA should provide guidance to clinicians on which incidents should be reported.

Recommendation 8

The IRG recommends that a small steering group be set up to prioritise, plan and monitor the following programme of research. Priorities should include:

- *research into the true incidence of rupture*
- *research into the aetiology of symptoms exhibited by a number of women who have had implants, in particular to elucidate the role, if any, of sub-clinical infection.*

The IRG recommends that the steering group should also consider the need to validate the results of other studies, such as those by Ellis et al.

The IRG concluded that the publications of Tenenbaum et al., and Smalley et al., were not conclusive and are open to legitimate scientific criticisms. However, in view of concerns expressed by women's groups, the IRG recommends that there would be scientific merit in determining whether the results of these studies can be reproduced by independent laboratories.

Recommendation 9

Although there is currently no justification for routine regular breast investigation to detect rupture, the IRG recommends that this subject should be kept under review and the decision revisited in the light of possible new information and technical advances relating to imaging techniques used in the detection of rupture.

1 Introduction: Why have an Independent Review Group?

1.1 The reason for the Independent Review Group

The Independent Review Group was established in response to concerns expressed by women in relation to silicone gel breast implants.

Because of these concerns the Minister of Health, Baroness Jay, asked the Chief Medical Officer to undertake a review of the use of silicone gel breast implants in the United Kingdom. The Chief Medical Officer addressed this request by setting up an Independent Review Group (IRG) with the remit:

'to review the evidence relating to the possible health risks associated with silicone gel breast implants, to examine the issues relating to pre-operative patient information, and to report to the Chief Medical Officer on its conclusions.'

The members of the IRG were selected for their independence, their knowledge and understanding of the issues, and their lack of vested interest in the conclusions reached. Members are listed at Annex 1.

The IRG set out to respond to concerns that silicone gel breast implants may be the underlying cause of medical problems which can severely affect the quality of women's lives, and that women perceived that their symptoms were not always taken seriously. Some women also complained that they were inadequately informed about the possible risks and complications of breast implants before they had surgery and were therefore unable to make a properly informed choice.

Although some men, for gender alteration purposes, undergo breast implantation, the vast majority of breast implant procedures are carried out in women. In this report we refer, therefore, solely to women.

The IRG has taken a fresh look at the existing and emerging scientific evidence for a link between silicone gel breast implants and effects on health. In so doing the IRG identified two key questions:

- why are some women ill?
- what information do women considering breast implant surgery need and how best can that information be presented?

To address these questions the IRG:

- reviewed the existing reports and evidence
- identified and considered new evidence
- considered the possible existence of a new, undefined syndrome
- considered the range of risks associated with silicone gel breast implants

- examined whether patient information is satisfactory
- considered how good clinical practice can be assured.

The IRG specifically addressed the problems associated with silicone gel breast implants. Silicone injections, hydrogel filled implants or other filling materials such as oil or saline were excluded from the remit given to the IRG.

1.2 How the IRG went about its work

The IRG considered evidence from a number of sources, including:

- oral evidence from representatives / nominees of patient groups, lawyers, researchers, physicians, plastic surgeons, industry and the National Breast Implant Registry
- written evidence from interested parties, including women with breast implants, replies to requests for information, and additional information from those who gave oral evidence
- plaintiff and defence submissions to the scientific panel appointed to review the scientific merits of evidence presented in litigation in the United States
- unpublished scientific information, legal submissions, letters from women with silicone gel breast implants, Internet and press articles
- scientific publications
- data provided by manufacturers.

The IRG appointed a number of advisors who were asked to consider specific information on behalf of the IRG. The names of the advisors are listed at Annex 1. The names of those who gave oral evidence are provided at Annex 2.

In considering the range of evidence, the IRG examined all relevant scientific data. Great emphasis was placed on considering the scientific quality of each study in addition to the conclusions drawn.

The IRG noted the large number of scientific papers and other material published in the past five years on the possible link between silicone gel breast implants and the development of connective tissue disease. The 1994 review by the Medical Devices Agency (Gott and Tinkler, 1994) commented on the poor scientific quality of some of the papers reviewed and on how this limited the conclusions that could be drawn from much of the research. This view was repeated by scientific and clinical witnesses to the IRG concerning some papers published in the past five years.

The IRG also expressed concern that some papers were not subject to adequate peer review. Similarly, a number of seemingly authoritative reviews of the literature were highly selective in the papers they included, thus appearing to support certain hypotheses which were not supported by the evidence as a whole.

Peer reviewed science
The judgement of scientific investigations by independent experts to ensure that the conclusions recorded are justified by the methods used and the results obtained.

This introduced the additional problem that the public and media would not be aware of the lack of scientific rigour and could be persuaded and alarmed by the results of what was, in fact, poor science and selective reporting.

During the past five years there have been sustained campaigns by interested parties to put across their points of view in the media. The amount of published, or electronically distributed material advocating a particular point of view is huge. While such parties are entitled to campaign, it is not surprising that the evidence they cite is chosen to support their case, rather than for its scientific quality. It needs to be remembered that this is not the same process as drawing unbiased conclusions after evaluating all the relevant scientific and medical evidence.

Glossary
While every effort has been made to make the text explicit, a glossary of terms is provided at the end of the report. The terms are highlighted in the text by the letter G.

2 The Report and How it is Organised

2.1 Target readership for the report

This report is intended for a variety of groups who have particular interests in silicone gel breast implants:

- women considering, or who have had, breast implants, and their families
- plastic surgeons and other clinicians in the NHS and independent sectors
- manufacturers
- lawyers
- policy makers in health care
- scientists.

2.2 Integrated report and Website

The IRG considered immense amounts of complex evidence. This report necessarily contains analysis of the evidence together with the IRG's key findings and recommendations. Some readers will wish to access further information or more detailed discussion of certain aspects. The IRG has therefore provided a dedicated Website which contains this information. The IRG's aim has been to provide highly accessible information about its work. It is the IRG's intention that the Website be updated regularly to reflect the latest evidence about silicone gel breast implants. The Website also contains the references to the literature considered by the IRG. This published report contains only those references relevant to the IRG's key findings and recommendations.

2.3 Addressing concerns and making recommendations

The IRG has considered the scientific evidence on the subject of silicone gel breast implants and areas of particular concern among women and the public, such as the possibility of silicone poisoning, chronic fatigue syndrome, non-specific pain, effects on children of women with breast implants, and immune responses to silicone. After considering the evidence, the IRG has made recommendations with the specific aims of:

- addressing the concerns of women with silicone gel breast implants
- encouraging further research into important areas of concern
- enabling clinicians to give women considering implants the most up-to-date advice about possible associated problems
- enabling clinicians, manufacturers, scientists and women to work in partnership to ensure the highest levels of confidence in the production, use and monitoring of silicone gel breast implants.

In preparing this report, the IRG has considered carefully a wide range of evidence from individual women, patient representative groups, plastic surgeons, scientists, epidemiologists, immunologists, pathologists, lawyers and manufacturers of silicone gel breast implants.

This report presents the IRG's conclusions from the evidence and sets out recommendations to help ensure that women have access to reliable information and are enabled to make informed choices about silicone gel breast implants; that surgeons make relevant information readily available; and that data are collected on an ongoing basis so that the health effects of silicone gel breast implants can be monitored.

3 Silicone Gel Breast Implants

3.1 How common are silicone gel breast implants?

Breast enlargement is the most common cosmetic procedure performed on women in the United Kingdom. It is estimated that around 8,000 such operations are performed each year. It is difficult to obtain accurate figures because a large number of unrecorded operations are carried out in the independent sector. Four groups of women seek breast enlargement:

- women who are dissatisfied with the size of their breasts
- women with congenital absence of one or two breasts
- women who have had normal breast development but the breast size has decreased following pregnancy or with increasing age
- women who have undergone mastectomy for treatment of breast cancer or because of a strong family history of breast cancer.

Silicone gel breast implants have been available since the early 1960s and have been the subject of investigation and monitoring since the mid-1980s. The time line, shown at Figure 1, outlines the history of silicone gel breast implants.

It is worth noting that in 1992 the USA's Food and Drug Administration limited the use of silicone gel breast implants to clinical trials. The increase in US

What is silicone?

It is important to understand the differences between silicon, silica and silicone because of the implications in the interpretation of scientific studies.

- **Silicon** is the second most abundant element, making up about 28% of the earth's crust.
- **Silica** is a three dimensional network of silicon dioxide and is most commonly encountered as sand.
- **Silicones** are not found naturally. They are man-made polymers used in a wide variety of products as fluids, gels and rubbers. They have a high degree of chemical inertness, thermal stability and resistance to oxidation. Modified silica is bound into silicone rubbers to provide strength.

Throughout this report the word silicone will be used for polydimethylsiloxane[G] (PDMS) polymers including their low molecular weight components.

litigation that followed led the manufacturers to reach a commercial decision to minimise the potential costs of litigation by offering a global settlement without admitting liability.

In the 1990s a number of countries, including the United Kingdom, Canada, the USA and France, carried out systematic reviews[G] focusing on the possible health implications of silicone gel breast implants. The time line at Figure 1 summarises the outcomes of these reviews.

3.2 What is a breast implant?

Silicone gel breast implants are made of an outer shell of silicone elastomer filled with silicone gel. The composition of the shell is important. There have been three generations of implant since they were made available in the 1960s. The time line, shown at Figure 1, indicates the periods of use of these three generations, although there has been some overlap.

1st generation implants: were made with a thick silicone shell. They had a smooth surface and were filled with silicone gel, which is a mixture of silicone solid and fluid. These implants are associated with significant gel bleed[G] from the implant and capsular contracture[G], that is shrinkage of scar tissue, but are believed to have a low rupture rate. These implants were manufactured from the 1960s and were superseded during the mid-1970s.

2nd generation implants: were made with a thin silicone shell. They had a smooth surface and were filled with silicone gel. The shell was reduced in thickness in an unsuccessful attempt to decrease the amount of capsular contracture. The gel bleed was similar to the 1st generation implants. It is now widely accepted that 2nd generation implants are more susceptible to rupture. They were manufactured from the 1970s to the late-1980s.

3rd generation implants: are made with a thicker shell of silicone, incorporating a barrier layer. They have a textured surface and are filled with silicone gel. The composition of the shell acts as a barrier to minimise gel bleed, the textured surface decreases the incidence of capsular contracture. The rupture rate of these implants is believed to be low but there are few relevant studies. The gel bleed and contracture rates are lower than with earlier implants. They have been manufactured since the mid-1980s.

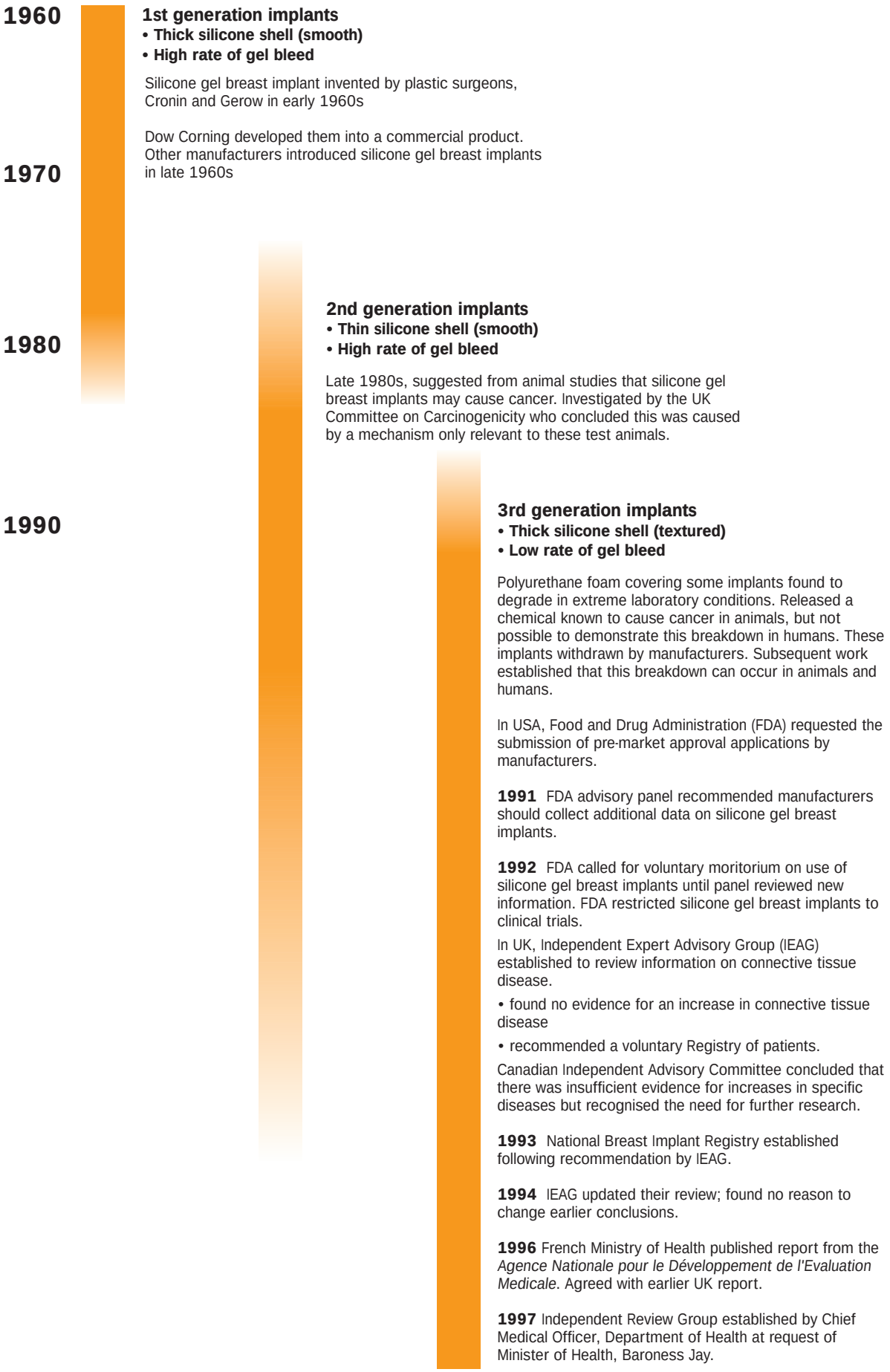
3.3 Exposure to silicone

It is essential to consider the issue of silicone gel breast implants in the context of the widespread exposure to silicones in the environment generally. Silicone is used in both personal and domestic products, including cleaning solvents, handcreams, hair and skin products, and antiperspirants. Silicone from these sources is absorbed primarily through the skin.

Silicone is used in food processing and packaging including canning and pre-prepared meals, babies' teats and dummies. Silicone from these sources is absorbed primarily through the gastro-intestinal tract.

Silicone is also incorporated in some medicines and medical devices. For example, silicone oil is commonly used as a lubricant in syringes. People with insulin dependent diabetes are therefore exposed to small but regular doses of silicone oil, resulting in a large, cumulative exposure to silicone over a period of time. Liquid silicone is injected into the eye during surgery to treat retinal detachment.

Figure 1 **Three Generations of Silicone Gel Breast Implants**



4 Health Risks: The Evidence

4.1 The evidence: introduction

The IRG considered the concerns expressed by women relating to possible health risks associated with silicone gel breast implants such as gel bleed, capsular contracture, rupture, and infection.

The IRG examined evidence relating to:

- local effects, that is those which depend on the silicone gel being present and which occur at the site of the implant (see Section 5)
- tissue responses to the presence of silicone (see Section 6.1)
- systemic health effects, that is those which do not require the silicone gel to be present and which occur at sites at a distance from the implant (see Section 6)
- the possible effects of silicone gel breast implants on the health of children of women with implants (see Section 6.5)

4.2 Safety

Before considering the detail of the evidence, it is important to understand the concept of 'safety' in the context of the scientific evidence relating to silicone gel breast implants.

The IRG has been asked by its remit to go further than previous UK reviews (Tinkler *et al.*, 1993; Gott and Tinkler, 1994) and to interpret the evidence in relation to the safety of silicone gel breast implants: to answer the question, are they safe?

However, safety is not a simple concept. It is widely accepted by lawyers, ethicists, doctors and regulators to mean freedom from an undue risk of harm. The word 'undue' is critical. It is impossible to guarantee that any given set of conditions can be completely free from any possibility of harm: safety is not an absolute concept. This is particularly so in medical practice, where deliberate invasive procedures carry a risk to health.

It follows therefore that any decision about medical intervention is a calculated risk, taken in partnership by the surgeon and the individual, with the aim of improving the overall circumstances for the individual. Balancing risks and benefits makes safety a difficult concept to define in any given situation and, consequently, it is important to consider 'safety' carefully in the context of individual circumstances.

5 Local Effects

5.1 Capsular contracture

The body puts a wall of scar tissue (fibrous capsule[G]) around any implanted foreign material and breast implants are no exception. Scar tissue shrinks, but the extent of shrinkage varies from person to person and even from breast to breast. This shrinkage, or capsular contracture, is noticeable to the woman as an apparent hardening of the breast.

With the older smooth surface implants (1st and 2nd generation) noticeable capsular contracture occurred in 40% to 60% of implantations. When implants with a textured surface were introduced in the mid-1980s (3rd generation), the reported rate of capsular contracture fell to around 10% with these implants.

The type of filling used in the implant has not been shown to have any effect on the incidence of contracture. Other factors, such as subclinical haematoma[G], shrinkage of the surgical pocket or subclinical infection with organisms such as Staphylococcus epidermidis[G], a bacterium normally found on the skin, have also been implicated as possible causes of capsular contracture.

5.2 Infection

The IRG considered the published evidence relating to the risk of infection from silicone gel breast implants. It is important to recognise that the introduction into the body of any foreign material such as a hip replacement, intravenous catheter, prosthetic heart valve, or silicone implant constitutes a risk of introduction of bacteria from the patient's own skin.

The IRG concluded that the possible influence of infection on capsular contracture is not proven. Capsular contracture may, however, be exacerbated by bacterial infection.

Chronic low grade infection may occur with any surgical implant. Such infection, at any site in the body, may be associated with a number of symptoms including tiredness, weakness, intermittent febrile periods and muscle aches and pains. There is a need for more scientific research into this area to determine how frequently low grade infection occurs in women with breast implants and whether this contributes to the symptoms complained of by some women.

5.3 Gel bleed

The term gel bleed describes the diffusion of small molecules of liquid components of silicone gel through the intact shell of the implant. There is no agreed method of measuring gel bleed and this, therefore, limits its accurate quantification. However, these small molecules of silicone comprise less than 1% of the gel. Gel bleed occurs from all breast implants; the concern is whether the material that bleeds causes illness.

These small molecules are handled by the body in exactly the same way as small silicone molecules from other sources, (see Section 3.3).

5.4 Rupture

Rupture means the development of a split or hole in the shell of a breast implant. The causes of rupture may include:

- deterioration of the implant shell with time - the most common cause
- undetected damage at the time of operation
- a shell weakness due to a flaw introduced during manufacture
- trauma to the breast, such as damage from a seat belt in a traffic accident, or external (closed) capsulotomy[G] (disruption of the fibrous capsule).

The effects of a rupture may be local and / or regional. There are reports of silicone gel having migrated to distant parts of the body such as the arm or trunk, but these are rare.

Local effects of a rupture

With a silicone gel filled implant there may be no very dramatic change in the breast because if the shell ruptures, the gel is often still contained within the body's fibrous capsule (intracapsular rupture). There may, however, be some slight change in shape or firmness of the breast.

Regional effects of a rupture

If there is a spread of gel through the ruptured shell beyond the fibrous capsule (extracapsular spread), the rupture will be more obvious with a change in the shape of the implant and possibly a reduction in size due to extrusion of gel beyond the breast area.

In the vast majority of extracapsular ruptures the gel is still in the region of the original pocket and can be removed when the ruptured implant is removed.

In a small number of cases the gel has been found in breast tissue, the muscles under the breast, the armpit, the axillary lymph nodes[G] in the armpit, or rarely around the nerves to the arm (brachial plexus[G]) in the depths of the armpit. In rare cases this may require removal of part of the breast and muscle tissue.

Gel outside the capsule can cause some inflammatory reaction with the development of lumps that can be felt. If the gel does move out of the breast area there may have been some severe physical trauma to account for this, such as compression from a seat belt in a car accident or a closed capsulotomy.

Detection of a rupture by imaging techniques

Intracapsular rupture can be difficult or impossible to detect by current imaging techniques (mammography, ultrasound and magnetic resonance imaging). Often it is only discovered at operation. However, these imaging techniques continue to be developed and evaluated. By contrast, extracapsular rupture is often easier to detect by imaging techniques.

Rupture rates

There is little information on the overall rupture rate of breast implants. Breast implants have a finite life and inevitably some will rupture. There is little information on rupture or the relationship between rupture, time, and indeed, the generation of implant. The available estimates of rupture rates are derived mainly from studies using a highly selected sample of implants. These studies are further complicated by their use of different criteria in defining rupture, for example some include gel bleed within the definition of rupture.

The difficulties of establishing the rate of rupture are compounded by the use of imaging techniques which in a percentage of cases fail to detect ruptures or incorrectly identify intact implants as ruptured.

6 Distant and Systemic Effects

6.1 Immunological and pathological effects

The possibility that silicone gel breast implants may lead to an autoimmune reaction[G] in women has been a major cause of concern for several years and a central focus of the controversy over breast implants. It was therefore a subject that the IRG explored in some depth. The IRG has no doubt that some women who have had a silicone gel breast implant are indeed suffering serious symptoms. The question is whether these symptoms are attributable to silicone gel breast implants or to some other cause. Therefore, one of the principal questions considered by the IRG was: *Do silicone gel breast implants lead to the development of an autoimmune disorder?* In this section of the report, this question is considered in some detail.

The body has two basic ways of reacting to infection or foreign materials; these are:

- inflammation
- immune reactions.

The nature of the inflammatory response to silicones is the same as would be expected with any other foreign material. If a prolonged inflammatory reaction occurs, fibrous tissue forms to isolate the site of the injury. Although evidence for an immune reaction to silicone has been reported previously, earlier reports concluded that the evidence was weak at best. The most recent studies on immune reactions and silicone implants have been considered by the IRG, and the conclusions are given later in this report. Immune reactions may lead to the formation of antibodies[G] and to the generation of reactive T-lymphocytes[G] (a type of white blood cell). The IRG has therefore examined reports claiming that antibodies or specifically reactive T-lymphocytes are found in women with silicone implants.

It has also been suggested that women with silicone implants may develop immune responses against their own tissues - autoimmune disorders, for example, rheumatoid arthritis, and other connective tissue diseases. These disorders are characterised by the presence of antibodies to particular components of the patient's own tissues (autoantibodies) and by specifically autoreactive T-lymphocytes. The IRG therefore set out to investigate the evidence for these changes. The possible mechanisms through which an autoimmune reaction might occur have been extensively reviewed. The most prominent recent advocates of this theory have been Professors

Radford Shanklin and Robert Garry whose views have been cited particularly by patient groups. This evidence was therefore examined in detail.

Professor Shanklin presented two forms of evidence to the IRG to demonstrate that there is an immune reaction in women with silicone gel breast implants.

1. He provided pathological slides of capsular tissue taken from women with breast implants. He pointed out a pathological feature in these slides, which he referred to as vasculitis (inflammation of the blood vessel wall). This is an indicator of an immunological component in a tissue response.
2. He described immunological studies he had carried out, using blood samples taken from implanted women with symptoms of disease. These claimed to show activation of T-lymphocytes, which is a marker for an immune effect. Further evidence from Professor Garry, indicating the presence of anti-polymer antibodies in the blood of women with implants, was also cited as evidence of an immune effect.

Professor Shanklin used these same forms of evidence to support his further hypothesis that silicones escaping from the implant into the tissues are broken down to silica and that both silicone and silica are implicated in the immune reaction seen.

- He pointed to the crystalline appearance of certain features in the tissue slides he provided as evidence for the presence of crystalline silica.
- He presented evidence which suggested to him that lymphocyte activation occurs in the presence of silicone as well as silica.

He suggested that the presence of crystalline silica would be an important factor, since it can induce silicosis, which has autoimmune features.

In examining the evidence for this hypothesis, the IRG had the assistance of two immunologists and three histopathologists with relevant experience. The immunologists reviewed evidence from the published immunological studies to ascertain what immune responses were encountered in women with implants. The pathologists considered the pathological changes in tissues from women with breast implants supplied by Professor Shanklin. They looked, in particular, at whether there was an immune component in the response and they carried out studies to establish whether silica was present in the tissue samples supplied.

In addition, published evidence was examined for the presence of autoantibodies[G] or genetic markers for autoimmune disease in groups of women with implants. These latter studies provide an indication of whether autoimmune effects are operating in the groups studied.

Epidemiological studies, which are discussed in Section 6.2, provide further insight into this aspect of the subject. Published studies of the incidence of disease in women with silicone gel breast implants were reviewed to see whether there was a correlation between the presence of implants and the occurrence of rheumatological diseases or symptoms.

The IRG arrived at nine conclusions in relation to questions relevant to the hypothesis presented.

1. *What pathological responses are associated with the presence of silicones in the tissues?*

After considering the pathological slides supplied by Professor Shanklin, the IRG concluded that silicone gel breast implants, like other surgical implants, are associated with a typical local inflammatory response to the foreign material and that implants are associated with local fibrosis and the formation of a membrane between the implant and the body.

The foreign material may occasionally be seen in sites other than the breast, particularly the regional draining lymph nodes. If overt rupture of the implant occurs and the silicone material escapes, clearly the possibility arises that a more substantial amount of silicone could accumulate elsewhere in the body. The extent of gel bleed and the likelihood of rupture depend primarily on factors related to the implant (see Section 5.4). A local inflammatory response is also likely to occur at the site of silicone accumulation. The consequences of this will depend on the site at which the silicone accumulates and the amount of material present.

2. *Does silicone break down to silica in the tissues?*

The IRG commissioned scientific tests to examine the claim that silica was present in tissue samples provided by Professor Shanklin. The investigating laboratory demonstrated the presence of silicone in Professor Shanklin's sections, but no silica was present in the samples examined. The IRG also

heard evidence that conversion of silicone to silica is not possible under the conditions prevailing in the body.

3. *Do the silicones used in breast implants provoke antibody responses against silicones or their biological breakdown products?*

The IRG concluded that the evidence in the scientific literature does not suggest that silicones themselves provoke antibody responses. Outside the body, the physical conditions necessary to cause breakdown of silicone polymers are extreme. Such conditions do not occur within the body. In addition, there is no published evidence that any identified biological breakdown products of silicone are capable of inducing an immune response.

4. *Does exposure to silicones lead to antibody responses to other body substances absorbed to the silicones?*

Experimental animal work indicates that self (and foreign) proteins absorbed to silicone polymers can induce an antibody response and that silicones may sometimes have a modest adjuvant[G] effect on antibody production. There is thus evidence for normal immune reactions occurring in response to combinations of silicone and protein. There is no evidence, however, that the response can cause tissue damage.

5. *Do silicones provoke an antibody response to partially polymerised polyacrylamide?*

Professor Garry discussed his findings, presented in a recent paper (Tenenbaum *et al.*, 1997) with the IRG. His findings suggested that antibodies specific for partially polymerised polyacrylamide are seen more frequently in women with breast implants with severe symptoms than in women with mild or no symptoms. The IRG concluded that this study is not conclusive, that the work is subject to legitimate criticism and that further studies would be needed to determine whether the findings are reproducible. The chemical structure of polyacrylamide is unrelated to that of silicone and no rationale was put forward to explain why cross-reactivity might occur; nor was any cross-reactivity reported, although this should have been readily demonstrable. Given this situation, independent confirmation of this work would be essential before the IRG could accept any conclusions drawn from it.

6. *Does exposure to silicone lead to the provocation of a lymphocytic response?*

T-lymphocytes are a particular type of white blood cell that play a crucial role in immune responses and their proliferation indicates that such a response has occurred. Recent papers (Smalley, Shanklin *et al.*, 1995-7) demonstrated proliferation of T-lymphocytes in blood samples taken from patients with silicone gel breast implants when they were cultured in the presence of silica. This work was used to support the suggestion that there is a breakdown of silicones to silica in the body and that the silica (which is known to produce immune effects) induces an autoimmune process. The work was poorly controlled and the findings were reported in a way that made them difficult to interpret. The IRG considered that this work was so deficient that valid conclusions could not be drawn.

Another recent study (Ellis *et al.*, 1997) showed proliferation of lymphocytes in women with silicone gel breast implants, in response to various autoantigens. The IRG considered that they would have to reserve judgement about this work and it would need to be independently confirmed. The relationship between the lymphocytic response and reported symptoms would also need to be investigated before conclusions could be drawn.

7. *Is there histopathological evidence for an immune response in the tissue surrounding breast implants?*

Following a careful consideration of the histopathological material provided by Professor Shanklin, the IRG did not agree with him that any of the changes seen constituted evidence of an immune response. In particular, neither vasculitis (inflammation of the blood vessels, indicative of immunological involvement) nor any other histological change suggesting an immune response could be seen in the tissues examined.

8. *Do silicones cause inflammatory reactions that indirectly provoke immune responses to the recipient's own tissues?*

It is well established that fluid silicones injected into tissues may produce a local inflammation, depending upon the amount injected. It has been suggested that one possible effect of silicone gel breast implants would be to cause an inflammatory reaction that can result in the development of an autoimmune reaction. Several studies have examined whether there is an increased frequency of autoantibodies in women with silicone gel breast implants. While some studies claim an increased frequency, none of this work is adequate to permit this conclusion. The IRG concluded that this question remains incompletely resolved.

There is no suggestion that the majority of women with silicone gel breast implants will go on to develop immune responses to their own tissues. It is inevitable, however, that a small proportion of women with implants will do so through chance alone. At this stage, the IRG cannot rule out the possibility that a sub-group of the women who develop an autoimmune response do so as a consequence of their implant rather than due to other factors. The likelihood of this being the case is remote and the prevalence of any disease due to silicones can be determined from an analysis of epidemiological data (see Section 6.2) which allows an estimate to be made of the relative risk of women with implants developing connective tissue disease, in comparison with the women without implants. Further studies would be needed to substantiate or refute this possibility, and to identify any sub-group of women at risk and the nature of any particular autoimmune response.

9. *Are autoimmune syndromes found in women with silicone gel breast implants associated with particular HLA variants?*

T-lymphocytes, including those that take part in autoimmune reactions, recognise fragments of their specific target molecule that become bound to a cell membrane carrier protein, called HLA, which shows extensive genetic variation. It is known that the likelihood of developing autoimmune diseases depends, in part, upon which particular HLA variant an individual possesses. Therefore, finding that an unknown syndrome tends to occur more frequently in individuals with a particular HLA variant is important evidence that autoimmune mechanisms are involved in causing tissue damage.

Conversely, the absence of reproducible, statistically significant associations between the unknown syndrome and a specific HLA variant is evidence against an autoimmune pathology.

One detailed study on HLA variants in women with breast implants has been published (Young *et al.*, 1995). The study claims that in women with symptoms of pain and fatigue there is a higher frequency of particular HLA variants. However, there are technical criticisms of this paper, which are discussed in the Website. No independent study confirming this claim has been published. The IRG judges that there is inadequate evidence to support the claim.

6.2 Long-term systemic effects

The IRG considered two groups of questions in relation to the impact of silicone gel breast implants on long-term systemic illness. The first related to an increased risk of previously well recognised disorders, particularly of connective tissue diseases. Although a number of connective tissue disorders have been proposed as being linked, much attention has focused on scleroderma. Such disorders are accepted as being rare in both implanted and non-implanted subjects.

Scleroderma is a generalised disorder which causes hardening of the skin as well as some of the internal organs. It has been suggested that scleroderma may be increased in women who have had silicone gel breast implants.

The second relates to the development of disorders which may be a specific consequence of silicone gel breast implants. Reports from patient series suggest that such complaints consist of combinations of symptoms such as fatigue and muscle weakness. These symptoms are often encountered in a variety of less easily defined disorders such as chronic fatigue syndrome and fibromyalgia.

Fibromyalgia is a disorder characterised by diffuse muscle aching and fatigue, often associated with depression as well as other physical symptoms. There is no specific diagnostic test or tests for this disorder which occurs at a frequency of 1-2% in the general population.

The IRG considered that purely descriptive studies, either of the rare but specific connective tissue disorders or the more frequently occurring symptoms of general ill health, are of limited value in the absence of similar data from a comparison group of women without breast implants. The results of such series cannot be used to demonstrate that the disorder resulted from an implant. Such studies, however, are useful to generate the issues and questions that can be explored in a more rigorous way. The appropriate means of investigating this is through epidemiological studies, which look at groups of women who have had silicone gel breast implants to see if they have a greater risk than the general population of developing such conditions.

6.2.1 The role of epidemiological studies to assess risk

Before considering the published evidence relating to connective tissue disease, it is useful to have an overall understanding of how a rigorous epidemiological study is constructed. As has already been indicated, the IRG was concerned about the quality of some of the evidence presented to them and it is important to recognise the characteristics of a reliable study.

There are two main types of epidemiological study that can be used to evaluate the presence and strength of any increased risk: the cohort study and the case control study.

Cohort study

In a cohort study, a group of people with a specific exposure, are followed up over a period of time to determine the occurrence of any events during that period, the incidence and nature of any changes can then be compared with a randomly identified group of people.

In this way a group of women with silicone gel breast implants can be followed over a period of time and then compared with a randomly selected group of women who did not have an implant.

Using this approach, the occurrence of a number of symptoms and disease features can be investigated. In the majority of reported cohort studies related to silicone gel breast implants, the outcome is based on diagnosis reported by a doctor. The alternative is a systematic examination of all women studied with the aim of identifying disease features which might otherwise not be brought to the attention of the doctor. This latter exercise is unlikely to be a feasible proposition in women with silicone gel breast implants, given the size of study and duration of follow-up that would be necessary to identify a sufficient number of cases.

Case control study

In a case control study a group of people, the cases, with a particular symptom or combination of symptoms, is compared with an unaffected group, the controls, who are free of that disorder. Typically controls are selected to be of similar age and sex as the cases.

Thus in studying the influence of silicone gel breast implants on disease risk, it is necessary to compare the frequency of prior implantation between new cases with the disorder under investigation and controls over an equivalent time period.

The statistical analysis of both cohort and case control studies is complex. Interpretation of the results has to be undertaken with care, particularly as the number of women investigated in the published studies might not be sufficient to provide a definitive answer.

Given concerns that no individual study, particularly in relation to rare connective tissue disorders, is likely to be strong enough on its own to answer the question of risk, epidemiologists have also published analyses attempting to combine the results from the individual studies using the technique of meta-analysis.

Meta-analysis
A meta-analysis is a technique used in a systematic review where special statistical methods are used to combine the results of several studies to arrive at an overall statistical conclusion. There are problems with this approach as it may not be appropriate to combine data from studies where the selection factors and methods of investigation are substantially different.

6.2.2 Association or causation

The nature of epidemiological studies is to describe the strengths of the relationship between, in this instance, having an implant and development of systemic disease. If an increased risk was to be demonstrated from epidemiological studies, this does not necessarily imply causation. Alternative explanations for such a link are (i) chance findings due to studying small numbers and (ii) the influence of other factors common to both implants and the disease under investigation that might give the false impression of a direct link. As an example, there are data that suggest women with breast cancer have an increased risk of scleroderma. Therefore, women who had a mastectomy following breast cancer and subsequently had an implant may be at an increased risk of scleroderma, which is unrelated to their implant. It is possible that the development of non-specific symptoms following breast implantation may be related to the *reasons* for having the implant rather than being a *direct consequence* of the implant itself.

6.2.3 Relative and absolute risk

Most epidemiological studies considered present their results in terms of relative risk, that is the number of times a women with an implant is at increased (or decreased) risk compared with the background population risk. It may be more important in public health terms to consider the absolute increased risk. Thus a 50% increase in the occurrence of a rare disease, which affects only one per hundred thousand women in the general population per year, would be of substantially less concern than a 10% increase in the occurrence of a disorder which occurred substantially more frequently.

6.2.4 Specific connective tissue diseases

The IRG examined case control and cohort studies conducted between 1970 and 1998, together with reviews, overviews and meta-analyses investigating the incidence of established connective tissue diseases.

Having considered the evidence, the IRG arrived at six main conclusions.

1. From the case control studies, the proportion of all women with established connective tissue disease who have had a silicone gel breast implant is small and probably no greater than the proportion of women without such a disease who have had an implant.

2. From the cohort studies, the risk of development of established connective tissue disease in women who have had a silicone gel breast implant is very low and no higher than from a similar group of women who have not had an implant.

3. Given the rarity of these specific connective tissue diseases under study, and the relatively low frequency of women who have had a silicone gel breast implant, it is not possible even on the studies published to date to exclude with certainty that there may be a small increase of relative risk, possibly as high as 1.5 times that of someone without an implant. These same data, however, are compatible also with the equivalent degree of protection *against* the development of such disorders.

4. The studies reviewed only refer to specific diagnostic groups. There may be other diseases linked to the development of silicone gel breast implants for which information has not yet been gathered or not gathered in a sufficiently robust manner.

5. Unless a specific disease entity can be identified that is worthy of further investigation, it does not

seem appropriate to undertake further epidemiological investigations into the defined connective tissue diseases at the present time.

6. In advising women whether they should or should not undergo breast implantation, it would be useful to compare the absolute and excess risks of development of a connective tissue disease following an implant with risks of other adverse outcomes following other medical interventions or procedures. As examples, the risks observed are substantially lower than the risk of thrombosis following the use of the oral contraceptive pill or the risk of major gastric bleed following the use of aspirin or aspirin-like drugs.

In short, if there is a risk of connective tissue disease, it is too small to be quantified.

6.2.5 Non-specific systemic illness

There have been a wide range of non-specific symptoms attributed to silicone gel breast implants. The most commonly reported symptoms are fatigue, headaches, dry eyes and dry mouth, musculo-skeletal aches and pains and memory loss. Some investigators have suggested that this collection of symptoms should be recognised as a new syndrome. This suggested syndrome has been given a variety of names, including 'human adjuvant disease' and 'silicone poisoning'.

The IRG recognises that a significant number of women who have had breast implants complain of this cluster of symptoms and this is being proposed as evidence that such a new syndrome exists.

However, these symptoms are common to a large number of conditions which are prevalent in the community such as depression, fibromyalgia, chronic infection, anaemia and chronic fatigue syndrome. There have been very few studies comparing an *unselected* group of women with implants with a matched population group to examine the frequency of such symptoms. This is particularly important as some of the symptoms, such as chronic widespread pain, occur in 10% of the normal population. (Croft *et al.*, 1994). Those studies that have been carried out do not suggest, for example, any important increase in pain and fatigue over background population risk.

It is, therefore, difficult on the available data to identify a specific syndrome associated with silicone gel breast implants when the symptoms are so diverse and could be related to other conditions, occurring in women with an implant but unrelated to it. The IRG noted, however, that chronic infection around silicone gel breast implants has been reported. It is possible that such chronic infection could account for the fatigue and musculoskeletal pains noted by some women and further research would be required to determine the presence and frequency of such infection associated with implants and its relationship to the level of symptoms reported.

6.3 Neurological disorders

A number of researchers have suggested that silicone gel breast implants may be the cause of a variety of neurological effects or of a multiple sclerosis-like syndrome. The available literature and unpublished data were reviewed by the Practice Committee of the American Academy of Neurology in 1997. The Committee concluded that the existing studies came from the weakest of their three possible categories of evidence and did not support any association or causal relationship between silicone gel breast implants and neurological disorders. They recognised that well conducted observational studies were needed to examine this issue.

Two observational studies were published in April 1998. Both were epidemiological studies, one from Denmark (Winther *et al.*, 1998) using their national register and the other from Sweden (Nyren *et al.*, 1998) based on their national discharge register. The controls were women undergoing breast reduction surgery. There was no statistically significant difference in the occurrence of neurological disorders between the study group and the control group. However both groups had more cases than were expected although this was not statistically different from the historical data on the general population.

6.4 Hormonal disorders

The possibility that some low molecular weight silicones may possess oestrogenic activity and act in an analogous manner to environmental oestrogens has been raised. At present there are no data to support these putative actions. There is as yet no consensus on which chemicals act as environmental oestrogens and major research efforts are underway to validate a methodology to identify such compounds and assess their effects.

6.5 Effects on children of women with breast implants

There is understandable concern among women, and resultant media interest, in the possible effects of silicone gel breast implants on the health of their children.

A number of women with silicone gel breast implants have reported that their children have developed swallowing difficulties, irritability, non-specific skin rashes, fatigue and a range of other symptoms similar to those that occur in some women with silicone gel breast implants.

The IRG considered the papers published on these issues. The majority of the papers report individual case studies and there are no epidemiological cohort or case control studies comparing the symptoms of children born to women who have an implant with children of women who do not have an implant.

The IRG examined papers relating to swallowing difficulties, to autoantibodies in children of women with an implant, and to T-lymphocyte responses to silica. They also examined relevant studies in animals and looked at whether there was any evidence of silicone being present in breast milk.

The IRG concluded that the published literature does not substantiate the claims that there are significant, clinically apparent, effects in children of women who have had an implant. While immunological abnormalities have been reported in some of these children, the methodological problems associated with the published studies mean that this cannot be interpreted as a clear effect of the presence of the implant. There is no evidence that the incidence of immunological abnormalities is any greater than in the general childhood population. Because of the presence of silicone in many forms, the exposure of children born to women with an implant is no greater than that to which they are exposed from other sources of silicone in the diet and in the environment.

6.6 Silicone toxicity

Understanding the risks to human health of chemicals requires knowledge of their toxicity. The IRG considered evidence reviewed in previous publications, detailed reports from manufacturers and publications in the medical and scientific literature.

The information supplied about the local and systemic toxicity, genetic toxicity, reproductive toxicity and carcinogenicity showed that silicones were relatively bland substances. There was little local reaction, except to older smooth-surfaced implants, which tended to excite local scarring and contraction over a period in animal studies. There has been no evidence of sensitisation of animals to implants or extracts of them, pathological changes in the tissues of the immune system in animals have not been seen after implantation of implant materials, nor were alterations found in specific tests of immune function in animals exposed to certain silicones.

Tests looking with reliable, validated analytical techniques for the dissemination of silicones from implants in the body have shown either no dissemination, or the presence of only very small amounts at distant sites following rupture of gel-filled implants, or after deliberate injection of the gel.

The substantiated risks of implants, as shown in experiments in animals and in other laboratory studies, and as borne out by the much more limited investigation of samples from women with implants, are local inflammatory and scarring reactions, and local infection, as around any foreign body in the tissues. If a silicone fluid is released from a ruptured gel implant, the inflammatory and fibrotic reaction will affect a wider area. There does not appear to be any evidence of a conventional or validated type of systemic reaction, or of abnormalities of the immune system, in women who have received implants, but these aspects are further discussed in this report and previous publications (Tinkler *et al.*, 1993; Gott and Tinkler, 1994).

The overall pattern of the findings in the toxicity tests, both the general studies of systemic actions and the experiments examining local actions, has been consistent with conventional forms of toxic responses. There has been no clinical, laboratory or pathological indication of unusual or unique types of reaction.

The IRG concluded that the relevant studies have shown only local reactions to silicones. Systemic damage and dispersal of silicone polymers

throughout the body has not been well demonstrated, despite various claims, even after rupture of gel-filled implants. The overall pattern of the findings is consistent with conventional forms of toxic response, rather than any unusual reaction.

6.7 Cancer

Analyses of large groups of women both with and without breast implants have shown that there is a slightly reduced incidence of breast cancer in women with breast implants. Studies looking at the incidence of other cancers have failed to demonstrate a statistically significant increase among women with breast implants.

Women with breast implants should continue to be screened. Breast screening arrangements are not affected by the presence of an implant. However, women should inform those carrying out the screening of the presence of an implant so that screening techniques can be modified appropriately.

7 Overall Conclusions from the Scientific Evidence

Having reviewed all the available evidence, the IRG have reached a number of conclusions.

1. There is no histopathological or conclusive immunological evidence for an abnormal immune response to silicone from breast implants in tissue.

2. There is no epidemiological evidence for any link between silicone gel breast implants and any established connective tissue disease. If there is a risk of connective tissue disease, it is too small to be quantified. The IRG cannot justify recommending further epidemiological studies to investigate this hypothesis.

3. Good evidence for the existence of atypical connective tissue disease or undefined conditions such as 'silicone poisoning' is lacking. It is possible that other conditions such as low grade chronic infection may account for some of the non-specific illnesses noted in some women with silicone gel breast implants.

4. The overall biological response to silicone is consistent with conventional forms of response to foreign materials, rather than an unusual toxic reaction.

5. There is no evidence that children of women with breast implants are at increased risk of connective tissue disease.

6. The IRG recognised that there were issues such as the precise incidence of rupture where the scientific data were incomplete so that rigorous conclusions could not be drawn.

8 Responding to Concerns: Conclusions and Recommendations

The IRG recognises the physical and psychological benefits of breast implantation but at the same time is aware that many women are concerned about the effects of the procedure. The IRG also recognises that there is some risk associated with the use of any implant. On the basis of information available, the IRG concludes that risks to patients associated with the use of silicone gel breast implants are no greater than for other implants. It is, however, important to ensure that women are able to make informed decisions by providing clear and comprehensive information about potential advantages and disadvantages of particular products and treatments.

Two major areas of concern were brought to the attention of the IRG by women giving oral and written evidence. These were:

- poor quality of information available to assist women in making informed decisions about breast implant surgery
- inadequate follow-up which makes it impossible to establish the true incidence of any short- and long-term complications.

The IRG makes recommendations to address these areas of concern.

8.1 Provision of adequate information before consultation

The IRG was concerned that some organisations promote breast augmentation as a simple procedure and do not provide adequate information to women.

Women have difficulty in obtaining reliable information about breast implant surgery. Information may be gathered from friends who have had similar surgery or from advertisements in the media. However, these sources give no information about the quality of the products, the service, or the follow-up care. Women who are contemplating breast implantation should see their GP and obtain the names of surgeons who are on the General Medical Council (GMC) Specialist Register.

Recommendation 1

The IRG recommends that all patients undergoing cosmetic breast augmentation surgery should be able to obtain, free of charge, from a designated body, comprehensive information about the benefits and risks of such surgery. This should be accompanied by a checklist of topics (see Figure 2) which should be covered when the possibility of an operation is discussed.

Recommendation 2

The IRG recommends that advertisements in all media promoting breast implant surgery should include a statement indicating that anyone contemplating this type of surgery can obtain information about the operation and its risks from a designated body.

8.2 Provision of adequate information at the consultation

The IRG's work has shown that women are frequently given inadequate information about the operation and any possible problems associated with it. They may be pressurised into going ahead with the operation before they have considered fully the advantages and disadvantages. They may not be given full information about the possible short- and long-term medical and financial implications of the operation. The IRG believes that women should be given comprehensive information about the surgery and about any short- and long-term risks connected with silicone gel breast implants.

8.3 Post-operative care

The IRG considered the need for women to be given comprehensive information about post-operative care and possible associated problems. The IRG agreed that:

- women should receive instructions about immediate and continuing aftercare including advice on physical activity, pain management, time off work and what circumstances might indicate the need to seek medical advice
- women should be informed of the type, manufacturer and batch number of their implants and told to keep this information. They should be given an explanation of why this may be important
- women should be informed that a letter will be sent to their GP giving details of the operation. The purpose of the letter should be explained; should women develop problems associated with surgery in the short- or long-term, the GP will need to be aware of previous surgery since it may be related to the prevailing condition
- every GP surgery should have a copy of the report *Silicone Gel Breast Implants, The Report of the Independent Review Group* and should be aware of the existence of the information pack referred to at Recommendation 1.

8.4 Follow-up

The IRG considered the need for systematic follow-up for women who have silicone gel breast implants.

Women and surgeons had expressed their concerns about the lack of long-term follow up. It was also suggested that the lack of effective follow-up explained the low rate of complications seen by plastic surgeons. Because reports about problems are spasmodic, it is impossible to identify the true incidence of complications.

The IRG agreed that:

- women should be followed-up for a minimum of one year with the option of longer follow-up at the woman's request
- women should be given advice about how to recognise signs of rupture and told to return for a follow-up appointment if they suspect this may have occurred
- women should be told that if capsular contracture occurs, they should make an appointment with the surgeon as soon as possible.

Recommendation 3

The IRG recommends that all women undergoing or proposing to undergo cosmetic breast augmentation surgery should be offered the following:

1. an initial appointment with the surgeon carrying out the operation

2. an opportunity to discuss the checklist of issues with that surgeon. Figure 2 contains a list of issues that should be included in any checklist

3. information on the likely financial implications of breast implant surgery including the fact that further treatment and expenditure may be necessary at some time in the future. These costs may include not only initial consultations and operation but also regular follow-up, screening for rupture if this is thought to have occurred, explantation and reimplantation

4. a 'cooling off' period of several days between the initial consultation with the surgeon and the operation

5. a guarantee that any deposit or payment for the operation will be fully refunded if for any reason the woman changes her mind, even at the very last moment, and cancels the operation

6. an assurance that they will not come into direct contact with a representative of a particular manufacturer prior to agreeing to surgery.

Figure 2

Suggested checklist of issues to be discussed with women considering breast implantation

- ☐ The experience of the surgeon in performing this operation (together with information on whether on the GMC Specialist Register, and whether a member of the British Association of Plastic Surgeons/British Association of Aesthetic Plastic Surgeons)
- ☐ The types of implants generally available, the advantages and disadvantages of each and the reason for the individual decision
- ☐ Cosmetic effects of the operation including:
  - position of pocket
  - position of implants
  - appearance of scar
- ☐ Information on the possible immediate post-operative effects including:
  - bruising
  - pain
  - swelling
  - bleeding
  - infection
  - nipple sensitivity
  - likely recovery time
- ☐ Information on longer term, local effects including:
  - wrinkles, folds
  - capsule formation
  - gel bleed
  - rupture linked to the expected lifetime of the implant, the incidence of rupture, screening for rupture, what it means if rupture occurs, symptoms that may be noted if rupture occurs, and what actions need to be taken under these circumstances
- ☐ Follow-up, including:
  - minimum follow-up of one year
  - further follow-up at woman's request or on development of certain symptoms
- ☐ Possible association between silicone and generalised illness such as connective tissue disease or autoimmune effects or a new connective tissue disease-like syndrome. There is no evidence for a significant association over and above the normal risk
- ☐ Breast cancer. There is no evidence for an association with either breast cancer or any other malignancy
- ☐ Effect on breast cancer detection and screening. Women with breast implants should continue to be screened. Breast screening arrangements are not affected by the presence of an implant. However, women should inform those carrying out the screening of the presence of an implant so that screening techniques can be modified appropriately
- ☐ Effect on the children of women with breast implants. There is no evidence for an increase of illness in children of women with silicone gel breast implants
- ☐ Effect on breast feeding. There is no interference with the ability to breast feed
- ☐ Information on financial implications:
  - the initial consultation
  - operation
  - follow-up
  - possible screening for rupture, possible explantation and re-implantation
- ☐ Letter to the GP. Letter will be sent to GP giving details of the operation. Explanation of this action
- ☐ The National Breast Implant Registry
  - details of implant and procedure
  - option to participate in future follow-up

8.5 Consent for the operation

The IRG's concerns about adequate information for women focused on the important issue of consent to treatment.

In 1993, the Department of Health defined consent in the following way:

> *"Consent is the voluntary and continuing permission of the patient to receive a particular treatment based on an adequate knowledge of the purpose, nature and likely risks of the treatment including the likelihood of its success and any alternatives to it. Permission given under any unfair or undue pressure is not consent".*

Consent to medical treatment may be oral or written, express or implied. For the purposes of surgery it is usual to obtain written consent from the patient except in an emergency.

One matter of concern is that it appears from the evidence presented to the IRG that there is no uniformity in the approach taken to counselling of women, and that in some instances women are given far too little information about what to expect as normal both in the immediate post-operation period and in the long-term.

One of two civil actions might be available in circumstances when consent is deficient. These are the actions for trespass to the person (assault and battery) and the action for negligence.

Trespass to the person

Assault and battery are forms of the civil action of trespass to the person. They are also crimes, though it would be very unusual for criminal proceedings to be brought against a doctor who treated a patient without consent.

Assault (putting a person in fear of immediate battery), usually accompanies battery as a matter of course.

In medical cases, battery may be committed if the individual:

- is treated against his or her will
- consents to one treatment but receives another or an additional treatment
- is given treatment without being told that this will happen
- is treated under duress
- agrees to treatment after being provided deliberately with information that is wrong.

A hypothetical example might be the case of a woman who has consented to a mastectomy, and at the same time reconstruction with a silicone gel implant is performed without her consent to that procedure having been obtained before surgery.

Negligence

If the individual consents to a particular treatment but this was without having received appropriate information beforehand, this is described in legal terms as 'negligence'.

In the United Kingdom, the general rule is that a patient is entitled to receive information concerning the material risks associated with the treatment. The nature and extent of that information is currently determined by the Bolam test. This means that a doctor would not be found to be negligent even if a woman claimed that she was given insufficient information about certain risks, if the doctor had acted, in good faith, on the basis of responsible, currently held medical opinion. In breast surgery, as in many other areas of care, medical opinion can be divided.

According to the Bolam test, as long as the doctor is found to have acted in accordance with a responsible body of medical opinion, there can be no finding of negligence.

Despite this, the IRG is strongly of the opinion that doctors should give women comprehensive information about the risks and benefits of silicone gel breast implants.

Recommendation 4

The IRG recommends that a specific consent form be developed which incorporates, as an integral part, the checklist of issues (see Figure 2). The consent form should confirm that the different types of implant available have been discussed with the surgeon and the type agreed, and that all subjects on the checklist have been discussed to the woman's satisfaction along with any other concerns that the woman wishes to address. This consent form should be signed by the surgeon and the woman. One copy should be kept by the surgeon in the notes, and one copy kept by the woman.

8.6 Regulation of private clinics

The IRG was concerned about varying standards of quality assurance among the variety of organisations offering breast implant surgery.

Recommendation 5

The IRG recommends that measures should be introduced to ensure that proper standards of care are implemented in clinics carrying out breast implantation within the private sector. In particular, a quality assurance system, including the sending of a routine letter to the woman's GP and clinical audit procedures should be standard practice within such clinics.

8.7 National Breast Implant Registry

There has been a National Breast Implant Registry since 1993. Currently the Registry is voluntary and women can decide whether to have their details included.

The purposes of the Registry are to identify information about short-term complications such as rupture, and to provide a source of data for future research studies on the long-term effects of breast implants. It is only by having access to a comprehensive systematically collected database that concerns about the possible effects of breast implants can be investigated. The IRG emphasised the value of a Registry for this purpose.

If the Registry is to be used for future research which will benefit all women with breast implants, it is essential to have information included on the Registry about all implant procedures carried out in both the NHS and the independent sector.

The IRG gave careful consideration to the issues of confidentiality and to the use of information on the Registry for research purposes. It was agreed that the principles of confidentiality should continue to be maintained in relation to this information.

Recommendation 6

The IRG recommends that prospective registration of details of each breast implant and explant operation on the National Breast Implant Registry should be compulsory.

In addition all women should be given the opportunity to participate in long term follow-up projects with the full understanding that they may be contacted in the future to provide information to facilitate research.

It should be explained to the woman that the Registry will be used to gather accurate data on the outcomes associated with silicone gel breast implants, including the incidence of rupture.

8.8 Adverse incidents

It is essential to have information about the clinical performance of implants during use to be able to assess and monitor their safety and suitability in the long-term. Information about adverse incidents can provide an early indication of a problem with a product and the IRG recognised the value of the Medical Devices Agency (MDA) adverse incident reporting system. Under this system a report is made to the MDA about any suspected problems with poorly designed or malfunctioning medical products. Similar systems exist elsewhere such as the FDA's Medical Device Reporting scheme in the USA and the Vigilance reporting system set up under the European Directives.

The IRG emphasises the importance of using the adverse incident reporting system to ensure that any problems are recognised as quickly as possible.

Recommendation 7

The IRG recommends that all clinicians should report breast implant related adverse incidents to the Medical Devices Agency Adverse Incident Centre. The MDA should provide guidance to clinicians on which incidents should be reported.

8.9 Future research

The IRG is concerned that future research should enable women with silicone gel breast implants, clinicians, manufacturers and scientists to work together to ensure the highest levels of confidence in the use of silicone gel breast implants. The IRG therefore make the following recommendations about future areas of research.

Recommendation 8

The IRG recommends that a small steering group be set up to prioritise, plan and monitor the following programme of research. Priorities should include:

- *research into the true incidence of rupture*
- *research into the aetiology of symptoms exhibited by a number of women who have had implants, in particular to elucidate the role, if any, of sub-clinical infection.*

The IRG recommends that the steering group should also consider the need to validate the results of other studies, such as those by Ellis et al.

The IRG concluded that the publications of Tenenbaum et al., and Smalley et al., were not conclusive and are open to legitimate scientific criticisms. However, in view of concerns expressed by women's groups, the IRG recommends that there would be scientific merit in determining whether the results of these studies can be reproduced by independent laboratories.

Recommendation 9

Although there is currently no justification for routine regular breast investigation to detect rupture, the IRG recommends that this subject should be kept under review and the decision revisited in the light of possible new information and technical advances relating to imaging techniques used in the detection of rupture.

Annex 1

Members of the Independent Review Group

Professor R D Sturrock, The McLeod / Arthritis Research Campaign Professor of Rheumatology, University of Glasgow (Chairman)

Professor J R Batchelor, Emeritus Professor of Immunology, Imperial College of Science, Technology and Medicine on the Campus of Hammersmith Hospital

Mrs V Harpwood, Senior Lecturer, Cardiff Law School, University of Cardiff

Professor D R London, Emeritus Professor of Medicine, University of Birmingham; Registrar of the Royal College of Physicians

Mr T M Milward, Consultant Plastic Surgeon, Leicester Royal Infirmary

Professor A J Silman, Arthritis Research Campaign Professor of Rheumatic Disease Epidemiology, University of Manchester Medical School

Professor J P Sloane, Professor of Pathology, University of Liverpool

Secretariat provided by the Medical Devices Agency

Mr G A Crosbie

Dr D M Gott

Dr S M Ludgate

Mr J J B Tinkler

Declaration of Interests

At their first meeting, members of the Independent Review Group were asked to declare any existing relevant interests. Mr Milward stated that he had resumed the use of silicone gel breast implants in line with the conclusions of the previous Independent Expert Advisory Group. Professor Silman stated that he had summarised the findings of previous epidemiological studies in scientific publications on the epidemiology of connective tissue disease.

Advisors to the Independent Review Group

Dr A J Darby, Consultant Histopathologist, Robert James and Agnes Hunt Orthopaedic Hospital, Oswestry

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Dr C Gemmell, Reader in Medical Microbiology, University of Glasgow

Professor R I Lechler, Professor of Immunology, Imperial College of Science, Technology and Medicine on the Campus of Hammersmith Hospital

Professor F D Lee, Professor of Pathology, Glasgow Royal Infirmary

Dr D E Woolley, Reader in Cell Biology, University of Manchester

Annex 2

Oral Evidence considered by the Independent Review Group

Mr P Balen	Freeth Cartwright Hunt Dickens	(Solicitors)
Ms N Bazire	National Breast Implant Registry	
Ms M Cameron	Silicone Support UK	(Women's Group)
Mrs A Clwyd	Member of Parliament	
Ms E Coomber	Survivors of Silicone	(Women's Group)
Professor R Garry	Tulane University, USA	
Ms S Green		
Ms M Heasman	Breast Implant Information Service	(Women's Group)
Mr R Levy	Leigh Day and Co.	(Solicitors)
Dr S Myhill	General Practitioner and Allergist	
Mr M Notaras	British Association of Cosmetic Surgeons	
Dr P O'Leary	International Association of Prosthesis Manufacturers: McGhan	
Dr B Purkait	International Association of Prosthesis Manufacturers: Mentor	
Dr P Shakespeare	National Breast Implant Registry	
Professor D R Shanklin	University of Tennessee, USA	
Professor D Sharpe	British Association of Plastic Surgeons and British Association of Aesthetic Plastic Surgeons	
Professor D R Uhlmann	University of Arizona, USA	(Nominated by former manufacturers)
Ms R Urion	Survivors of Silicone	(Women's Group)

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Glossary

Adjuvant: a substance which enhances antibody production.

Antibody: a protein that is manufactured by certain lymphocytes (types of white blood cell) which reacts with a specific antigen in the body.

Antigen: a substance that can trigger an immune response resulting in the production of an antibody as part of the body's defense against disease.

Autoantibody: an antibody which reacts with the individual's own tissues because it recognises these as foreign antigens.

Autoimmune reaction: a response arising from and directed against the individual's own tissues.

Axillary lymph nodes: a group of glands in the armpit.

Brachial plexus: a group of nerves in the armpit which supply the arm.

Capsular contracture: shrinkage of the fibrous capsule, noticeable as an apparent hardening of the breast.

Capsulotomy: the creation of an opening through the scar tissue forming around the breast implant, by application of external pressure.

Fibrous capsule: a wall of scar tissue around the breast implant.

Gel bleed: diffusion of small molecules of the liquid component of silicone gel through the intact shell.

Haematoma: a mass of extra-vascular clotted or partially clotted blood, confined within a tissue or space.

Polydimethylsiloxanes (PDMS): polymers of dimethylsiloxane, referred to throughout this report as silicone.

Staphylococcus epidermidis: a bacterium which exists as part of the normal skin microflora causing no ill effects unless introduced into the human body.

Subclinical: this denotes the presence of a condition without obvious symptoms; may be an early stage in the evolution of a disease.

Systematic review: an exercise which aims to review all relevant published studies in the scientific literature on a specific topic, evaluates their quality and the results obtained with the aim of reaching an overall conclusion.

T-lymphocyte: a particular type of long-lived white blood cell.

Silicone Gel Breast Implants
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July 1998 / 30k