Results of the public consultation on SCENIHR's preliminary opinion on the safety of Poly Implant Prothèse (PIP) Silicone Breast Implants

(Update of the Opinion of February 2012)

A public consultation on this opinion was open on the website of the EU non-food scientific committees from 29 October 2013 to 3 January 2014.

Information about the public consultation was broadly communicated to national authorities, international organisations and other stakeholders.

Six organisations and ten individuals participated in the public consultation providing specific comments and suggestions, with the aim to improve the scientific basis of the opinion.

Each contribution was carefully considered by the SCENIHR and the scientific opinion has been reviewed to take into account relevant comments. The final opinion includes these changes; the literature has been updated with relevant publications.

Consideration of the contributions received during the consultation process

Some respondents appeared not to be aware that the purpose of the new opinion was to update the previous opinion produced in 2012 on the same topic. For this reason SCENIHR makes clear that:

- A comprehensive analysis of the literature relevant to this topic was not attempted. Only publications that were directly relevant for updating purposes were considered and the focus was on publications released in 2012 and 2013.
- Particular emphasis was given to data on rupture rates and studies by the competent Agencies of various countries. Information which could not be readily verified, although of interest, was not used in the opinion (in line with SCENIHR general policy[1]).
- Issues concerning risk management or legal aspects were not addressed because they are outside the remit of the SCENIHR mandate.

[1] SCENIHR Memorandum on the use of the scientific literature for human health risk assessment purposes – weighing of evidence and expression of uncertainty- 19 March 2012

Respondents made comments on the following relevant issues.

i) Rupture rates

Several respondents provided additional information based on their experience regarding variation in rupture rates, requesting to include this information in the opinion. One respondent also expressed concerns that the basis for the risk assessment was primarily through a comparison of data on PIP implants against implants from other manufacturers.

The response of the SCENIHR is that information provided by respondents has confirmed the statement in the opinion that rupture rates in different clinics show considerable variation. The cause(s) of this variability in rupture rates may be due to the differences between batches of implants in the quality of the silicon and/or poor control of the manufacturing process. Other factors contributing to the variability in rupture rates are the differences of the way the incidence is identified and reported by different clinics. As a conclusion, SCENIHR considers that adding more information on the variability of rupture rates between clinics is unnecessary. Moreover, SCENHIR states that equivalence with devices of other manufacturers was the best available basis for analysing the data in consideration of the task set by the Commission.

ii) Relationship between rupture and adverse effects

This issue was recognised by some respondents as critical. Some respondents referred to a series of references and medical claims related to the movement of silicone in the body (particularly in the armpits, neck and chest/lungs). Other respondents referred to some anecdotal information that around damaged PIP implants milky fluid is formed. A number of respondents underlined the importance of the release of polymeric silicones (gel) from ruptured implants in causing adverse effects such as local swelling and irritation and, finally, one contributor claimed that some of its work in the area of siloxane toxicity was inappropriately referenced.

The response of SCENIHR

- related to the contributions focused on the movement of silicon in the body, this issue is well covered in the opinion (see section 8.2).
- related to the list of references: the list of references was not taken into account because the most recent reference is from 2004 and therefore, the information is too dated to be considered again by the SCENIHR
- related to the information that around damaged PIP implants there is milky fluid: this issue is not discussed in the opinion as the available evidence/information is anecdotal. This is interpreted as an indicator of a formation of a silicone emulsion rather than formation of a new substance.
- related to the release of polymeric silicones (gel): unfortunately there are no new data in regard to PIP devices nor on the migration of the gel for non-PIP devices and therefore it is not known whether this is an issue related to particular batches of PIP devices. There were reports that some PIP implants were produced without a barrier layer /membrane and this would lead to higher diffusion of silicone from the implant. (SCENIHR PIP Opinion, 2012, page 22). A statement

concerning the lack of new data in regard to PIP devices and on the migration of the gel for non-PIP devices has been added to the opinion.

- The report on siloxane toxicity was fully considered in the preparation of the preliminary opinion and is now appropriately referenced.

iii) Psychological effects and their causes

The opinion notes that psychological effects may arise in patients who have, or have had PIP implants and it draws attention to the effects of the extensive and adverse publicity concerning PIP implants as an important contributor to these psychological effects. This view was challenged by one respondent.

The response of the SCENIHR is to acknowledge that for individual patients there may be other contributing factors, but the SCENIHR does not wish to change its view that adverse publicity is the major contributor for most patients suffering psychological effects. A note has been added to indicate that for individual patients there may be additional contributing factors.

Additions suggested by SCENIHR members

In reviewing the preliminary opinion it was noted that a mention of factors limiting explantation should be added, namely that replacement of an implant cannot be carried out if the tissue around the explant is substantially inflamed. This mention has now been included in the final opinion.

The table below shows all the comments made about each of the questions posed in the opinion and SCENIHR's response to them. It is also indicated if the comment resulted in a change of the opinion.

Comments received during the public consultation on the SCENIHR preliminary opinion on "The safety of Poly Implant Prothèse (PIP) Silicone Breast Implants (2013 update)"

SUBMISSIONS				SCENIHR'S COMMENTS
Name of individual/ organisation	**Do you agree with the observations made by the Scientific Committees?**	**The nature of disagreement**	**The evidence (s) with the reference(s)**	**SCENIHR's response**
Task 1: Obtain reliable data on the incidence of implant failure of PIP devices in different countries				
Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	Pierre Blais: ADVERSE PHENOMENA FROM BREAST IMPLANTS - GENESIS OF THE PROBLEMS http://web.archive.org/web/20040804215346/implants.clic.net/tony/Blais/001.html Pierre Blais: BACKGROUND ON FOAM COVERED PROSTHESES http://web.archive.org/web/20040804215624/http://implants.clic.net/tony/Blais/002.html Pierre Blais: BREAST FEEDING AND PROSTHESES: Individuals with implants in general and in particular users with a history of problems or with evidence of hematomas, seromas or nipple discharge should be strongly advised against breast feeding. In many such instances, the risk may be greater to the offspring than to the mother.http://web.archive.org/web/20040804220056/http://implants.clic.net/tony/Blais/003.html	The most recent reference is in 2004 and therefore falls outside the scope of the SCENIHR search. The references seem to be general in nature, that is: they are about silicone and all implants rather than specifically related to PIP and the cyclo-siloxanes. SCENIHR deliberately covered the low molecular weight cyclo-siloxanes in respect of toxicity and migration, but that is because a relative abundance of these compounds appears to be the only physico-chemical differences between PIP and other implants. The opinion sufficiently covers the aspects of migration in the toxicology section.

			Pierre Blais: BREAST IMPLANT PROMOTION PRACTICES Since about 1994, promotional activity has been on the increase. As a result, implantation of new subjects has risen dramatically and, as expected, adverse reactions have followed. Paradoxically, products sold for breast augmentation have not improved. Some have actually diminished in quality. There is also a large segment of illegal importation of low quality products mainly from Brazil and Europe. http://web.archive.org/web/20040804220437/http://implants.clic.net/tony/Blais/004.html	No changes to the opinion are required in relation to this comment.
			Pierre Blais: BREAST IMPLANTS AND CANCER http://web.archive.org/web/20040804221033/http://implants.clic.net/tony/Blais/005.html	
			Pierre Blais: REAST PROSTHESES - A CASE HISTORY OF POOR CLINICAL TRIAL MANAGEMENT experimenteren Wetboek van neurenberg http://web.archive.org/web/20040804221454/http://implants.clic.net/tony/Blais/006.html	
			Pierre Blais: BBRIEFING NOTE ON FOAM PROSTHESES http://web.archive.org/web/20040804222031/http://implants.clic.net/tony/Blais/007.html	
			Pierre Blais: CAUSES OF IMPLANT RUPTURE AND RESULTING INJURIES Primary impact and crushing injuries to the upper chest area include mostly hard tissue damage, rupture of blood vessels leading to hematomas and seromas, glandular tissue injury leading to oedema, nerve damage culminating in late pain, cartilage trauma, and separation of muscle attachment points, muscle damage associated with overextension and deep trauma involving transmission of energy to more fragile internal organs, such as the liver. In many patients, this translates most frequently as rib cage injury such as fractures with associated secondary soft tissue damage. These are commonly encountered under trauma conditions and are generally expected by clinicians who habitually treat accident victims. For subjects with prostheses, all of the above damages are possible http://web.archive.org/web/20040804222605/http://implants.clic.net/tony/Blais/008.html	

			Pierre Blais: ETIOLOGY OF SHELL RUPTURE http://web.archive.org/web/20040805031136/http://implants.clic.net/tony/Blais/014.html FOAM-COATED PROSTHESES - DESIGN AND RISK ISSUES http://web.archive.org/web/20030515190516/http://implants.clic.net/tony/Blais/015.html	
			Pierre Blais: COMPLICATIONS AND PROBLEMS FROM FOAM-COATED IMPLANTS http://web.archive.org/web/20040804222840/http://implants.clic.net/tony/Blais/009.html	
			Pierre Blais: COSMETIC AUGMENTATION OF SOFT TISSUE WITH OIL INJECTIONS http://web.archive.org/web/20040804223733/http://implants.clic.net/tony/Blais/010.html	
			Pierre Blais: CODOW CORNING: HISTORY AND BREAST IMPLANT http://web.archive.org/web/20040804223859/http://implants.clic.net/tony/Blais/011.html	
			Pierre Blais: DOW CORNING: HISTORY AND BREAST IMPLANT – http://web.archive.org/web/20040804224605/http://implants.clic.net/tony/Blais/012.html Ethics of Publication, Abuse of Process - Control of Information: http://web.archive.org/web/20040804224757/http://implants.clic.net/tony/Blais/013.html	
			Pierre Blais: GENERAL CULTURAL AND COMMERCIAL ASPECTS OF BREAST PROSTHESES USAGE http://web.archive.org/web/20031020190452/http://implants.clic.net/tony/Blais/016.html	
			Pierre Blais: HISTORY AND PROBLEMS WITH SALINE-FILLED TISSUE EXPANDERS http://web.archive.org/web/20031020191055/http://implants.clic.net/tony/Blais/017.html	

			Pierre Blais: INJURIES ARISING FROM SUPERFICIALLY UNDAMAGED BREAST PROSTHESES http://web.archive.org/web/20031228073607/http://implants.clic.net/tony/Blais/018.html The intracapsular fluid mixtures vary	
Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	I have several clients that suffer from health problems related to their silicone breast implants. Especially the PIP-implants cause serious harm because of the high rupture rate the PIP implants. Lots of females have silicon substance in their armpit. From the armpit on it appears for several women the silicon substance moves to the neck, the lungs (and lung area hili) and the ventrum and cervix area. I will send some documents by e-mail about this observations.	See the response formulated above. No changes to the opinion are required.
			Dokter Nanayakkara from VUMC did research over 80 women: http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/140420/VUmc-waarschuwt-voor-siliconen-borstprothese.htm. He concluded women's health restored after the removal of the implants.	
			Patients organisation www.meldpuntklachtensiliconen.nl is collecting data relating to health problems regarding silicone implants. They have already 500 questionnaires registering health problems regarding silicon breast implants. The Allergan implants in the Netherlands appear to cause the same problems like PIP. I will send some documents by e-mail about this. In my opinion the health incidents with silicone breast implants the Netherlands are quite serious. I think this is related to the regulatory failure by the Dutch Health inspection (IGZ). This is also reported by the commissie Sorgdrager that researched the supervisory practices of IGZ. A special focus was on the PIP-implants. I will send the most important conclusions of this report by e-mail or wetransfer. Incidents are not registered in the Netherlands and not evaluated, what is an obligation regarding article 10 of the medical devices directive.I contacted also the FAGG in Belgium. In my opinion the Belgian authorities are registering incidents far more better than the Netherlands. It appears lots of PIP implants before 2001 are used in the Netherlands, while the CE-mark was first provided in 2001 by TUV. I do not understand which notified body did the conformity assessment before 2001. It appears some illegal implants were used (without a PIP or Rofil stamp, however the females were informed	

			their implants are PIP implans. After removal it appears there is no stamp. This also is seen with the Mentor and Allergan (inamed, Mcghan) implants. It appears to me that breast implants are dumped on the Dutch market because of the regulatory failure. In Europe many companies know about this. It also happened with the meshes and hip-implants.	
Individual *No agreement to disclose personal data*	Agree		Nothing	No changes to the opinion are required.
Organisation; Other; Adveniunt Medical International Limited haroon@qualityfirstint.com	Disagree	Other	Please refer to document - Extract from Poly Implant Prothèse (PIP) silicone breast implants	SCENIHR took note and analysed the report 'Extract from Poly Implant Prothèse (PIP) silicone breast implants' and concluded that no changes to the opinion are required.
Organisation; Other; PIP Action Campaign; pip.action.campaign@gmail.com	Disagree	Disagreement with the interpretation of the existing scientific and other data	1. Criminally NON COMPLIANT PIP Implants have failed to meet the essential requirements referred to in Article 3; Article 8; Article 10; Article 14b, Article 15 (6) and ANNEX I ESSENTIAL REQUIREMENTS I. GENERAL REQUIREMENTS of the COUNCIL DIRECTIVE 93/42/EEC http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:EN:PDF 2. INVALID 'equivalence' Scenihr is using 'equivalence' to compare fraudulently manufactured NON COMPLIANT high risk Category III medical devices with COMPLIANT Medical devices as a basis for its opinion. EVIDENCE: French Police reports show there were no technically qualified staff at the PIP factory. Unknown raw materials Unknown manufacturing processes	While SCENIHR sympathizes with the women offended by PIP breast implant fraud, it is not in the mandate of the SCENIHR to consider issues such as criminality and fraud or how such issues have been managed by a National Authority. No changes to the opinion are required.

Individual; Douglas Cross BSc, CSci. CBiol. FSB; doug@ukcaf.org	Disagree	Relevant scientific and other information missing from the analysis	The risk assessment process employed by SCENIHR for its examination of this matter is too restricted in its scope. The analysis is essentially confined to the examination of toxicological, carcinogenic and other health risks of the substances found in the product, compared with those of authorised filler materials and enclosures. In the Abstract to the Opinion, it is stated that 'There is currently no convincing medical, toxicological or other data to justify removal of intact PIP implants as a precautionary approach.' This conclusion is subject to peer review, and I will leave this to those more qualified to comment further on this aspect of the Opinion. However, in this specific case the Committee appears not to have complied fully with its own remit, which states that 'This Committee deals with questions related to emerging or newly identified health and environmental risks and on broad, complex or multidisciplinary issues requiring a comprehensive assessment of risks to consumer safety or public health and related issues not covered by other Community risk assessment bodies.' (my emphasis added). In a retrospective review of evidence in a case such as this, where there is clear evidence of existing and long-standing non-compliance, the additional issues of 'consumer safety or public health and related issues specified in the committee's remit must also be addressed, and at the same level as those dealing with the clinical effects of the product's chemical constituents. It is in SCENIHR's apparently arbitrary dismissal of these 'related issues' that this 'Opinion' fails to fulfil its own mandate. Unlike most 'Risk Assessments' this is a retrospective analysis of an actual incident. Whilst a detailed scrutiny of the physical effects of the supply of this product is entirely justified, the Committee should also assess the extent and severity of those 'related issues' that have emerged within the community as a whole. This is particularly the case where failure to identify and terminate criminal deception in such a sensitive social context may lead to serious psychological impacts.	SCENIHR considers that use of equivalence with other manufacturers is the only appropriate approach. No changes to the opinion are required.

			Public investigations of such incidents, especially when misrepresented as 'risk assessments', routinely down-play their social impacts. They often dismiss public concern as mere 'hysteria' caused by media coverage, as in the Camelford water poisoning of 1988. There is clearevidence of this bias in this Opinion. It correctly identifies a significant increase in the actual suicide rate in women with cosmetic implants (s.4.1.4) and the 'marked psychological impact' of public awareness of the defective PIP implants on a considerable number of women (s.10.4.2). But then it implies that much of this might be attributed to the media "scandal" that accompanied the exposure of the non-compliance (s. 7.4.2). In the original publication, and in many of its citations, the word scandal is not enclosed in quotation marks, but in both the emboldened text in the Opinion's Table of Contents and in s. 7.4.2 these are inserted, whereas in the text itself and in the reference citation (p.72) it is not. The impression given to the reader by this deliberate misrepresentation is that the psychological impacts of this "scandal" might be attributable merely to media hype and alarmism The result of this bias emerges in section 10.5 - Generic Risks and Benefit of removal of PIP silicone breast implants, it is stated that 'With regard to explantation of intact PIP implants as a precautionary approach . . . based on individual assessment, explantation could be considered for women who experience psychological impairment due to carrying PIP implants, even in the absence of implant malfunction.' This reveals an unacceptable prejudice of the Committee against recognising the relevance of the very real trauma of those caught up in this fraud, of the many other women whose implants have not failed, and the effects on their immediate families and contacts.	
Individual; Marga van Amersfoort; m.g.j.van.amersfoort @hetnet.nl	Uncertain		My comment: uncertain..... as uncertain as words like probably, reasonable and likely used in the opinion.	No changes to the opinion are required. When scientific evidence is not strong enough; conclusion should reflect that.
Organisation; Other; SVS Stichting voor Vrouwen met Siliconenimplantatie; meldpuntklachtensili	Disagree	Relevant scientific and other information missing from	At the SVS-mks (A non-profit organization representing the interests of women with complaints or became ill after breast implants. We provide information, maintain contact with medical care, breast cancer societies, gathering information to stay informed of developments. Founded in 1992, since about 4000 registered	In the SCENIHR opinion it was clearly stated that the rupture rates reported varied considerably due to: • Variations in the physicochemical properties of the PIP implants over time and perhaps

conen@hotmail.nl		the analysis	women) women who were 'victims' of the PIP-implants could apply through a questionnaire, regardless the status of their implants, these 228 women reported: 45% one or both implants ruptured 27% no failure 5% not removed 23%, unknown. The average age of implants was 7 years	also between markets • Differences in the denominator used to express the failure rates (eg is the rate based on all women with a PIP implant or only those responding to a questionnaire or attending a clinic after the issue received much publicity. No changes to the opinion are required.
Individual; Darren Stuart; Darren.stuart@ntlworld.com	Mostly agree		I agree with the findings that the implants were of an inferior quality, however the true rupture rate and the timescales when a rupture occurs cannot be fully determined without a worldwide or Europe wide program of scanning with ongoing monitoring.	The opinion is based on data available in 2013. No changes to the opinion are required.
Organisation; Public authority; BfArM - Federal Institute for Drugs and Medical Devices; medizinprodukte@bfarm.de	Agree		By 30 November 2013, BfArM has received 1569 case reports concerning explantation of silicone gel-filled breast implants manufactured by PIP. In 1352 reports (86%) there was information on findings at explantation. In 48% of these cases a rupture / defect or bleeding was reported; in 52% the implants were intact at explantation. Overall, the case reports include 2429 implants with information on findings at explantation. Bleeding was reported for 21% of all the implants, rupture / defect for 19%. 60% of the implants were intact at explantation. The failure mode "bleeding" includes all forms of gel-bleed (light/moderate/severe).	SCENIHR considers that there is too little information included in the comments. 48% ruptured or leaking implants among roughly 1500. No information as to how these data were gathered, there could be a heavy selection bias - or none about how long have these implants been implanted is unknown. The data could have been offered when SCENIHR asked for the data. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Agree		personal series (unpublished) of 99 exchange patients would concur with the above rupture rates	This comment supports the opinion. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Disagree	Other	Evidence as presented at the meeting	No information about age of implants/ implantations or year, which makes the results impossible to compare with others. No changes to the opinion are required

Organisation; NGO; European Social Insurance Platform (ESIP ; marina.schmidt@esip.eu	Mostly agree		---	No changes to the opinion are required.
Organisation; Public authority; Medical Products Agency in Sweden; meddevcentral@mpa.se	Agree		No comments	No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Disagree	Other	I got pip 2007 in Sweden .since 2010 I have been very sick in my lungs and body. 2013 they took out my implant. I have silicon in my glands, have a lot of pain. I have problems With My lungs and chest. Food and Drug Administration analysed my implant and the found that they are the toxic one. They have never seen so high levels of toxic in other implants. Other implant :D4 på 77-134 ppm My implants :300 and 220 D4 ppm They don't help me in Sweden and no dr knows anything about this. Please help me! I am so sick ! Please contact	This is a report of a personal case which is reflected in clinical studies analysed. National contact has been provided to the contributor. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Mostly agree		There is no doubt that the PIP manufacturing process was at best ad hoc and so any individual implant cannot be guaranteed to be compliant with the CE mark. As a consequence, none of the implants comply with the CE mark and as such are not fit for implantation in the human. If allowed to remain in situ, it makes a mockery of CE marking. .	This comment refers to risk management, which falls outside the remit of SCENIHR. No changes to the opinion are required.

SUBMISSIONS				SCENIHR'S COMMENTS
Name of individual/ organisation	**Do you agree with the observations made by the Scientific Committees?**	**The nature of disagreement**	**The evidence (s) with the reference(s)**	**SCENIHR's response**
Task 2: Identify the physicochemical factors that might influence PIP implant failure in particular the influence of the implant contents				
Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	There is also a large segment of illegal importation of low quality products mainly from Brazil and Europe. http://web.archive.org/web/20040804220437/http://implants.clic.net/tony/Blais/004.html	See the replies in the previous section. No changes to the opinion are required.
			Pierre Blais: BREAST IMPLANTS AND CANCER http://web.archive.org/web/20040804221033/http://implants.clic.net/tony/Blais/005.html	
			Pierre Blais: BREAST PROSTHESES - A CASE HISTORY OF POOR CLINICAL TRIAL MANAGEMENT experimenteren Wetboek van neurenberg http://web.archive.org/web/20040804221454/http://implants.clic.net/tony/Blais/006.html	
			Pierre Blais: BRIEFING NOTE ON FOAM PROSTHESES http://web.archive.org/web/20040804222031/http://implants.clic.net/tony/Blais/007.html	

			Pierre Blais: CAUSES OF IMPLANT RUPTURE AND RESULTING INJURIES Primary impact and crushing injuries to the upper chest area include mostly hard tissue damage, rupture of blood vessels leading to hematomas and seromas, glandular tissue injury leading to oedema, nerve damage culminating in late pain, cartilage trauma, and separation of muscle attachment points, muscle damage associated with overextension and deep trauma involving transmission of energy to more fragile internal organs, such as the liver. In many patients, this translates most frequently as rib cage injury such as fractures with associated secondary soft tissue damage. These are commonly encountered under trauma conditions and are generally expected by clinicians who habitually treat accident victims. For subjects with prostheses, all of the above damages are possible http://web.archive.org/web/20040804222605/http://implants.clic.net/tony/Blais/008.html	
			Pierre Blais: COMPLICATIONS AND PROBLEMS FROM FOAM-COATED IMPLANTS http://web.archive.org/web/20040804222840/http://implants.clic.net/tony/Blais/009.html	
			Pierre Blais: COSMETIC AUGMENTATION OF SOFT TISSUE WITH OIL INJECTIONS http://web.archive.org/web/20040804223733/http://implants.clic.net/tony/Blais/010.html	
			Pierre Blais: DOW CORNING: HISTORY AND BREAST IMPLANT http://web.archive.org/web/20040804223859/http://implants.clic.net/tony/Blais/011.html	
			Pierre Blais: DOW CORNING: HISTORY AND BREAST IMPLANT – http://web.archive.org/web/20040804224605/http://implants.clic.net/tony/Blais/012.html Ethics of Publication, Abuse of Process - Control of Information: http://web.archive.org/web/20040804224757/http://implants.clic.net/tony/Blais/013.html ETIOLOGY OF SHELL RUPTURE http://web.archive.org/web/20040805031136/http://implants.clic.net/tony/Blais/014.html	
			Pierre Blais: FOAM-COATED PROSTHESES - DESIGN AND RISK ISSUES http://web.archive.org/web/20030515190516/http://implants.clic.net/tony/Blais/015.html	

			Pierre Blais: GENERAL CULTURAL AND COMMERCIAL ASPECTS OF BREAST PROSTHESES USAGE http://web.archive.org/web/20031020190452/http://implants.clic.net/tony/Blais/016.html	
			Pierre Blais: HISTORY AND PROBLEMS WITH SALINE-FILLED TISSUE EXPANDERS http://web.archive.org/web/20031020191055/http://implants.clic.net/tony/Blais/017.html	
			Pierre Blais: INJURIES ARISING FROM SUPERFICIALLY UNDAMAGED BREAST PROSTHESES http://web.archive.org/web/20031228073607/http://implants.clic.net/tony/Blais/018.html The intracapsular fluid mixtures vary from very mobile, water-like and nearly without color, to thick, paste-like media with intense amber colorations. White pasty fluids are most common for users of devices that have been in situ for more than 6-7 years. The space always contains large quantities of emulsified oils and detergent-like substances which are formed through biodeterioration of blood products. When micro-organisms populate the site, overt infections do not always result. The most common micro-organisms do not culminate in florid infective manifestations. Instead, colonies form and are comparatively well tolerated by the host. Microbiological activity proceeds and metabolites formed by the entities become part of the toxic burden produced by the intracapsular medium.	
			Pierre Blais: INJURY FROM BREAST IMPLANTS http://web.archive.org/web/20031228041108/http://implants.clic.net/tony/Blais/019.html	
			Pierre Blais: INJURY FROM SALINE INFLATABLE BREAST IMPLANTS welke patiënten zijn het meest kwetsbaar http://web.archive.org/web/20031228042737/http://implants.clic	

Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	I miss the studies by Jan Willen Cohen Tervaert, the studies by Rita Kappel, professor Vernooy and Nanayakkara in the report: http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/140420/VUmc-waarschuwt-voor-siliconen-borstprothese.htm http://link.springer.com/article/10.1007/s00238-013-0914-4 http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCgQFjAA&url=http%3A%2F%2Fwww.inchem.org%2Fdocuments%2Fehc%2Fehc%2Fehc236.pdf&ei=h9vGUvGODYaO0AWaxYCgBQ&usg=AFQjCNEuzgvnUf3S5uDqMkoy2q1oT7df5g&bvm=bv.58187178,d.d2k and the reports on the website www.meldpuntklachtensiliconen.nl or www.svs.nl.	See the replies in the previous section No changes to the opinion are required.
			In my opinion environmental studies show serious concerns regarding siclosiloxanes in the shell and the volume material. http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCoQFjAA&url=http%3A%2F%2Foehha.ca.gov%2Fmultimedia%2Fbiomon%2Fpdf%2F1208cyclosiloxanes.pdf&ei=7-DGUue5Ks-10QXKnoHgCw&usg=AFQjCNEXmjjfilly3R_iK8BKz1ufr700ww&bvm=bv.58187178,d.d2k In my opinion such studies should also be done regarding health issues. In my opinion lost of research over silicone material is done and financed by Dow Corning. Dow Corning has a special interest not to be to critical over silicone material, because the still produce this. For this reason I think really independent research over the risks regarding silicones is necessary and should be financed by a neutral party.	

Individual *No agreement to disclose personal data*	Disagree	Other	The data cited in the preliminary opinion and provided by MHRA (documents cited in the preliminary opinion), failed to identify most of the silicone substances present in PIP filler silicone (see the low match coefficients for almost all peaks in GC-MS analyses, evidently wrong attributions and compounds reported as unknowns). A more complete and substantiated characterization of the filler silicone has been reported in Beretta and Malacco (2013), a paper cited in the preliminary opinion only concerning the presence of intra-implant cholesterol. In that study, apart the presence of the polydimethylsiloxanes D4, D5 and D6, that of the series of the higher homologues species D7-D23 is described. This series is moreover the more quantitatively significant. The potential consequences deriving from the exposure of human body to these non volatile and persistent substances has been completely neglected in the preliminary opinion. It should be kept in mind that the toxicological profile of these substances are currently unknown, although some clues about their local and systemic proinflammatory effects following direct injection in different body parts are reported in the literature (see citations in Beretta and Malacco 2013 and Beretta Richards Malacco 2013). G. Beretta, M. Malacco. J Pharm Biomed Analysis. 2013; 78-79: 75-82. G. Beretta, A. Richards, M. Malacco. J Pharm Biomed Analysis. 2013; 84: 159-167.	SCENIHR considered carefully these comments; these issues are addressed in the opinion, Chapter 6. The references quoted are already included in the reference list. No changes to the opinion are required.
Organisation; Other; Adveniunt Medical International Limited; haroon@qualityfirstint.com	Mostly agree		Please refer to document - Extract from Poly Implant Prothèse (PIP) silicone breast implants	The SCENIHR took note of this paper and consider it carefully. No changes to the opinion are required.
Organisation; Other; PIP Action Campaign; pip.action.campaign@gmail.com	Disagree	Disagreement with the interpretation of the existing scientific and other data	1. Criminally NON COMPLIANT PIP Implants have failed to meet the essential requirements referred to in Article 3; Article 8; Article 10; Article 14b, Article 15 (6) and ANNEX I ESSENTIAL REQUIREMENTS I. GENERAL REQUIREMENTS of the COUNCIL DIRECTIVE 93/42/EEC http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:EN:PDF	This falls outside the remit of SCENIHR which is related to risk assessment. It is not in the mandate of the SCENIHR to consider issues such as criminality and fraud or how such issues have been managed by a National Authority. No changes to the opinion are required.

			2. INVALID Assertions Scenihr 'notes' invalid generalisations about REACH Substance TOXIC D4. EVIDENCE: Repro-Toxic D4 Octamethylcyclotetrasiloxane CAS 556-67-2, identified in tests on sterile PIP implants, was drawn to the attention of international health and safety regulators in 2011 by the AFSSAPS. In 2012, the European Commission responded to PIP Action Campaign's request for details of the classification of D4. This confirmed D4 as ReproToxic in humans with labeling exemptions in personal care products and High Risk Category III implantable Medical Devices. We were informed of the substance review and environmental evaluation of D4 underway by UK Competent Authority for REACH, HSE. According to the HSE: "Based on the available information, D4 meets the Annex XIII criteria for both a 'persistent, bioaccumulative and toxic' (PBT) and a 'very persistent and very bioaccumulative' (vPvB) substance in the environment. This conclusion was endorsed by the ECHA PBT Expert Group in November 2012." HSE has confirmed that following the completion of this evaluation and the conclusion reached, EA is now working on a detailed project that may result in a formal proposal for restriction on the basis of the environmental concerns. The criteria in REACH, Article 57 for Substances of Very High Concern SVHC's include: • Substances which are persistent, bio-accumulative and toxic (PBT) in accordance with the criteria set out in Annex XIII of the REACH Regulation; • Substances which are very persistent and very bio-accumulative (vPvB) in accordance with the criteria set out in Annex XIII of the REACH Regulation; D4 is currently classified as follows: Human health Repro. Cat 3 R62: Possible risk of impaired fertility. Human health Hazard class and category: Repr. 2. Hazard statement: H361f: Suspected of damaging fertility. D4 is categorized as an endocrine disruptor (cat 1) Octamethylcyclotetrasiloxane - Sin List Database accessed 30/07/2013 03:29 - D4 is found in silicone breast implants and in higher concentrations in criminally manufactured PIP breast implants. - D4 has been found in the prosthetic fluid associated with PIP implants. http://www.sciencedirect.com/science/article/pii/S0731708513002525 - The Majority of women with PIP breast implants are of reproductive age. - Women with fraudulent PIP implants report immunological, neurological and endrocrinal symptoms. - Women	See the comments in the section above. No changes to the opinion are required.

			with fraudulent PIP implants are known to be undergoing a number of corrective surgeries including the removal of massively silicone saturated lymph nodes. http://pipactioncampaign.org/PACTheLiteratureReview.pdf	
Individual; Douglas Cross BSc, CSci. CBiol. FSB; doug@ukcaf.org	Uncertain		I am unqualified to provide an opinion	This comment does not need a response. No changes to the opinion are required.
Individual; Marga van Amersfoort; m.g.j.van.amersfoort @hetnet.nl	Uncertain		Following a thorough toxicological review on the properties of the two most studied siloxanes, D4 and D5, the conclusion of the SCENIHR is that these compounds are of low acute and chronic toxicity. Used for >25years before decent studies were conducted and again..... denied	This issue is addressed in Chapter 6. No changes to the opinion are required.
Organisation; Other; SVS Stichting voor Vrouwen met Siliconenimplantatie; meldpuntklachtensiliconen@hotmail.nl	Disagree	Relevant scientific and other information missing from the analysis	First: perhaps an answer on the question about failure rates The transport of octamethylcyclotetrasiloxane (D4) and polydimethylsiloxane (PDMS) in lightly cross-linked silicone rubber. This suggests that the permeation of D4 out of any encapsulation device, such as a silicone breast implant, is linearly dependent upon the concentration of D4 in the prosthesis. Swelling is isotropic and was measured by dimensional changes in rectangular samples and correlates well with the volume of D4 sorbed. J Biomater Sci Polym Ed. 2001;12(7):801-15. Wolf CJ, Jerina KL, Brandon HJ, Young VL. In the 90s D4/D5 'were partly responsible for the ban in America; www.fjc.gov/BREIMLIT/ORDERS/order37.rtf because it turned out that there was little research done on these substances ,while they were implanted for more than> 25 years in women. From 2006 the implants according to the FDA contain <69ppm at 300cc implant D4 and D5 as well. Much higher concentrations were used : http://www.ncbi.nlm.nih.gov/books/NBK44794/#a200067c8ddd00045 We quote: A silicone gel implant is said to contain about 855 parts per million (ppm) of D4, or about 256 mg in an average-size (300-cc) gel implant (T.H. Lane and J.J. Kennan, personal communication, 1998). The sad thing is that the first studies were not published until 1995. A total of 40 studies on octamethylcyclotetrasiloxane, decamethylcyclopentasiloxane even less, about dodecamethylcyclohexasiloxane a total of nine studies including 4 more related to all siloxanes. Some quotes from the	SCENIHR considered carefully these comments; this issue is addressed in Chapter 6. No changes to the opinion are required.

			different studies	
			· Silicone gel taken from a commercial breast implant thus is capable of mediating collagen induced arthritis in the DA rat. However, silicone gel alone does not appear to be arthritogenic	
			· Rats immunized with BSA mixed with the highest molecular size silicone oil tested (M.W. approximately 60,000) showed a significant increase in anti-BSA antibodies as compared to the lower molecular size oils. The three silicone gel preparations showed no difference in their adjuvancy effect. Thus, the humoral adjuvancy of silicone oil appears to be dependent on molecular weight. Differential shearing of the silicone gel does not alter its humoral adjuvancy	
			· The results indicate that both D4 and the silicone gel potentiate antibody production to BSA in mice. Known adjuvants have been shown to induce autoimmune syndromes in animal models. Whether silicones can act in a similar mechanism is still unclear.	
			· The results of this study show that low molecular weight siloxanes produce lethal effects on B-lymphocyte derived target cells in vitro and permeabilize the plasma membranes at lower sublethal concentrations	
			· Histopathologic evaluation of the injection sites reveals granulomas for mice injected with IFA and D4 preparations. Whether D4 or silicone gel acts as an adjuvant against self-antigens has yet to be determined.	
			· Thus it has been demonstrated that D4 can induce denaturation and conformational changes in Fbg and Fn and it can be expected that protein molecules that have undergone denaturation or conformational change induced by D4 may act as antigens and stimulate the immune system to generate antibodies, ultimately resulting in autoimmune disease	

			• D4 appeared to be a higher potency inducer than phenobarbital (PB). Dose-response curves for increased liver weights had N/mS 1.0 and Kd/mS 3.4 microM, very different values from those for enzyme induction. Exposure concentration leading to a 0.1% increase in CYP2B1/2 protein predicted by the 1- and 5-compartment models were 2.1 ppm and 5.1 ppm, respectively. The 1- and 5-compartment liver models provided very similar fits to the whole liver induction data, excluding the lowest dose, but the 5-compartment liver model had the additional advantage of simultaneously describing the regional induction of CYP2B1/2.	
Individual; Darren Stuart; Darren.stuart@ntlworld.com	Disagree	Relevant scientific and other information missing from the analysis	Testing that has taken place has been on new implants that have not been placed in the human body, therefore no information is available of the effects of the substandard gel when a rupture occurs. A program of testing on explanted material should be undertaken and monitoring of patients who have experienced a rupture for common symptoms. I have seen many women reporting signs of tiredness, night sweats, ongoing rashes, the response for these women has been inadequate and has not reassured them.	In the SCENIHR opinion it was clearly stated that the rupture rates reported varied considerably due to: • Variations in the physicochemical properties of the PIP implants over time and perhaps also between markets • Differences in the denominator used to express the failure rates (eg is the rate based on all women with a PIP implant or only those responding to a questionnaire or attending a clinic after the issue received much publicity. No changes to the opinion are required.
Organisation; Public authority; BfArM - Federal Institute for Drugs and Medical Devices; medizinprodukte@bfarm.de	Uncertain		Additional scientific data on the mentioned siloxanes cannot be provided at the moment.	No changes to the opinion are required.

Individual *No agreement to disclose personal data*	Agree		No evidence in my patients of increase in toxicity	This comment agrees with SCENIHR opinion. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Agree		Agree	No changes to the opinion are required.
Organisation; NGO; European Social Insurance Platform (ESIP; marina.schmidt@esip.eu	Uncertain		Since industrial grade silicone does not meet the same stringent quality requirements as medical grade silicone, for example containing higher amounts of low molecular weight siloxanes in the PIP implants, the uncertainty remains that it could have adverse long term health consequences for patients when released due to leakage or rupture.	This issue is addressed in the opinion at page 20 (section 5.1). No changes to the opinion are required.
Organisation; Public authority; Medical Products Agency in Sweden; meddevcentral@mpa.se	Mostly disagree	Disagreement with the interpretation of the existing scientific and other data	In conclusion the Swedish Medical Products Agency (MPA's) assessment is that, with exception of a possibly more pronounced local irritative effect, PIP implants manufactured from raw material with higher contents of D4, D5 and D6 are from a toxicological point of view not considered to pose an increased risk to humans as compared to implants manufactured from raw material approved for implants. However, SCENIHR presents a too generalised view of findings concerning chemical contents of PIP implants, which have implementation on exposure and toxicological effects. Furthermore, data concerning physio-chemicals properties may have been misinterpreted. The comments below are divided into four parts concerning chemical composition, exposure, toxicology and physio-chemical properties.	SCENIHR considered carefully these comments and modified some text for the sake of clarity at page 20 (section 5.1) and page 23 (section 5.4).

			Chemical composition Throughout the SCENIHR opinion the terminology is confusing since siloxanes, cyclosiloxanes, silicone and silicon have been mixed. PIP implants are stated to contain higher amounts of D4, D5, and D6 (cyclic siloxanes) compared to other implants. However, chemical analyses by the MPA and AFSSAPS/ANSM have shown three different formulas of PIP gel, where "PIP Nusil" is made from the raw material (MED3-6300 part A+B) approved for use in implants. PIP Nusil gel has no or very low levels of D4, D5 and D6 as other implants on the market made of the same raw material. For the other two PIP gel formulas MPA agrees that the main difference to other implants on the market is the presence of higher levels of the D4, D5 and D6 (Ref 1, SCENIHR ref SMPA, 2013 c). MPA detected xylene (an organic solvent) in PIP implants which is omitted in the SCENIHR opinion; instead a result is referenced (p.21) that no volatile organic compounds could be detected. Table 4 in the SCENIHR opinion has misleading referral to MPA results. For PIP2 (n=6) the highest level of D5 is 499 ppm and D6 777 ppm. For PIP Nusil (n=5) the highest level of D5 is 55 ppm and D6 71 ppm (SCENIHR ref SMPA, 2013 c).	
			Exposure: The fibrous capsule is stated in the SCENIHR opinion to act as a barrier to dispersal of siloxanes within the body. This is not in agreement with the capsule being well vascularised (SCENIHR ref Wolfgang et al., 2004). Furthermore, Flassbeck has shown that siloxanes are spread into other tissues (SCENIHR ref Flassbeck et al., 2001, 2003). SCENIHR states (no reference) that released D4, D5, and D6 are to be cleared from the blood and lymph over time. In fact, Flassbeck observed a poor clearance rate. Furthermore the SCENIHR opinion lacks data on background levels that comparison is made to (SCENIHR ref Flassbeck et al., 2001, 2003). Negative results in skin irritation tests cannot exclude that PIP implants may cause irritation since the route of exposure differ.	

			Toxicology SCENIHR refers to properties of PIP gel. To be able to draw conclusions about toxicity, the levels of cyclic siloxanes in the PIP gel needs to be confirmed since PIP gel comprises of three different formulas. In the aspect of cytotoxicity, Pfleiderer performed a study including intramuscular (i.m.) injection of aqueous emulsion with cyclic polysiloxanes, linear polysiloxanes or without polysiloxanes. Only cyclic polysiloxanes, mainly D4, caused tissue reactions. This result confirms that the observed pronounced tissue reactions are not caused by the i.m. injection but by cyclic polysiloxanes (SCENIHR ref Pfleiderer B et al., 1999).	
			Physio-chemical properties PIP implants are stated to be of comparative quality to other implants. This is not in agreement with findings by Yildimer investigation of mechanical and viscoelastic properties (SCENIHR ref Yildirimer et al., 2013). The reference to Strömberg is misleading since only morphology was studied by FTIR and FE-SEM (SCENIHR ref Strömberg and Atarijabarzadeh, 2013). Reference 1: ANSM (2012) Situation update on checking procedures performed by the health authorities on the poly implant prothèse company.	
Individual *No agreement to disclose personal data*	Mostly disagree	Disagreement with the interpretation of the existing scientific and other data	You become so much sicker than you say.	Personal case which is reflected in clinical studies analysed. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Disagree	Relevant scientific and other information missing from the analysis	The inflammation around a proportion of implants remains unexplained I have experienced on explanation and reports by the French and other surgeons remains unexplained. If not the implant, other factors need to be examined as this has not been seen around any implant previously. The surgeon, technique, wash fluids and hospitals should be investigated.	This statement is reflected in the opinion at pages: 11 (section 1.5 and 1.6), 19 (section 4.3.3), 26 (section 6.31), 30 (section 6.3), 32, 33, 35 (section 7.2.1), 38 (section 7.2.2), 41 (section 7.4.4), 42 (section 7.2.5), 44 (section 7.3.1), 48 (section 7.3.4), 50(sections 7.3.5 and 7.3.6), 53, 54 (section 8.2), 54, 55 (section 8.3), 60 (section 10.4.2), 61 (section 10.5) and 89, 90 (Appendix II). No changes to the opinion are required.

SUBMISSIONS				SCENIHR'S COMMENTS
Name of individual/ organisation	**Do you agree with the observations made by the Scientific Committees?**	**The nature of disagreement**	**The evidence (s) with the reference(s)**	**SCENIHR's response**
Task 3: comparison to the environmental risks				
Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	Pierre Blais: INJURY FROM BREAST IMPLANTS http://web.archive.org/web/20031228041108/http://implants.clic.net/tony/Blais/019.html	See the reply in the first section (Task 1). No changes to the opinion are required.
			Pierre Blais: INJURY FROM SALINE INFLATABLE BREAST IMPLANTS welke patiënten zijn het meest kwetsbaar http://web.archive.org/web/20031228042737/http://implants.clic.net/tony/Blais/020.html	
			Pierre Blais: LIMITATIONS & RISKS FROM MAMMOGRAPHIC STUDIES voor RIVM WITH IMPLANTS IN SITU http://web.archive.org/web/20031020191947/http://implants.clic.net/tony/Blais/021.html	
			Pierre Blais: MEDICAL ENGINEERING AND SURGITEK PROSTHETIC SYSTEMS, hartkleppen, kinimplantaten, neuscorrectie enz. http://web.archive.org/web/20031020191329/http://implants.clic.net/tony/Blais/022.html	
			Pierre Blais: PENILE PROSTHESES penis implantaten, plooien, lekken, infecties, opblaasbaar, sluit niet goed af, bloed en micro-organismen in implantaat, zorgt voor ernstige infecties. http://web.archive.org/web/20031228051625/http://implants.clic.net/tony/Blais/023.html	
			Pierre Blais: ADIATION AND ITS IMPACT ON TISSUE - IMPLICATIONS FOR IMPLANT USERS bestraald weefsel is reactief, natuurlijke genezing wordt vertraagd. Na bestraling meer infecties, die jaren	

			aanhouden http://web.archive.org/web/20031228053348/http://implants.clic.net/tony/Blais/024.html	
			Pierre Blais: RADIOLOGICAL EVALUATION OF MAMMARY PROSTHESES voor RIVM http://web.archive.org/web/20031228054726/http://implants.clic.net/tony/Blais/025.html	
			Pierre Blais: RRATIONALE FOR THE STUDY OF RECOVERED IMPLANTS te weinig kennis zorgt voor problemen http://web.archive.org/web/20031020192520/http://implants.clic.net/tony/Blais/026.html	
			Pierre Blais: RISKS FROM IMPLANT REUSE - AN UNSANCTIONED PRACTICE (niet hergebruiken, ook niet na sterilisatie) http://web.archive.org/web/20040315231538/http://implants.clic.net/tony/Blais/027.html Sending Specimens for Research http://web.archive.org/web/20040315232222/http://implants.clic.net/tony/Blais/028.html	
			Pierre Blais: UPPRESSIONS OF INFORMATION Bv. Promotiemateriaal vermomd als wetenschappelijke publicaties behoort tot fraude. Informatie over producten moet door onafhankelijken en zonder belangenconflict http://web.archive.org/web/20040315232222/http://implants.clic.net/tony/Blais/029.html	
			Pierre Blais: TECHNOLOGY AND COMPOSITION OF SILICONE BREAST IMPLANTS http://web.archive.org/web/20040315233146/http://implants.clic.net/tony/Blais/030.html	
			Pierre Blais: TECHNOLOGY OF STERILIZATION - IMPACT ON PRODUCTS http://web.archive.org/web/20040315233701/http://implants.clic.net/tony/Blais/031.html	
			Pierre Blais: HE COX UPHOFF INTERNATIONAL CORPORATION (CUI) overgenomen door Inamed '89, oa polyurethaan implantaten http://web.archive.org/web/20040315234030/http://implants.clic.net/tony/Blais/032.html	

			Pierre Blais: THERAPEUTIC RADIATION TREATMENTS AND IMPLANTS bijwerkingen met bestralen door vervuiling implantaat http://web.archive.org/web/20040315235256/http://implants.clic.net/tony/Blais/033.html	
			Pierre Blais: Platina from Dr Pierre Blais. platinol is geen goede katalysator, niet geschikt voor implantaten omdat het in water oplosbaar is. http://web.archive.org/web/20040501181120/http://implants.clic.net/tony/Blais/034.html	
			Pierre Blais: Dr. Blais Testimony to the FDA http://web.archive.org/web/20040501083819/http://implants.clic.net/tony/Blais/035.html TEXT OF LETTER TO DR. D.W.. FEIGAL Nov 18.99 http://web.archive.org/web/20040501181821/http://implants.clic.net/tony/Blais/036.html	
			Pierre Blais: ALINE-FILLED BREAST IMPLANTS - A CONTINUING AREA OF CONCERNS, afsluitbare doppen slecht, veel kapselvorming, verkalking omliggend weefsel, hierdoor schuren implantaten en slijt de envelop. http://web.archive.org/web/20040409144241/http://implants.clic.net/tony/Blais/037.html	
			Pierre Blais: Implant Critic Converts Government Crusade Into Business (ontslag Blais) http://web.archive.org/web/20040501182406/http://implants.clic.net/tony/Blais/038.html	
			Pierre Blais: INJURY FROM BREAST IMPLANTS http://web.archive.org/web/20031228041108/http://implants.clic.net/tony/Blais/019.html	
			Pierre Blais: DEPARTMENT OF HEALTH & HUMAN SERVICES http://web.archive.org/web/20040501175720/http://implants.clic.net/tony/Blais/039.html	

Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	I miss the studies by Jan Willen Cohen Tervaert, the studies by Rita Kappel, professor Vernooy and Nanayakkara in the report: http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/140420/VUmc-waarschuwt-voor-siliconen-borstprothese.htm http://link.springer.com/article/10.1007/s00238-013-0914-4 http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCgQFjAA&url=http%3A%2F%2Fwww.inchem.org%2Fdocuments%2Fehc%2Fehc%2Fehc236.pdf&ei=h9vGUvGODYaO0AWaxYCgBQ&usg=AFQjCNEuzgvnUf3S5uDqMkoy2q1oT7df5g&bvm=bv.58187178,d.d2k and the reports on the website www.meldpuntklachtensiliconen.nl or www.svs.nl. In my opinion environmental studies show serious concerns regarding siclosiloxanes in the shell and the volume material. http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCoQFjAA&url=http%3A%2F%2Foehha.ca.gov%2Fmultimedia%2Fbiomon%2Fpdf%2F1208cyclosiloxanes.pdf&ei=7-DGUue5Ks-10QXKnoHgCw&usg=AFQjCNEXmjjfilly3R_iK8BKz1ufr700ww&bvm=bv.58187178,d.d2k In my opinion such studies should also be done regarding health issues.	See the reply in the first section (Task 1). No changes to the opinion are required.
			In my opinion lost of research over silicone material is done and financed by Dow Corning. Dow Corning has a special interest not to be to critical over silicone material, because the still produce this. For this reason I think really independent research over the risks regarding silicones is necessary and should be financed by a neutral party. I have several clients that suffer from health problems related to their silicone breast implants. Especially the PIP-implants cause serious harm because of the high rupture rate the PIP implants. Lots of females have silicon substance in their armpit. From the armpit on it appears for several women the silicon substance moves to the neck, the lungs (and lung area hili) and the ventrum and cervix area. I will send some documents by e-mail about this observations.	

			Dokter Nanayakkara from VUMC did research over 80 women: http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/140420/VUmc-waarschuwt-voor-siliconen-borstprothese.htm. He concluded women's health restored after the removal of the implants. Patients organisation www.meldpuntklachtensiliconen.nl is collecting data relating to health problems regarding silicone implants. They have already 500 questionnaires registering health problems regarding silicon breast implants. The Allergan implants in the Netherlands appear to cause the same problems like PIP. I will send some documents by e-mail about this. In my opinion the health incidents with silicone breast implants the Netherlands are quite serious. I think this is related to the regulatory failure by the Dutch Health inspection (IGZ). This is also reported by the commissie Sorgdrager that researched the supervisory practices of IGZ. A special focus was on the PIP-implants. I will send the most important conclusions of this report by e-mail or wetransfer. Incidents are not registered in the Netherlands and not evaluated, what is an obligation regarding article 10 of the medical devices directive.I contacted also the FAGG in Belgium. In my opinion the Belgian authorities are registering incidents far more better than the Netherlands. It appears lots of PIP implants before 2001 are used in the Netherlands, while the CE-mark was first provided in 2001 by TUV. I do not understand which notified body did the conformity assessment before 2001. It appears some illegal implants were used (without a PIP or Rofil stamp, however the females were informed their implants are PIP implans. After removal it appears there is no stamp. This also is seen with the Mentor and Allergan (inamed, Mcghan) implants. It appears to me that breast implants are dumped on the Dutch market because of the regulatory failure. In Europe many companies know about this. It also happened with the meshes and hip-implants.	

Individual *No agreement to disclose personal data*	Disagree	Other	The conclusion that "there is no good evidence that the adverse consequences of a PIP silicone breast implant failure are greater than those resulting from failure of an implant from other manufacturer" is at least questionable. Reliable scientific conclusions should be drawn based on bodies of data reliable to the assumed purposes. The current bodies of data, although highly useful to deduce important information, about development of siliconomas, lymphadenopathy, lumps etc are far to be complete enough to draw such conclusion. Studies have considered these complications. Few observations reported in some of the recent studies cited in the preliminary opinion, and some data from the huge French explantation program, explicitly point to the opposite conclusions. In a study (Beretta, Richards, Malacco 2013) not cited in the preliminary opinion a rational model that explains the massive silicone lymphadenopathies in PIP patients has been described, linking this complication to the non cohesive nature of the PIP gel/shell permeability/silicone-periprosthetic fluid emulsion formation with further diffusion through the breast lymphatic system has been described. Also the conclusion that "there is no indication of a specific association between other effects (…) with PIP silicone breast implants may be misleading. A lack of "visible" association due to lack of data does not necessarily imply that the association does not exist. G. Beretta, M. Malacco. J Pharm Biomed Analysis. 2013; 78-79: 75-82. G. Beretta, A. Richards, M. Malacco. J Pharm Biomed Analysis. 2013; 84: 159-167.	SCENIHRs tried to collect as much data as possible and this opinion is the synthesis of the reported information. No changes to the opinion are required.
Organisation; Other; Adveniunt Medical International Limited; haroon@qualityfirstint.com	Mostly disagree	Other	Please refer to document - Survey answers. Answer 3.	

Organisation; Other; PIP Action Campaign; pip.action.campaign@gmail.com	Disagree	Disagreement with the interpretation of the existing scientific and other data	1. Criminally NON COMPLIANT PIP Implants have failed to meet the essential requirements referred to in Article 3; Article 8; Article 10; Article 14b, Article 15 (6) and ANNEX I ESSENTIAL REQUIREMENTS I. GENERAL REQUIREMENTS of the COUNCIL DIRECTIVE 93/42/EEC http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:EN:PDF	See the reply in the first section (Task 1). No changes to the opinion are required.
			2. INVALID 'equivalence' Scenihr is using 'equivalence' to compare fraudulently manufactured NON COMPLIANT high risk Category III medical devices with COMPLIANT Medical devices as a basis for its opinion.	
			3. VICTIMS & PATIENTS challenges SCENIHR to produce evidence for their assertions.	
			4. PATIENT SAFETY 93/42/EEC risks associated with corrective surgeries EVIDENCE: MHRA (UK) PIP Implant adverse reporting, ANSM (France) published reports, peer-reviewed clinical studies, victims testimonies, PIP Action Campaign Health Survey *202 respondents.	
Individual; Douglas Cross BSc, CSci. CBiol. FSB; doug@ukcaf.org	Uncertain		I am unqualified to provide an opinion	No changes to the opinion are required.
Individual; Marga van Amersfoort; m.g.j.van.amersfoort@hetnet.nl	Uncertain		Members of the Commission. I want to give my opinion as a concerned citizen who had no PIP's but became a victim of other implants after breast cancer. I want to appeal on your morality, not to you as ' scientist, professor, doctor ' but as a human being. What if your wife, girlfriend, mother or the women in the committee itself, would get breast cancer, would you choose breast implants or could you stand behind the choice of your loved ones? Knowing that there are thousands of women which have become sick, women who are	SCENIHR collected available scientific data about breast implants and really regret the incidents after breast reconstruction using implants. SCENIHR sympathizes with women offended by PIP fraud. However, it is out the scope of the committee to produce an opinion on the best way for reconstruction after cancer.

			not recognized worldwide. Some women who first had to enter a fight to survive, amputated, radiation treatments or chemotherapy with all consequences. After the treatment getting a product that ' s reasonable safe ' according to the conflicting science. By your decisions again denied. Would I have chosen 'implants ' after breast cancer if I had gotten fair information? and knew they were forbidden in America, partly because of the siloxanes D4/D5 when I got them!? Would I have set my health at stake for my appearance? Would I have chosen implants, knowing that there are thousands of studies on NBCI/Pubmed that does in fact have other outcomes? Would I have chosen implants at the time, if I had known, that economic interests turn out to go before public health? If so again, "at least" acknowledge that there are women who are / could get sick. Then you can look yourself in the mirror as the future shows that they are unsafe, like asbestos, DES etc.etc. ..... and my answer ... NO ... I definitely had not opted for a 'reasonable' safe product just for appearance (rather than other medical devices which give less pain/quality of life and really are needed). Marga	No changes to the opinion are required.
Organisation; Other; SVS Stichting voor Vrouwen met Siliconenimplantaties; meldpuntklachtensiliconen@hotmail.nl	Uncertain		If there are symptoms, different than those mentioned, these are not recognized, rather denied . This applies to all implants. Because there had 'never' been decent long-term scientific research done, it can't be seen. 492 surveys from all manufacturers showed: Ruptured / leak 44%, total deflated 2%, unknown 54%. Removed After 3 years 16%, after 5 years of 27% after 10 years 52%. At 20 years, 89% had been removed, whilst at implant time the majority of these women heard that this would be "lifetime" devices. 47% reported having had severe capsular contracture	Some sentences in the opinion were modified for better clarity. This issue was addressed in the opinion at the following pages: 11 (section 11), 15 (section 4.1.4), 33, 34 (section 7.2.1), 37, 38 (section 7.2.2) 42 (section 7.2.5), 43, 44 (section 7.3.1), 47 (section 7.3.4), 50 (section 7.3.5).
Individual; Darren Stuart; Darren.stuart@ntlworld.com	Disagree	Relevant scientific and other information missing from the analysis	I disagree that there is a high rupture rate associated with all implant manufacturers, the PIP Implants have been shown to be up to 10 times more likely to rupture. Symptoms of inflammation and irritancy associated with a ruptured PIP implant seem far more severe, the psychological effect caused by the uncertainty of the content of the PIP gel is far worse in PIP patients.	Data to substantiate this statement is needed. See the reply in the first section (Task 1). No changes to the opinion are required.

Organisation; Public authority; BfArM - Federal Institute for Drugs and Medical Devices; medizinprodukte @bfarm.de	Disagree	Disagreement with the interpretation of the existing scientific and other data	With regard to the high rupture/bleeding rates reported to BfArM (see answer to Task 1), the risk of PIP silicone emerging from the implant into the woman's body (due to either rupture of the implant or bleeding through the implant shell) has to be considered to be much higher than in case of comparable high-quality implants. According to advice given to BfArM by German medical societies, a reliable detection of implant failure/bleeding is complicated and in many cases not reliable. It is known that silicone, which has emerged into the body, may lead to adverse local tissue reactions. The silicone may also be transported to other areas of the body and may e.g. be concentrated in the axillary lymph nodes with unclear long-term effects. Above all, adverse local tissue reaction due to rupture and/or bleeding of the PIP implants may complicate or prohibit the implantation of a new implant during the same intervention.	See the reply in the first section (Task 1). No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Mostly disagree	Other	See above re adverse consequences of PIP rupture.	See the reply in the first section (Task 1) No changes to the opinion are required
Individual *No agreement to disclose personal data*	Agree		Agree	No changes to the opinion are required.
Organisation; NGO; European Social Insurance Platform (ESIP ; marina.schmidt @esip.eu	Mostly agree		---	No changes to the opinion are required.

Organisation; Public authority; Medical Products Agency in Sweden; meddevcentral@mpa.se	Mostly disagree	Disagreement with the interpretation of the existing scientific and other data	Three different formulas of PIP silicone gel The Swedish Medical Products Agency (MPA) has shown (SCENIHR ref SMPA2013c), and is confirming the ANSM data (Ref 1), that there are clearly three different formulas of PIP silicone gel. One of the formulas, named "PIP Nusil", is made of the raw material from NuSil Silicone Technology (MED3-6300 part A+B) approved for the use in silicone implants. It is also shown that this PIP Nusil gel has no detectable or very low levels of the cylic siloxanes D4, D5 and D6 just as other approved silicone implants on the market made of the same raw material. For the other two PIP gel formulas MPA agrees with the SCENIHR opinion that the main difference to other silicone implants on the market is the presence of considerably higher levels of cylic siloxanes. Both PIP implants made from PIP Nusil and PIP implants with high levels of cylic siloxanes have been manufactured in parallel at least 2005-2009 (SCENIHR ref SMPA2013c). Failure to discriminate on cyclic siloxanes As the SCENIHR opinion points out (p.9) the question is whether the higher levels of these cyclic siloxanes in the PIP implants could have adverse health consequences for women. To answer this question, in vitro and animal tests with PIP gel as well as clinical studies of women with PIP implants should discriminate on whether implants/gel of PIP Nusil or from PIP with verified high levels of cyclic siloxanes have been used. Studies on PIP gel/implants failing to discriminate on this factor cannot be used to prove whether cyclic siloxanes are irritating/causing inflammation or not since these substances may have been absent or in very low concentrations. Failure to reproduce the results of irritation tests may be due to the failure of verifying the concentration of cyclic siloxanes. This discrimination has not been done except for in a small group of women, with limited data, reported by the MPA (SCENIHR ref; SMPA2013b). In this group 12 of 32 women operated for rupture of PIP implant with D4 in a concentration of 77-134 ppm in the gel had thick opaque miscoloured exudates around the implant with no reported infection, whereas 0 of 8 women operated for rupture of PIP implants made of raw material from Nusil had any such exudates. Women with implants of PIP Nusil are not expected to have any different adverse effects related to the chemical composition of the implant than women with implants made of the same raw material	The new version of the opinion addressed this issue in Chapter 6.

			from other manufacturers. Thus, the question remains whether higher levels of cyclic siloxanes in PIP implants of the other two formulas could have adverse health consequences for women. There is no data to exclude that there may be a dose response relationship. There is no data showing that women with PIP implants with verified higher levels of cyclic siloxanes do not have a higher risk of adverse events compared with implants made of raw material from Nusil or from other approved raw materials, and thereby no clinical data to support the SCENIHR statement (p.30) "It can now be concluded that the silicone used in PIP implants is not irritant" Overall higher risks for PIP implants The MPA agrees with SCENIHR stating "In view of the high rupture rates, many women having PIP breast implants can be expected within their lifetime to experience ruptured implants. There is inevitably a higher intra- and postoperative risk associated with the removal of ruptured implants than with intact implants.", "The overall risk of adverse effects is higher for PIP-implants due to the higher risk of rupture." However, SCENIHR does not present the overall risk assessment made to conclude that "there is currently no convincing medical, toxicological or other data to justify removal of intact PIP implants as a precautionary approach" which is a possible overall risk reducing action. Reference 1: ANSM (2012) Situation update on checking procedures performed by the health authorities on the poly implant prothèse company	
Individual *No agreement to disclose personal data*	Uncertain		??	No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Disagree	Other	Logically, if any implant is not CE compliant it should not be in the human body whether there is evidence of harm or not.	This comment relates to risk management. No changes to the opinion are required.

SUBMISSIONS				SCENIHR'S COMMENTS
Name of individual/ organisation	**Do you agree with the observations made by the Scientific Committees?**	**The nature of disagreement**	**The evidence (s) with the reference(s)**	**SCENIHR's response**
Task 4: Knowledge gap				
Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	3M/McGHAN/INAMED CORPORATIONS (McGhan had zelf grondstoffen en deze geleverd aan Cox Uphoff en Heyer Schulte. Bedrijven sámen onder de vlag van Inamed) http://web.archive.org/web/20040501180235/http://implants.clic.net/tony/Blais/040.html	This falls outside the remit of SCENIHR to consider issues such as criminality and fraud. No changes to the opinion are required.
			AD HOC REGULATION OF HEALTH CARE PRODUCTS IN CANADA http://web.archive.org/web/20040501181631/http://implants.clic.net/tony/Blais/041.html	
			GEL-FILLED MAMMARY IMPLANTS FROM KOKEN CO. LTD. (Japan) http://web.archive.org/web/20040501182332/http://implants.clic.net/tony/Blais/042.html LES LABORATOIRE SEBBIN (FRANCE) http://web.archive.org/web/20040501182535/http://implants.clic.net/tony/Blais/043.html	
			LIPOMATRIX TRILUCENT™ OIL-FILLED PROSTHESES http://web.archive.org/web/20040603071559/http://implants.clic.net/tony/Blais/044.html	
			SALINE INFLATABLE BREAST IMPLANTS http://web.archive.org/web/20040603072743/http://implants.clic.net/tony/Blais/045.html	
			SILASTIC ™ AS A TRADENAME OR AS A GENERIC TERM http://web.archive.org/web/20040603073632/http://implants.clic.net/tony/Blais/046.html	

			SIMAPLAST, KLEIN AND MAMMATECH SALINE-FILLED MAMMARY IMPLANTS Vrijwel onmogelijk om ze steriel te houden http://web.archive.org/web/20040603074226/http://implants.clic.net/tony/Blais/047.html geschiedenis fabrikanten Inamed/ Mcghan/ Dow Corning	
			THE NOVAMED, VITEK AND BIOPLASTY CORPORATIONS http://web.archive.org/web/20040603074746/http://implants.clic.net/tony/Blais/048.html Fraud and misrepresentations in the breast implants trades http://web.archive.org/web/20040603112641/http://implants.clic.net/tony/Blais/049.html FDA – McGhan (costa rica) http://web.archive.org/web/20040616004546/http://implants.clic.net/tony/Blais/050.html McGhan, kibride industrial estate, Ireland Sterilisatie – temperatuur niet bijgehouden, blz 4 http://web.archive.org/web/20040617073411/http://implants.clic.net/tony/Blais/051.html vervolg McGhan Ireland http://web.archive.org/web/20040501181859/http://implants.clic.net/tony/Blais/052.html x VS district court – Mentor (defendants) http://web.archive.org/web/20040603052840/http://implants.clic.net/tony/Blais/053.html vervolg mentor http://web.archive.org/web/20080829000134/http://implants.clic.net/tony/Blais/054.html vervolg mentor http://web.archive.org/web/20081006132034/http://implants.clic.net/tony/Blais/055.html	
Individual; Shanta Marjolein Singh lawyer at Advocatenkantoor Rechtens Advies; info@rechtensadvies.nl	Disagree	Relevant scientific and other information missing from the analysis	I miss the studies by Jan Willen Cohen Tervaert, the studies by Rita Kappel, professor Vernooy and Nanayakkara in the report: http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/140420/VUmc-waarschuwt-voor-siliconen-borstprothese.htm http://link.springer.com/article/10.1007/s00238-013-0914-4 http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCgQFjAA&url=http%3A%2F%2Fwww.inchem.org%2Fdocuments%2Fehc%2Fehc%2Fehc236.pdf&ei=h9vGUvGODYaO0AWaxYCgBQ&usg=AFQjCNEuzgvnUf3S5uDqMkoy2q1oT7df5g&bvm=bv.58187178,d.d2k and the reports on the website www.meldpuntklachtensiliconen.nl or www.svs.nl.	This is outside the remit of SCENIHR to consider issues such as criminality and fraud. No changes to the opinion are required.

			In my opinion environmental studies show serious concerns regarding siclosiloxanes in the shell and the volume material. http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCoQFjAA&url=http%3A%2F%2Foehha.ca.gov%2Fmultimedia%2Fbiomon%2Fpdf%2F1208cyclosiloxanes.pdf&ei=7-DGUue5Ks-10QXKnoHgCw&usg=AFQjCNEXmjjfilly3R_iK8BKz1ufr700ww&bvm=bv.58187178,d.d2k In my opinion such studies should also be done regarding health issues.	
			In my opinion lost of research over silicone material is done and financed by Dow Corning. Dow Corning has a special interest not to be to critical over silicone material, because the still produce this. For this reason I think really independent research over the risks regarding silicones is necessary and should be financed by a neutral party. I have several clients that suffer from health problems related to their silicone breast implants. Especially the PIP-implants cause serious harm because of the high rupture rate the PIP implants. Lots of females have silicon substance in their armpit. From the armpit on it appears for several women the silicon substance moves to the neck, the lungs (and lung area hili) and the ventrum and cervix area. I will send some documents by e-mail about this observations.	
			Dokter Nanayakkara from VUMC did research over 80 women: http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/140420/VUmc-waarschuwt-voor-siliconen-borstprothese.htm. He concluded women's health restored after the removal of the implants.	

			Patients organisation www.meldpuntklachtensiliconen.nl is collecting data relating to health problems regarding silicone implants. They have already 500 questionnaires registering health problems regarding silicon breast implants. The Allergan implants in the Netherlands appear to cause the same problems like PIP. I will send some documents by e-mail about this. In my opinion the health incidents with silicone breast implants the Netherlands are quite serious. I think this is related to the regulatory failure by the Dutch Health inspection (IGZ). This is also reported by the commissie Sorgdrager that researched the supervisory practices of IGZ. A special focus was on the PIP-implants. I will send the most important conclusions of this report by e-mail or wetransfer. Incidents are not registered in the Netherlands and not evaluated, what is an obligation regarding article 10 of the medical devices directive.I contacted also the FAGG in Belgium. In my opinion the Belgian authorities are registering incidents far more better than the Netherlands. It appears lots of PIP implants before 2001 are used in the Netherlands, while the CE-mark was first provided in 2001 by TUV. I do not understand which notified body did the conformity assessment before 2001. It appears some illegal implants were used (without a PIP or Rofil stamp), however the females were informed their implants are PIP implans. After removal it appears there is no stamp. This also is seen with the Mentor and Allergan (inamed, Mcghan) implants. It appears to me that breast implants are dumped on the Dutch market because of the regulatory failure. In Europe many companies know about this. It also happened with the meshes and hip-implants.	
Individual *No agreement to disclose personal data*	Agree		Nothing	No changes to the opinion are required.
Organisation; Other; Adveniunt Medical International Limited ; haroon@qualityfi	Agree		Please refer to document - Extract from Poly Implant Prothèse (PIP) silicone breast implants	The SCENIHR took note of this paper and analysed it carefully. No changes to the opinion are required.

rstint.com				
Organisation; Other; PIP Action Campaign; pip.action.campaign@gmail.com	Disagree	Relevant scientific and other information missing from the analysis	1. Criminally NON COMPLIANT PIP Implants have failed to meet the essential requirements referred to in Article 3; Article 8; Article 10; Article 14b, Article 15 (6) and ANNEX I ESSENTIAL REQUIREMENTS I. GENERAL REQUIREMENTS of the COUNCIL DIRECTIVE 93/42/EEC http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:EN:PDF It is of deep regret to the many thousands of women affected by criminally manufactured PIP implants, that the SCENIHR scientific committee has failed to recognise the significance of the Regulations 93/42/EEC and of NON COMPLIANCE in the criminal fraud of PIP implants.	It is outside the remit of SCENIHR to consider issues such as criminality and fraud. No changes to the opinion are required.
Individual; Douglas Cross BSc, CSci. CBiol. FSB; doug@ukcaf.org	Disagree	Relevant scientific and other information missing from the analysis	This question conflates two entirely different problems. For any high-risk implantable device, strict examination of failed products is essential, to determine the cause, and how such failures may be avoided in the future, This should be carried out by independent laboratories, with the manufacturer being held responsible for the costs. This would introduce a stronger financial incentive to ensure the highest possible quality control of the product during manufacture But when a manufacturer attempts to downgrade the quality of a product to reduce costs, and even resorts to fraud, the current lofty approach to monitoring, in which a cosy, almost casual, relationship may develop between manufacturer and examining body, this inadequacy is totally unacceptable. Only random, unannounced sampling of products, both at the point of manufacture and from the post-production supply chain, before its actual use, by totally independent analytical specialists, can ensure that defective or fraudulent products are removed from the marketplace before they fail and cause harm to recipients. This must be entirely independent of the formal inspection of premises, materials and personnel that the current system imposes, and prior warnings of all inspections must be made a criminal offence.	It is outside the remit of SCENIHR to consider issues such as criminality and fraud. Risk management and activities of notifying bodies is also not in the scope of the committee. No changes to the opinion are required.

			But in addition, a new system must be established, that takes full account of the full range of potential risks arising from the licensing of manufacturers of all high-risk devices. It is therefore a matter of very serious concern that this consultation appears to be mainly aimed at the improvement of policies and practices supporting post-incident monitoring of products. But it seems to virtually ignore the urgent need to improve the precautionary licensing and quality assurance procedures necessary to ensure that the risks of such catastrophic fraudulent non-compliance incidents are prevented. Permitting manufacturers of questionable reputation to supply high-risk devices, whilst of high public concern, appears not to be in issue for SCENIHR There is a clear precedent for such an approach. In the UK, all adults who come into professional contact with children are subject to police security clearance before they may practice. Pre-approval scrutiny of the security records of both Jean-Claude Mas and of his American associate Donald McGhan should have alerted both regulators to potentially increased public risks arising from the licensing of this organisation to manufacture and supply such high-risk devices. But the role of the British regulator, the MHRA, in this fiasco also raises very serious security issues. When these devices were reclassified as high risk devices in 2003, specifically on the petition of both the British and French governments, the existing data on which their former prroduct license was awarded then became subject to review under the new legislation. This created an opportunity - indeed, a legal requirement - for the reappraisal of the product and its supplier at that time. Whilst I have no evidence of misconduct by the French regulator, this process was apparently ignored by the MHRA; the PIP products appear to have been 'nodded through', without ensuring that they were subjected to the required higher level of scrutiny and quality assurance before their use in patients. This was an inexcusable regulatory failure. I consider that the MHRA itself presented just as much a risk to public safety as did the proprietors of the PIP organisation. It has an unsavoury history of failing to act in accordance with European medicinal legislation, and is reported to have refused to accept and analyse samples of defective PIP implants offered to it by the Harley Street Clinic. Its role in this fiasco must therefore be subjected to critical scrutiny, to ensure that it is forced to exert a far greater level	

			of proactive diligence in the scrutiny of medical devices, and of their manufacturers, in the future.	
Individual; Marga van Amersfoort; m.g.j.van.amersfoort@hetnet.nl	Uncertain		As uncertain as confidence in medical science. There are so many studies which show otherwise ... totally ignored. If there were not so many conflicts of interest, studies would have different outcomes. This is what Frank Vasey, MD, learned a lot from the 2000 sick women with mostly, but not exclusively, gel-filled silicone breast implants. wrote So the status quo continues as I approach retirement… Basically, because a definitive study has not been done despite the fact that silicone breast implants have been placed since 1964. That is over 40 years. A 20-year prospective (into the future, not looking back) study of silicone patients and their similar best friends without implants would answer the question of the existence of the syndrome. The fact that a large number of typical symptoms (chronic fatigue, muscle & joint pain, etc.) were statistically worse in women with silicone breast implants over controls who had a breast reduction operation (Fryzeck et al. 2001) does not convince plastic surgeons. Neither does the improvement in symptomatic women post implant removal (Rohrich et al. 2000 & Vasey et al. 1996).	The references mentioned date 2000/2001 and therefore are outside the timeline used by SCENIHR (2012-2013). However, they were considered in the analysis to finalise the opinion. SCENIHR Memorandum of weight of evidence is followed (see footnote page 1). No changes to the opinion are required.
Organisation; Other; SVS Stichting voor Vrouwen met Siliconenimplantaties; meldpuntklachtensiliconen@hotmail.nl	Uncertain		How one character and different search terms changes the outcomes and 'reasonable' safe doesn't seem so safe anymore Asia OR shoenfeld OR Silicone induced AND breast implants results 248 studies fibromatosis OR desmoid AND breast implants results 22 studies lymphoma AND breast implants results 104 studies ALCL AND breast implants results 31 studies T cells OR macrophages AND breast implants results 95 studies Giant cell AND breast implants results 51 studies Autoimmune disease AND breast implants	SCENIHR Memorandum is followed in considering literature references. For many issues references outside the period of this opinion are provided (2012-2013). No changes to the opinion are required.

			results 227 studies	
			Autoimmune diseases AND breast implants results 206 studies	
			Immune disease AND breast implants results 342 studies	
			Immune diseases AND breast implants results 335 studies	
			Siliconoma OR granuloma AND breast implants results 125 studies	
			In 1992 Vojdani A, Campbell A, Brautbar N. wrote: Immune functional impairment in patients with clinical abnormalities and silicone breast implants.	
			Our findings here show definite abnormalities of the T helper/suppressor ratio, increased autoimmunity, as well as increased production of immune complexes. Silicone implants have been used in cosmetic and reconstructive surgery more than 30 years (Brown et al., 1960).	
			In 1994 Ojo-Amaize EA, Conte V, Lin HC, Brucker RF, Agopian MS, Peter JB. wrote: Silicone-specific blood lymphocyte response in women with silicone breast implants	
			Our data demonstrating that CD4 T cells are the target cells for silicone are consistent with previous reports on the involvement of CD4 T celles in the immune response against a related light metal, beryllium. In conclusion the silicone specific T cell proliferation test compared with a silicon-specific anti body test is less cumbersome to perform is more specific and sensitive and permits the gathering of information on an individual's cellular abnormal reaction to either elemental silicon SiO, or silicone gel.	
			In 2013 Kellogg BC, Hiro ME, Payne WG. wrote: Implant-Associated Anaplastic Large Cell Lymphoma: Beyond Breast Prostheses.	
			Anaplastic large cell lymphoma (ALCL) is a rare form of non-Hodgkin T-cell lymphoma potentially associated with silicone-shelled breast implants.	

			Whether low doses of EDCs influence certain human disorders is no longer conjecture, because epidemiological studies show that environmental exposures to EDCs are associated with human diseases and disabilities. We conclude that when nonmonotonic dose-response curves occur, the effects of low doses cannot be predicted by the effects observed at high doses. Thus, fundamental changes in chemical testing and safety determination are needed to protect human health.	
Individual; Darren Stuart; Darren.stuart@ntlworld.com	Agree		This should allow retrospective recording back to the year 2000 where documentation is available, all patients with PIP Implants should be able to record their details and any symptoms. This should be set up urgently and widely publicised in the European press, without a significant ongoing monitoring programme the long term effects of the PIP gel may never be known. There should be major improvements in the surveillance of products with unannounced inspections to verify standards are being maintained. This whole situation has revealed the need to review the CE licencing process to ensure confidence in the mark remains.	This issue has been already considered in the opinion (see section 4.3.3). A registry has been recommended by SCENIHR. No changes to the opinion are required.
Organisation; Public authority; BfArM - Federal Institute for Drugs and Medical Devices; medizinprodukte@bfarm.de	Agree		BfArM shares the view of SCENIHR that a breast implant registry could be very relevant.	No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Agree		Agree there needs to be an implant registery	No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Agree		agree	No changes to the opinion are required.

Organisation; NGO; European Social Insurance Platform (ESIP ; marina.schmidt@esip.eu	Mostly disagree	Other	We disagree with the observations of the committee regarding "recommendations for further work" to close knowledge gaps. These recommendations fall too short, as they focus solely on registration systems and post hoc assessments and explant analysis. We think a strong postmarket surveillance system of breast implants which really improves patient safety would include the following aspects:	Risk management is out of the scope of SCENIHR. These suggestions will be passed to competent Commission's Department. No changes to the opinion are required.
			1. A website listing all products available on the European market, together with product-specific labels that address the risks and benefits, known side-effects etc. of each product. The labels must be in separate formats for patients and doctors. Additionally, the safety and effectiveness data (pre-clinical, mechanic tests, clinical data) must be published on this site, together with a published letter of the responsible notified body stating the certification conditions (e. g. approved postmarket clinical follow-up plan, PMCF). At present it is even impossible to get reliable information about how many different breast implant products of which manufacturers are currently marketed in the member states. Evidence for the value of this information can be obtained from the U. S. Food and Drug Administration: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm063871.htm (Site lists all breast implant products currently available on the U. S. market) http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm354927.htm (Example for product-specific information: Product label (short and long version) for patients, product label for physicians, product-specific summary of safety and effectiveness data, consumer information, approval letter, post-approval studies).	See the comment above about risk management.

			2. Reliable, manufacturer-sponsored, prospectively planned clinical trials with long-term observations of implanted products, to assess long-term local complications (e.g., capsular contracture, re-operation, removal of implant, implant rupture) and less common potential disease outcomes (e.g., rheumatoid arthritis, breast and lung cancer, reproductive complications). Such trials (which usually include several thousands of patients) are mandatory post-approval in the US. Evidence for the value of this information can be obtained from the U. S. Food and Drug Administration: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm (For information about post approval breast implant studies e.g. scroll to P020056, P040046, P060028, P030053). http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/UCM260090.pdf (Update on safety of silicone breast implants, including preliminary results of post approval studies for implants of Allergan and Mentor).	
			3. An independent, EU-wide patient info addressing general and universal information about risks and benefits of breast implants, implication of side-effects, and cosmetic outcomes of potentially necessary explantations. At present, e. g. the MHRA offers a patient info about breast implants, while e. g. the German agency BfArM does not. We think it would be appropriate to offer this information in a barrier-free format for patients and people interested in cosmetic surgery. The information should be posted on the websites of the authorities of the member states; and the medical facilities offering the product should be obliged to hold printouts of this information available. A valuable example for patient information can be obtained from the U. S. Food and Drug Administration: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm259296.htm (Understandable language, possible outcomes illustrated with photographs, summary of “things to consider”, info available in a booklet format).	

Organisation; Public authority; Medical Products Agency in Sweden; meddevcentral@mpa.se	Mostly disagree	Other	Please see comments on Task 2 and Task 3.	See comments in previous sections. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Uncertain		Please kontact Klinisk utredare, Specialistläkare Enheten för Medicinteknik Box 26, 751 03 Uppsala Besöksadress: Dag Hammarskjölds väg 42 www.lakemedelsverket.se I am so sick and have so high level od D4 in my body.	See comments in previous sections. No changes to the opinion are required.
Individual *No agreement to disclose personal data*	Agree		Any implant for use in the the human body shall be CE marked, used on prescription only and and shall be registered on a national basis with Central European reporting of complications.	Risk management statements. No changes to the opinion are required.

SUBMISSIONS				SCENIHR'S COMMENTS
Name of individual/ organisation	**Do you agree with the observations made by the Scientific Committees?**	**The nature of disagreement**	**The evidence (s) with the reference(s)**	**SCENIHR's response**
Comments received via email				
Organisation; Other; SVS Stichting voor Vrouwen met Siliconenimplantaties; meldpuntklachtensiliconen@hotmail.nl			Silicone gel-filled breast and testicular implant capsules: a histologic and immunophenotypic study Conflict of interest Dow Corning, studies octamethylcyclotetrasiloxane D4 Induction of type II collagen arthritis in the DA rat using silicone gels and oils as adjuvant, J Autoimmun. 1995 Oct;8(5):751-61., Naim JO, Ippolito KM, Lanzafame RJ, van Oss CJ The effect of molecular weight and gel preparation on humoral adjuvancy of silicone oils and silicone gels. , Immunol Invest. 1995 Mar;24(3):537-47, Naim JO, Ippolito KM, Lanzafame RJ The adjuvancy of silicones: dependency on compartmentalization, Curr Top Microbiol Immunol. 1996;210:113-21, Klykken PC, White KL Jr Silicone gel and octamethylcyclotetrasiloxane potentiate antibody production to bovine serum albumin in mice., Curr Top Microbiol Immunol. 1996;210:139-44, Nicholson JJ 3rd, Wong GE, Frondoza CG, Rose NR	SCENIHR Memorandum is followed in considering literature references. For many issues references outside the period of this opinion are provided (2012-2013). No changes to the opinion are required.

			Cytotoxicity and membrane damage in vitro by inclusion complexes between gamma-cyclodextrin and siloxanes.	
			Curr Top Microbiol Immunol. 1996;210:93-9.	
			Felix K, Janz S, Pitha J, Williams JA, Mushinski EB, Bornkamm GW, Potter M.	
			Silicone gel and octamethylcyclotetrasiloxane (D4) enhances antibody production to bovine serum albumin in mice.	
			J Biomed Mater Res. 1996 Jul;31(3):345-53.	
			Nicholson JJ 3rd, Hill SL, Frondoza CG, Rose NR.	
			Protein denaturation induced by cyclic silicone.	
			Biomaterials. 1997 Dec;18(24):1593-7.	
			Sun L, Alexander H, Lattarulo N, Blumenthal NC, Ricci JL, Chen G	
			Extraction of octamethylcyclotetrasiloxane and its metabolites from biological matrices.	
			Anal Biochem. 1998 Feb 1;256(1):14-22.	
			Varaprath S, Salyers KL, Plotzke KP, Nanavati S.	
			Low molecular weight silicones are widely distributed after a single subcutaneous injection in mice.	
			Am J Pathol. 1998 Mar;152(3):645-9.	
			Kala SV, Lykissa ED, Neely MW, Lieberman MW	
			Evaluation of octamethylcyclotetrasiloxane (D4) as an inducer of rat hepatic microsomal cytochrome P450, UDP-glucuronosyltransferase, and epoxide hydrolase: a 28-day inhalation study.	
			Toxicol Sci. 1998 Jan;41(1):29-41.	
			McKim JM Jr, Wilga PC, Kolesar GB, Choudhuri S, Madan A, Dochterman LW, Breen JG, Parkinson A, Mast RW, Meeks RG.	
			Quantitative exposure of humans to an octamethylcyclotetrasiloxane (D4) vapor.	
			Toxicol Sci. 1998 Aug;44(2):206-13.	

			Utell MJ, Gelein R, Yu CP, Kenaga C, Geigel E, Torres A, Chalupa D, Gibb FR, Speers DM, Mast RW, Morrow PE	
			Acute respiratory exposure of human volunteers to octamethylcyclotetrasiloxane (D4): absence of immunological effects.	
			Toxicol Sci. 1998 Aug;44(2):214-20	
			Looney RJ,Frampton MW, Byam J,Kenaga C,Speers DM, Cox C,Mast R,Klykken PC, Morrow PE,Utell MJ	
			Cyclosiloxanes produce fatal liver and lung damage in mice.	
			Environ Health Perspect. 1999 Feb;107(2):161-5.	
			Lieberman MW, Lykissa ED, Barrios R, Ou CN, Kala G, Kala SV.	
			Identification of metabolites of octamethylcyclotetrasiloxane (D(4)) in rat urine.	
			Drug Metab Dispos. 1999 Nov;27(11):1267-73.	
			Varaprath S, Salyers KL, Plotzke KP, Nanavati S.	
			Toxicology and humoral immunity assessment of octamethylcyclotetrasiloxane (D4) following a 28-day whole body vapor inhalation exposure in Fischer 344 rats.	
			Drug Chem Toxicol. 1999 Nov;22(4):655-77.	
			Klykken PC, Galbraith TW, Kolesar GB, Jean PA, Woolhiser MR, Elwell MR, Burns-Naas LA, Mast RW, McCay JA, White KL Jr, Munson AE.	
			Genetic toxicity evaluation of octamethylcyclotetrasiloxane.	
			Environ Mol Mutagen. 2000;36(1):13-21.	
			Vergnes JS, Jung R, Thakur AK, Barfknecht TR, Reynolds V	
			Repeated inhalation exposure to octamethylcyclotetrasiloxane produces hepatomegaly, transient hepatic hyperplasia, and sustained hypertrophy in female Fischer 344 rats in a manner similar to phenobarbital.	
			Toxicol Appl Pharmacol. 2001 Apr 15;172(2):83-92.	
			McKim JM Jr, Kolesar GB, Jean PA, Meeker LS, Wilga PC, Schoonhoven R, Swenberg JA, Goodman JI, Gallavan RH, Meeks RG.	

			Potential estrogenic and antiestrogenic activity of the cyclic siloxane octamethylcyclotetrasiloxane (D4) and the linear siloxane hexamethyldisiloxane (HMDS) in immature rats using the uterotrophic assay.	
			Toxicol Sci. 2001 Sep;63(1):37-46.	
			McKim JM Jr, Wilga PC, Breslin WJ, Plotzke KP, Gallavan RH, Meeks RG.	
			The transport of octamethylcyclotetrasiloxane (D4) and polydimethylsiloxane (PDMS) in lightly cross-linked silicone rubber.	
			This suggests that the permeation of D4 out of any encapsulation device, such as a silicone breast implant, is linearly dependent upon the concentration of D4 in the prosthesis. Swelling is isotropic and was measured by dimensional changes in rectangular samples and correlates well with the volume of D4 sorbed.	
			J Biomater Sci Polym Ed. 2001;12(7):801-15.	
			Wolf CJ, Jerina KL, Brandon HJ, Young VL.	
			Bioavailability of octamethylcyclotetrasiloxane (D(4)) after exposure to silicones by inhalation and implantation.	
			Environ Health Perspect. 2001 Nov;109(11):1095-101.	
			Luu HM, Hutter JC.	
			Read also comments from Dow Cornings authors below	
			Inhalation toxicology of octamethylcyclotetrasiloxane (D4) following a 3-month nose-only exposure in Fischer 344 rats. , Int J Toxicol. 2002 Jan-Feb;21(1):39-53.	
			Inhalation toxicology of octamethylcyclotetrasiloxane (D4) following a 3-month nose-only exposure in Fischer 344 rats.	
			Int J Toxicol. 2002 Jan-Feb;21(1):39-53.	
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			J Biomater Sci Polym Ed. 2002;13(1):27-41.	

			Wolf CJ, Jerina KL, Brandon HJ, Young VL.	
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			Skin Pharmacol Appl Skin Physiol. 2002 May-Jun;15(3):184-94.	
			Zareba G, Gelein R, Morrow PE, Utell MJ.	
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			Environ Health Perspect. 2002 August; 110(8): A442–A448.	
			Robert G Meeks letter	
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			Environ Health Perspect. 2002 Aug;110(8):A444-5; author reply A445-8.	
			Andersen ME, Dobrev ID, Reddy MB, Sarangapani R, Reitz RH, Plotzke KP.	
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			Toxicol Sci. 2003 Jan;71(1):41-52.	
			Sarangapani R, Teeguarden J, Andersen ME, Reitz RH, Plotzke KP.	
			Determination of siloxanes, silicon, and platinum in tissues of women with silicone gel-filled implants.	
			Anal Bioanal Chem. 2003 Feb;375(3):356-62. Epub 2003 Jan 28.	
			Flassbeck D, Pfleiderer B, Klemens P, Heumann KG, Eltze E, Hirner AV.	
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			Toxicol Sci. 2003 Mar;72(1):1-2.	
			Fisher JW.	

			Physiological modeling of inhalation kinetics of octamethylcyclotetrasiloxane in humans during rest and exercise.	
			Toxicol Sci. 2003 Mar;72(1):3-18.	
			Reddy MB, Andersen ME, Morrow PE, Dobrev ID, Varaprath S, Plotzke KP, Utell MJ.	
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			Toxicol Appl Pharmacol. 2003 Nov 1;192(3):254-61.	
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			In vitro and in vivo evaluation of the estrogenic, androgenic, and progestagenic potential of two cyclic siloxanes.	
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			Quinn AL, Regan JM, Tobin JM, Marinik BJ, McMahon JM, McNett DA, Sushynski CM, Crofoot SD, Jean PA, Plotzke KP.	
			A two-generation reproductive toxicity study of octamethylcyclotetrasiloxane (D4) in rats exposed by whole-body vapor inhalation.	
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			Reprod Toxicol. 2007 Jun;23(4):532-40. Epub 2007 Mar 2.	
			Quinn AL, Dalu A, Meeker LS, Jean PA, Meeks RG, Crissman JW, Gallavan RH Jr, Plotzke KP.	

			Physiologically based pharmacokinetic modeling of the disposition of octamethylcyclotetrasiloxane (D4) migration from implants in humans.	
			J Long Term Eff Med Implants. 2008;18(2):133-44.	
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			Regul Toxicol Pharmacol. 2008 Mar;50(2):239-48. doi: 10.1016/j.yrtph.2007.11.003. Epub 2007 Nov 22.	
			Jovanovic ML, McMahon JM, McNett DA, Tobin JM, Plotzke KP.	
			Assessing kinetic determinants for metabolism and oral uptake of octamethylcyclotetrasiloxane (D4) from inhalation chamber studies.	
			Inhal Toxicol. 2008 Feb;20(4):361-73. doi: 10.1080/08958370801903743	
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			Toxicol Lett. 2008 Jun 30;179(2):85-92. doi: 10.1016/j.toxlet.2008.04.007. Epub 2008 Apr 22.	
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			Environ Int. 2013 Jan;51:82-7. doi: 10.1016/j.envint.2012.10.008. Epub 2012 Nov 28.	
			Hanssen L, Warner NA, Braathen T, Odland JØ, Lund E, Nieboer E, Sandanger TM.	
			in total 110 studies NBCI/pubmed Rest is about enviroment.	
			Studies decamethylcyclopentasiloxane (D5)	
			Low molecular weight silicones are widely distributed after a single subcutaneous injection in mice.	

			Am J Pathol. 1998 Mar;152(3):645-9.	
			Kala SV, Lykissa ED, Neely MW, Lieberman MW.	
			Toxicology and humoral immunity assessment of decamethylcyclopentasiloxane (D5) following a 1-month whole body inhalation exposure in Fischer 344 rats.	
			Toxicol Sci. 1998 May;43(1):28-38.	
			Burns-Naas LA, Mast RW, Klykken PC, McCay JA, White KL Jr, Mann PC, Naas DJ.	
			Inhalation toxicology of decamethylcyclopentasiloxane (D5) following a 3-month nose-only exposure in Fischer 344 rats.	
			Toxicol Sci. 1998 Jun;43(2):230-40.	
			Burns-Naas LA, Mast RW, Meeks RG, Mann PC, Thevenaz P.	
			Cyclosiloxanes produce fatal liver and lung damage in mice.	
			Environ Health Perspect. 1999 Feb;107(2):161-5.	
			Lieberman MW, Lykissa ED, Barrios R, Ou CN, Kala G, Kala SV.	
			Induction of hepatic xenobiotic metabolizing enzymes in female Fischer-344 rats following repeated inhalation exposure to decamethylcyclopentasiloxane (D5).	
			Toxicol Sci. 1999 Jul;50(1):10-9.	
			McKim JM Jr, Choudhuri S, Wilga PC, Madan A, Burns-Naas LA, Gallavan RH, Mast RW, Naas DJ, Parkinson A, Meeks RG.	
			Toxicology and humoral immunity assessment of octamethylcyclotetrasiloxane (D4) following a 28-day whole body vapor inhalation exposure in Fischer 344 rats.	
			Drug Chem Toxicol. 1999 Nov;22(4):655-77.	
			Klykken PC, Galbraith TW, Kolesar GB, Jean PA, Woolhiser MR, Elwell MR, Burns-Naas LA, Mast RW, McCay JA, White KL Jr, Munson AE.	
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			Determination of low molecular weight silicones in plasma and blood of women after exposure to silicone breast implants by GC/MS.	
			Anal Chem. 2001 Feb 1;73(3):606-11.	
			Flassbeck D, Pfleiderer B, Grümping R, Hirner AV.	
			Metabolites of hexamethyldisiloxane and decamethylcyclopentasiloxane in Fischer 344 rat urine--a comparison of a linear and a cyclic siloxane.	
			Drug Metab Dispos. 2003 Feb;31(2):206-14.	
			Varaprath S, McMahon JM, Plotzke KP.	
			Determination of siloxanes, silicon, and platinum in tissues of women with silicone gel-filled implants.	
			Anal Bioanal Chem. 2003 Feb;375(3):356-62. Epub 2003 Jan 28.	
			Flassbeck D, Pfleiderer B, Klemens P, Heumann KG, Eltze E, Hirner AV.	
			The measurement of conformational stability of proteins adsorbed on siloxanes.	
			J Biomater Sci Polym Ed. 2003;14(2):103-18.	
			Prokopowicz M, Banecki B, Lukasiak J, Przyjazny A.	
			Highly activated, silicone entrapped, lipase.	
			Chem Commun (Camb). 2003 Sep 21;(18):2314-5.	
			Ragheb A, Brook MA, Hrynyk M.	
			A two-generation reproductive toxicity study of decamethylcyclopentasiloxane (D5) in rats exposed by whole-body vapor inhalation.	
			Reprod Toxicol. 2007 Feb;23(2):216-25. Epub 2006 Nov 18	
			Siddiqui WH, Stump DG, Reynolds VL, Plotzke KP, Holson JF, Meeks RG.	
			In vitro and in vivo evaluation of the estrogenic, androgenic, and progestagenic potential of two cyclic siloxanes.	
			Toxicol Sci. 2007 Mar;96(1):145-53. Epub 2006 Dec 14.	

			Quinn AL, Regan JM, Tobin JM, Marinik BJ, McMahon JM, McNett DA, Sushynski CM, Crofoot SD, Jean PA, Plotzke KP.	
			Modeling of human dermal absorption of octamethylcyclotetrasiloxane (D(4)) and decamethylcyclopentasiloxane (D(5)).	
			Toxicol Sci. 2007 Oct;99(2):422-31. Epub 2007 Jul 14	
			Reddy MB, Looney RJ, Utell MJ, Plotzke KP, Andersen ME.	
			In vitro and in vivo percutaneous absorption of 14C-octamethylcyclotetrasiloxane (14C-D4) and 14C-decamethylcyclopentasiloxane (14C-D5).	
			Regul Toxicol Pharmacol. 2008 Mar;50(2):239-48. doi: 10.1016/j.yrtph.2007.11.003. Epub 2007 Nov 22.	
			Jovanovic ML, McMahon JM, McNett DA, Tobin JM, Plotzke KP.	
			Disposition of decamethylcyclopentasiloxane in Fischer 344 rats following single or repeated inhalation exposure to 14C-decamethylcyclopentasiloxane (14C-D5).	
			Inhal Toxicol. 2008 Mar;20(5):513-31. doi: 10.1080/08958370801935075 .	
			Tobin JM, McNett DA, Durham JA, Plotzke KP.	
			Survey of organosilicone compounds, including cyclic and linear siloxanes, in personal-care and household products.	
			Arch Environ Contam Toxicol. 2008 Nov;55(4):701-10. doi: 10.1007/s00244-008-9172-z. Epub 2008 Apr 29.	
			Horii Y, Kannan K.	
			Inhalation dosimetry modeling with decamethylcyclopentasiloxane in rats and humans.	
			Toxicol Sci. 2008 Oct;105(2):275-85. doi: 10.1093/toxsci/kfn125. Epub 2008 Jun 26.	
			Reddy MB, Dobrev ID, McNett DA, Tobin JM, Utell MJ, Morrow PE, Domoradzki JY, Plotzke KP, Andersen ME.	
			Low molecular weight cyclic volatile methylsiloxanes in cosmetic products sold in Canada: implication for dermal exposure.	

			Environ Int. 2009 Aug;35(6):900-4. doi: 10.1016/j.envint.2009.03.009. Epub 2009 Apr 10.	
			Wang R, Moody RP, Koniecki D, Zhu J.	
			In total there were 73 studies about D5 not mentioned were the studies about enviroment.	
			http://oehha.ca.gov/multimedia/biomon/pdf/1208cyclosiloxanes.pdf	
Organisation, CES – Silicones Europe Cefic (AISBL) -The European Chemical Industry Council			I am writing on behalf of CES – Silicones Europe concerning the public consultation on the SCENIHR preliminary opinion on "The safety of Poly Implant Prothèse (PIP) Silicone Breast Implants (2013 update)". CES – Silicones Europe is a non-profit trade organisation, sector group of the European Chemical Industry Council (Cefic) representing all major producers of silicones in Europe. Given the scope of the opinion and CES area of expertise, the report section dealing with the properties of the cyclics siloxanes, i.e. D4, D5 and D6 is the most relevant for CES members. Further to our experts analysis, CES would like to highlight the following imprecision in section 6.4.4 Chronic toxicity and carcinogenicity studies – Paragraph on D5 – Page 29: Endometrial adenomatous polyps and adenocarcinomas were observed in rats given D5 orally for one year followed by one year of recovery (Dow 2005). To our knowledge there is no 2a oral study with D5 and it looks like an inhalation study might have been mis-described. In our opinion, the relevant section of the report should be edited to correct this inaccuracy.	These comments were taken into account. Modification included at Page 29 in the final opinion.

			Please find below some specific comments on the statement in section 6.4.4 Chronic toxicity and carcinogenicity studies – Paragraph on D5 – Page 29: Endometrial adenomatous polyps and adenocarcinomas were observed in rats given D5 orally for one year followed by one year of recovery (Dow 2005): I. The study was conducted by the inhaled route, not oral II. The study comprised of groups that were administered D5 for 1 year, or 1 year followed by 1 year recovery, or for 2 years. Based a brief review of the results of that study the endometrial findings were only noted in the group of animals administered D5 by the inhaled route for 2 years, not 1 year plus 1 year recovery as currently stated III. The reference to the study (Dow 2005) does not appear in the reference section at the end of the document.	
Organisation, The Swedish Medical Products Agency (MPA)			The Swedish Medical Products Agency (MPA) has submitted comments in the web based template (IPM reference number: 480176929491434713) on the Preliminary Opinion on the safety of Poly Implant Prothèse (PIP) Silicone Breast Implants (2013 update) September 2013. Apart from references already listed in the SCENIHR opinion, the MPA is referring to: 1: ANSM (2012) Situation update on checking procedures performed by the health authorities on the poly implant prothèse company. This is published on the ANSM website (2013-12-09): http://ansm.sante.fr/var/ansm_site/storage/original/application/e044aa9eb27fc2eca49b93165c9020ae.pdf Please also find the document attached. On behalf of the Medical Products Agency	Please see the updated list of references.