Results of the public consultation on
SCENIHR’s preliminary Opinion on the safety of surgical meshes used in urogynaecological surgery

A public consultation on this Opinion was opened on the website of the scientific committees from 12 June 2015 to 19 July 2015. Information about the public consultation was broadly communicated to national authorities, international organisations and other stakeholders.

52 organisations and individuals (providing in total 178 comments) participated in the public consultation providing input to different chapters and subchapters of the Opinion. Among the organisations participating in the consultation, there were universities, professional associations, institutes of public health, industry representatives and NGOs.

Comments received during this time have been considered carefully by the SCENIHR. Where appropriate, the text of the relevant sections of the opinion has been modified or explanations have been added to take account of relevant comments. The literature has been accordingly updated with relevant publications. The scientific rationale and the opinion section were clarified and strengthened. In the cases where the SCENIHR, after consideration and discussion of the comments, has decided to maintain its initial views, the opinion (or the section concerned) has remained unchanged.

The SCENIHR thank all contributors for their comments and for the references provided during the public consultation.

The table below shows all comments received on different chapters of 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 surgical meshes used in urogynaecological surgery"

<table>
<thead>
<tr>
<th>No</th>
<th>Name of individual /organisation</th>
<th>Table of content to which comment refers</th>
<th>Submission</th>
<th>Additional documents submitted by contributors</th>
<th>SCENIHR response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>BALZARRO MATTEO, AOUI VERONA, <a href="mailto:matteo.balzarro@ospedaleuniverona.it">matteo.balzarro@ospedaleuniverona.it</a>, Italy</td>
<td>ABSTRACT</td>
<td>We agree with the SCENIHR recommends limiting the amount of meshes for all procedures where possible. Moreover, the use of synthetic meshes for POP repair via a transvaginal route should only be used when other surgical procedures have already failed or are expected to fail.</td>
<td>SCENIHR agrees with the comment, No changes to the Opinion are required.</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>BALZARRO MATTEO, AOUI VERONA, <a href="mailto:matteo.balzarro@ospedaleuniverona.it">matteo.balzarro@ospedaleuniverona.it</a>, Italy</td>
<td>ABSTRACT</td>
<td>Any recommendation on the learning curve is supported by low level of evidence (LE4) and sparse data from the Literature.</td>
<td>Learning curve is a well-known overarching issue. No changes to the Opinion are required.</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Ras Adri, <a href="mailto:adri.admara@gmail.com">adri.admara@gmail.com</a>, Netherlands</td>
<td>ABSTRACT</td>
<td>Het implanteren van mesh voor behandeling van verzakking mag niet worden overwogen,dient te worden verboden. De risico's van mesh die niet meer verwijderbaar is zijn te gevaarlijk en veroorzaken meer en ernstigere lichamelijke klachten dan de eerst bestaande verzakkingsklachten met alle gevolgen van dien. Door krimp van de mesh uiten deze gevolgen zich voor mij in: 1.Recidive enterocele “oplossing” mesh heeft niet geleid tot opheffing eerder bestaande klacht. 2. Ondraaglijke pijn waardoor veroordeeld tot herhaalde pijnblokkades op OK en langdurig/levenslang gebruik sterk verdovende pijnstilling waaronder verschillende soorten opiaten. Met alle bijwerkingen en beperkingen die deze geven. (autorijden b.v. niet meer mogelijk) 3. Zenuwbeschadiging. (pudendus) waaronder Unintended side effects have been addressed in the Opinion. No changes to the Opinion are required.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

verstoringen in blaas en darm waaronder pijnlijke lozing en wisseling in incontinentie en obstipatie en seksuele activiteit. 4. Sterke beperkingen in zitten, beperking in langdurig staan en lopen/ traplopen. 5. Beperkingen in tillen, bukken, duwen en alle bewegingen die druk geven op de buik en het bekkenbodemgebied. 6. Daarnaast nog door beperkingen kwijtraken van betaalde baan en inkomsten en beperkingen in uitoefenen eigen hobby’s en sociale activiteiten.

4. Sterk Thecla, Eucomed, thecla.sterk@eucomed.org, Belgium

<table>
<thead>
<tr>
<th>ABSTRACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eucomed welcomes the SCENIHR’s preliminary Opinion on “The safety of surgical meshes used in urogynecological surgery” and would like to offer the following comments to the Committee for consideration. From a practical point of view, it is important to clearly define from the beginning the methodology used to carry out this assessment including a description of the selection process of the experts consulted. Specifically for the literature search methodology, we would recommend the following: 1. Describe and list search terms used so that an independent entity would be able to use the same methodology and reproduce the outputs of the search 2. Medline was the only search database used. Consider using others to ensure the most thorough search for appropriate articles 3. Define how literature was selected. What were the inclusion and exclusion criteria? 4. What was the Level of Evidence of the articles selected? 5. Provide a flow diagram of articles obtain with the selected search terms and then the decisions made to eliminate articles down to the final bibliography Consideration on surgical techniques should also be considered throughout the Opinion as this could have an impact on the potential health risks of meshes used in urogynaecological surgery. To provide a balanced Opinion, we</td>
</tr>
</tbody>
</table>

The comment has been considered and the respective changes in the Opinion have been made.
would also welcome an analysis of the benefits associated with the use of meshes, including the benefits of POP repair, in urogynaecological surgery and not only to the risks associated with these devices. It would appear that the abstract bears the hallmark of British, French and Australian surgeons and often stands in contradiction to the interdisciplinary D-A-CH guidelines. As a result, relationships that can still be found in detail in the text will be scored differently in the summary. In the abstract, therefore, conclusions are sometimes drawn which are not always related to the data. It is also not worked out that there are a variety of meshes and technologies, which are / were used by different surgeons on different patients, resulting in differences in the results. The advantages of modern mesh surgery, which can be found in the latest D-A-CH-guideline as well as the view that in certain situations not implanting a surgical mesh would be far more detrimental to the health of the patient in certain situations, is not included. Lastly, we believe that the MHRA's guidelines on the benefits and risks of vaginal mesh implants may be a useful source of information as it provides a good overview.

5. JACQUETIN Bernard, OBGYN department-Estaing University Hospital-Clermont-Ferrand FRANCE, bjacquetin@chu-clermontferrand.fr, France

ABSTRACT

- ABSTRACT:
  o P.4: "colposuspension is associated with greater surgical morbidity" is not at a good place in the transvaginal surgery chapter.
  o P.5: do you confirm “or are expected to fail” (See above)

1. EXECUTIVE SUMMARY:

P.7, L.41: the Directive 93/42/EEC (including amendment 2007/47/EC) (also mentioned P. 17 etc.. ) in not provided in Annex
o P.8, L. 17: add "or are expected to fail" (see above)

The comments have been considered and the Opinion was changed as follows:

ABSTRACT:

p. 4: SCENIHR agrees with the comment. The text has been changed accordingly.

p5: No changes in the Opinion are required

1. EXECUTIVE SUMMARY:

The reference has been added and the reference list has been updated.
Taking into account the lack of long term data...” and P.11, L.29-30: “establish scientific studies to assess the long term (at least 5 years) safety and performance...”; I understand very well the interest of the long term studies...so why don’t mention them, particularly the two prospective and parallel studies performed by the French TVM group and the US Miller D. et al group? I will come back on this criticism.

4. SCIENTIFIC RATIONALE:
- P.17, L.25: concerning the national standard in France (AFNOR S94-801), it’s inaccurate to mention “for stress urinary incontinence”; this norm is dedicated to SUI and/or POP (see slide 1, inner part).
- P.29, L.22: please add pore...“mesh PORE size”
- P.31, L.1-3: the Figure 1 is not understandable: 7 different meshes are mentioned but only 4 curves are on the graph?
- P.33, L.15-34: it’s a good synthesis of the host response to implanted biomaterials.
- P.34, L.15: the sentence is incomplete
- P.34, L.24: correct “bowel INJURY”
- P.34, L.41: be careful with the abbreviation SIS, used in the text with two different meanings: “Single Incision Slings” and “Small Intestine Submucosa”.
- P.51, L.18: I cannot understand why and how, in a multiple compartment repair (according to Table 3) including anterior AND posterior mesh, there are de novo POP in untreated compartments?
- P.51, L.23-24: I agree totally with the lack of long term results of RCT; it’s a very important weak point well illustrated in this paper from OU et al (Ou R, Xie XJ, Zimmern PE: Prolapse follow-up at 5 years or more: myth or reality? Urology 2011, 78:295-299.)
- P.52, L.36-40 and P.53, L.1-19: I don’t understand at all, in the UK guidelines, the...
reason and the interest of this long chapter about infracoccygeal sacropexy, compared to other guidelines (US, Dutch, French...) only quoted; I will come back later (P. 59) on the UK's recommendations.

o P.55, L.8: could you clarify the meaning of “decade”: 10 days, 10 years or 10 operations?

o P.55, L.30: clarify this Error!

o P.58-60: Risk assessment and recommendations by National Associations: Important comments about French recommendations (erroneous!) and UK recommendations (NOT mentioned!)

§ P.58, L.35-40 and P.59, L.1-3: I disagree totally with the abstract of the French National Authority for Health (HAS), particularly the point 3) “the use of polypropylene meshes for POP surgery by vaginal route was not recommended”. In 2006 the HAS conclusion was “vaginal meshes are in the field of the clinical research”, but in January 2008, the conclusion was “vaginal meshes may have an interest in case of recurrence or in a particular clinical situation increasing the recurrence risk” (see slide 1, upper part), i.e. exactly the same conclusion than the today SCENIHR’s one (if you maintain “…are expected to fail”).

§ P.58-60: There are recommendations from France, USA, Australia/New-Zealand, Canada, Australia again, but NOTHING from UK! It’s a pity, because this country, although considered doing less vaginal mesh implants than all others OECD countries (about 3.3% for anterior repair) according to Haya et al (Haya N, Baessler K, Christmann-Schmid C, Tayrac R, Dietz V, Guldberg R, Mascarenhas T, Nussler E, Ballard E, Ankardal M, Boudemaghe T, Wu JM, Maher CF: Prolapse and continence surgery in countries of the Organization for Economic Co-operation and Development in 2012. Am.J Obstet.Gynecol 2015), published very good reviews and recommendations,
particularly:

- The NICE in 2008 published a very complete review with clear comparisons between the different implants compared to autologous repairs (see slide 2 for a short abstract)
- The MHRA produced this year a large compilation with a “courageous” conclusion: “…on the safety of vaginal mesh implants and their use and has concluded that, from a regulatory perspective, the benefits of the use of these devices outweigh the risks.” (see slide 3).

5. OPINION:

- 5.1. Terms of reference:
  § P.61-64: The answers to the questions Q1-Q8 are very similar, but not exactly identical to those in the P.8-11; a little bit disturbing...
- 5.2. Recommendations:
  § I agree with these general recommendations, quite similar to these mentioned P.11 excepted improved technologies...Why?

6. Costantini Elisabetta, Department of Medical-Surgical Specialties and Public Health, Section of Urology and Andrology, University of Perugia, Perugia, Italy, elisabetta.costantini@unipg.it, Italy

ABSTRACT

I am a urology with a long experience in the field of female urology and in the time I have used different materials in Pelvic organ prolapse repair and mid-urethral slings. I agree with the majority of the conclusions of SCENIHR and I think that EAU message on the safety of surgical meshes used in urogynecological surgery is a must. My only comment regards: PAGE 8 "Current evidence suggests: Type 1 (macroporous, monofilament) polypropylene is considered to be the most appropriate synthetic mesh for insertion via the vaginal route. Type 1 (macroporous, monofilament) polypropylene and Type 3 (microporous, multifilament) polyester are the most appropriate synthetic meshes for insertion via the abdominal route" From to 2010 I am using Polyvinylidene fluoride (PVDF meshes) during

The comment has been considered. The text has been changed accordingly.
sacrocolpopexy. At today I am following the patients prospectively to check the outcomes in terms of functional results and erosion rate. My data are unpublished because the 64 patients have a mean follow-up of 25 ± 15 months and the study is ongoing. PVDF, approved by FDA and CE mark, is an alternative material primarily used in hernia repair and recently applied to POP repair. Abstracts and clinical studies are present in the literature and recently and interesting application regards the use of PVDF MRI-Visible Mesh Implant. Many data suggest that this material has favorable properties: it is macroporous with high porosity, good biocompatibility and low foreign body reaction. Obviously its role in POP repair is still under observation but at the moment my data are in line with those of other experiences. The majority of the patients after surgery do not complain sexual problems and the erosion rate is 4.6% with all the erosions in patients who underwent hysterectomy and sacrocolpopexy. My comment is only to avoid that interesting materials, actually available and alternative to polypropylene and polyester are not considered although they are used in clinical application with similar or better results. As final comment I completely agree with the SCENIHR recommendations which invite to assess the long-term (at least 5 years) safety and performance of synthetic non-absorbable meshes and to Encourage further research into novel design and materials and improved technologies for manufacturing meshes.

ABSTRACT

For civilians it is impossible to evaluate the Preliminary Opinion, as it based on medical report and medical language. As co-founder of the Dutch and Belgian mesh sufferers (MeshedUp.eu , with over 600 severely handicapped people due to use of surgical mesh) it became clear to me, that more less nobody is able to react to this Opinion. These sufferers represent the main medical evidence, that using surgical mesh is a very dangerous treatment. This in view of the fact that in most cases treatments with less risks and complications are available, also after a first treatment that has failed. In the group of MeshedUp meanwhile four women died due to

The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents. SCENIHR sympathises with people suffering due to the use of surgical meshes. However, this is an opinion produced for Commission policy makers in a scientific language. An easy to read fact-sheet has been produced to explain this opinion in a language accessible also to
the complications of mesh. In this group it is also clear that much more complications occur than presented in the related international medical surveys, such as cancer and autoimmune diseases, also when SUI operations were applied. We strongly recommend the committee to start with public hearings to find out the real situation with regard to the risks of surgical mesh. Doctors and Professors in their surveys left many complications out. Objective surveys including the variety of findings with the thousands of heavily wounded victims are needed. Best regards, Maria Smit Co-founder of MeshedUp.eu Tel. +31 492 525305

the general public.

8. Schotman Frank, frank_schotman@wxs.nl, Netherlands

ABSTRACT

1 ABSTRACT Committee: Why are there no members or external experts involved representing the patients? A first request to the committee is to add a chapter related to the huge existing group of sufferers of complications due to surgical mesh: will this group be taken seriously with extensive search for personal solutions to their dramatic change of life since the implant of the mesh, or are they left as “outcasts”, giving no attention at all to this group of thousands of desperate women and men? When assessing synthetic mesh risks there is a need surgery from those of POP mesh surgery. Maybe, but the number of patients suffering from severe complications seems to be growing, when looking at the recent complaints received by MeshedUp.eu in the Netherlands. Long term effects are still unknown. There is still no registration system monitoring the real situation of patients with SUI sling surgery. The implantation of any mesh for the treatment of POP, in particular after failed primary repair surgery. Who is judging the situation for a patient on a professional and objective way, and how is this systemized? However, synthetic sling SUI surgery is an
accepted procedure with proven efficacy and safety in the majority of patients with moderate to severe SUI of appropriately trained surgeons and detailed counselling of patients about the associated risk/benefits. How can patients recognize their surgeon to be well-trained and experienced? How can patients find out details about the success rate of their surgeon? Based on the available scientific evidence, the SCENIHR recommends that due to increased risks associated surgical procedures have already failed or are expected to fail: Who is judging the situation for a patient on a professional and objective way, and how is this systemized? Based on the currently marketed products, assessment of the risks reported for vaginal use and polypropylene type 1 and polyester type 3 for insertion via the abdominal route. To which extent does the committee accept risks for patients and to which extent does the committee accept the seriousness of complications? Does the committee realize that the (compared to conventional surgery by far more dramatic) complications of mesh are irreversible? However, there is a need for further improvement, in particular for POP surgery. How does the committee expects this to be realized? By continuing using patients as laboratory animals as in the past 25 years? The SCENIHR recommends the introduction of a certification system for surgeons based on existing international guidelines with the relevant European Surgical Associations. Can the committee give an advise with regard to setting up such a system, the funding, the planning etc.? What will be the situation for patients for the years up to the introduction of the system? Appropriate patient selection and counselling, further clinical evidence, which should be collected in a systematic fashion for all of these devices. Does the committee realize, that the situation at this moment does
not give any security yet to patients? The current uncontrolled situation led to many casualties. Only the pressure from TV, internet and newspapers with dramatic reports related to mesh patients led to the situation that more and more patients became known with the risks of the mesh. What suggestions does the committee have to increase the security of SUI and POP patients?

9. **Schotman Frank**, frank_schotman@wxs.nl, Netherlands

**ABSTRACT**

In my reaction to the preliminary Opinion I found it impossible to keep within the 3800 characters per chapter. It occurred to me that it was also impossible to present my comments in a for the Committee workable way. That is why I had to choose in sending my comments in a pdf file as attached. I trust you will accept my file as my reaction to the preliminary Opinion chapters Abstract, Executive Summary, 4.2 Treatment (including sub chapters) and 5.2 Recommendations.

See response to comment above.

No changes to the Opinion are required.

10. **Shields Charles**, International Urogynecology Association, chuck@iuga.org, USA

**ABSTRACT**

Page 4: Paragraph 8 Line 8 "colposuspension is associated with greater morbidity in the context of POP surgery" Do the authors mean colpopexy?

SCENIHR agrees with the comment. The text has been changed accordingly.

11. **Prof. Dr. med. Klinge Uwe**, Department for General, Visceral and Transplant Surgery at the University Hospital of the RWTH Aachen, Uklinge@ukaachen.de, Germany,

**EXECUTIVE SUMMARY**


SCENIHR agrees with the comment. The text has been changed accordingly.

Prof. Dr. med. B. Klosterhalfen Bernd, Institute of Pathology Düren, bernd.klosterhalfen@web.de, Germany

**EXECUTIVE SUMMARY**

page 8, lines 40+41 page 9, lines 1+2+3 Being an expert for biomaterial research for over 20 years, in particular for biocompatibility and local tissue reaction and textile structures for pelvic floor repair and hernia repair I have personally published over 60 publications in this special field. I am expert witness and currently involved in various mesh litigations in the US for more than 3 years and personal owner of the largest data pool of mesh explants worldwide.

1.) Classification of AMID is not up to date

1) The AMID classification has been used because this is cited in most clinical guidelines. No changes to the Opinion are required.

2) SCENIHR accepts the comment. The text has been changed accordingly.
15


2.) Due to our research Polyvinylidene fluoride PVDF and PES monofilaments are also suitable materials for surgical meshes. In particular PVDF indicates in all our preclinical experiments an improved biocompatibility and tissue reaction compared to PP mono- and PES multifilament. These results are confirmed by analysis of more than 600 mesh explants used in pelvic floor repair and more than 1000 explants of surgical meshes used in hernia surgery. Therefore PVDF must be included into the recommended materials. Klinge et al. PVDF as a new polymer for the construction of surgical meshes. Biomaterials. 2002 Aug;23(16):3487-93. Klink et al. “Comparison of Long-Term Biocompatibility of PVDF and PP Meshes”. Journal of Investigative Surgery: The Official Journal of the Academy of Surgical Research 24, Nr. 6 (2011): 292–99.

EXECUTIVE SUMMARY

17, 8 "there is a limited use for mesh for CFD, mainly in specialist centres" There is no coding system (register) within hospital systems (worldwide) which could determine an accurate account of implantations and excisions of all surgical mesh. CFD surgical mesh procedures SHOULD be included and focused on in this Opinion. Until there is a true understanding of the scope and scale of mesh complications, this statement cannot be validated. As a health advocate for mesh sufferers I come into contact with many CFD do not fall exactly within the scope of this Opinion. No changes to the Opinion are required.

13. New Zealand No agreement to disclose personal data
14. New Zealand  
*No agreement to disclose personal data*  
**EXECUTIVE SUMMARY**  
16,17,18 "Taking into account the lack of long-term data on performance and safety of the use of synthetic non-absorbable mesh for POP repair, the SCENIHR recommends being cautious about using these in younger age groups". Because there is a lack of long term data, caution in the use of surgical mesh should be used in all age groups not just in the younger age group category.  
The text has been changed for clarification.

15. New Zealand  
*No agreement to disclose personal data*  
**EXECUTIVE SUMMARY**  
28,29,30,31 The SCENIHR acknowledges the efficacy and use of implanted meshes for SUI in the majority of patients with moderate to severe SUI. It considers that the associated risk is limited, but recognises the absence of long-term data. Most complications associated with mesh insertion are related to the route of insertion. Complications that are established quickly can be identified more easily as being related to mesh insertion. When there is a delayed onset of symptoms, SUI mesh related complications are commonly misdiagnosed and attributed to other conditions and therefore are underrepresented in the current statistics. Although the route of insertion is identified as the main concern, it should not be the only underlying factor considered as the cause.  
The comment is in agreement with SCENIHR. No changes to the text are required.

16. New Zealand  
*No agreement to disclose personal data*  
**EXECUTIVE SUMMARY**  
"Before a decision for surgery is made, it is important to explore non-surgical solutions for SUI, POP and colorectal functional disorders (CFD). If non-surgical solutions are unfeasible or unacceptable to the patient, in a shared decision process the surgeon and the patient must determine whether to use a surgical approach with or without mesh."

The comment is in agreement with SCENIHR. No changes to the text are required.
| 17. New Zealand  
No agreement to disclose personal data | EXECUTIVE SUMMARY | "If non-surgical solutions are 11 unfeasible or unacceptable to the patient, in a shared decision process the surgeon and 12 the patient must determine whether to use a surgical approach with or without mesh". The wide variety of surgical treatments available for prolapse indicates the lack of consensus as to the optimal treatment. There are no guidelines that exist to guide the surgeon and the patient as to the preferred surgical intervention. | No changes to the text are required. |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>18. Dr. Obolenski Boris, FEG Textiltechnik Forschungs- und Entwicklungsgesellschaft mbH, <a href="mailto:b.obolenski@feg-textiltechnik.de">b.obolenski@feg-textiltechnik.de</a>, Germany</td>
<td>EXECUTIVE SUMMARY</td>
<td>Chapter 1 Executive Summary: Page 8, lines 40-41 Page 9, lines 1-5 Without any doubt is Polypropylene the mostly used polymer as mesh material, but it is not justified at all to conclude that it is the only optimal material. The actual research status shows that other non-absorbable synthetic polymers such as PVDF are convincing or even superior alternatives and should not be excluded by being not mentioned in the report. Joukhadar et al „A Novel Operative Procedure for Pelvic</td>
<td>The SCENIHR agrees with the comment. The text has been changed accordingly.</td>
</tr>
</tbody>
</table>

Open letter to the SCENIHR committee: To whom it may concern, First of all congratulations to the initiative to analyse the problems, which led to the FDA warnings. Being a technology-driven manufacturer of meshes used in urogynaecological surgery, we strongly support every advancement in knowledge. FEG Textiltechnik is an independent fully integrated SME manufacturer of synthetic, non absorbable textile implants for hernia, incontinence and prolapse repair. Our product range consists of state-of-the–art open pore, surface-minimised warp knitted structures made from Polypropylene (PP) and/or Polyvinylidene fluoride (PVDF) monofilaments. The company consists of dedicated and highly qualified staff, in-house R&D, and intelligent production facilities, all under one roof in Aachen Germany. Under the brand name DynaMesh®, an internationally protected trademark, FEG’s mesh products are successfully used in more than 50 countries around the world. Constant contact with major scientific, medical and technical institutions ensures that FEG’s high-quality products meet the latest requirements in terms of patient safety and comfort. The sophisticated quality management system at FEG Textiltechnik mbH is fully certified to DIN EN ISO 13485 standards for the manufacture of medical devices. All FEG products bear the CE mark.
and are approved under all relevant national regulations. Furthermore PVDF and PP products are certified by FDA and CFDA and have obtained the approval in various other countries in Asia and South America. Since 2005 more than 27,500 meshes (customer's choice: 96% PVDF and only 4% PP) have been used for incontinence and prolapse repair via vaginal or abdominal route. Since 2003 more than 240,000 meshes (50% PVDF for abdominal and intraperitoneal use, 50% PP for markets outside EU or extraperitoneal use) in hernia repair. FEG supports various registries and sets a high value on Post Market Surveillance. In the last 10 years no serious reportable events or product recalls have taken place. PVDF is one of the best evaluated high-tech polymers (over 2142 publications in Pubmed). Independent studies and tests show that PVDF is superior to PP regarding material properties, such as biocompatibility, long-term stability, elasticity, aging and performance in contaminated fields.

Beside FEG other international companies like Lintex or Medlinx, Acacia has chosen PVDF as an optimal polymer for surgical meshes. Ethicon (Johnson&Johnson) funded a research project for the intra-abdominal use of PVDF with convincing results and reduced inflammatory tissue reaction compared to PP. Further PVDF is used as suture material due to its outstanding material properties by companies around the world (e.g. Ethicon J&J, Resorba, Acufirm, Centeniel).

19. Dr. Müllen Andreas, DynaMesh FEG Textiltechnik mbH, a.muellen@dyna-mesh.com, Germany

EXECUTIVE SUMMARY

Chapter 1. EXECUTIVE SUMMARY Page 11, line 25 - 38 I fully agree to the SCENIHR recommendations but like to amend these in the field of further material research. There are strong doubts about absorbable materials for the use in the pelvic floor as already described in the actual draft report. Limiting or even focussing further research to this

The SCENIHR agrees with the comment. The topics mentioned in the Opinion are only given as examples ("such as"). No changes to the text are required.
<table>
<thead>
<tr>
<th></th>
<th>Executive Summary</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>20. Hardacre Ingrid, Mesh injured patient member of the public – living in England UK, <a href="mailto:ingrid.hardacre@talktalk.net">ingrid.hardacre@talktalk.net</a>, United Kingdom</td>
<td><strong>EXECUTIVE SUMMARY</strong> Dear Sirs Having read your report and trying to understand it to the best of my ability allow me to respond to your SCENHIR report. You invite comments but on your submission form there is no provision, (like “other”) for patients to make comments? Patients are not medically trained and their understanding only comes through their anecdotal experience and their own research. Although these experiences are individual the adverse incidents and disappointed and unexpected outcomes are as a direct result of the implantation of a “global” mesh product made of plastic (Polypropylene)! These injuries are also global as we now come forward to bring our stories to on-line Self Help Support Group websites and blog sites. Most patients then discover that they are not unique and the “only one” with problems, as they are led to believe when they go back with their problems, to their inputting centre, Trust and consultants. Although you mention that overall there is a lack of evidence and long term studies, especially long term outcomes on mesh surgeries you condone the use of mesh. I find this upsetting and puzzling as a mesh injured patient. As a result please find my comments in, I hope in the correct categories. Although some US research has been listed You have not taken into consideration the very frank and clear warnings from the eminent doctors in the US who remove mesh. These are:- Prof Shlomo Raz and Mr Thomas Margolis on the dangers of mesh and their experience in removing mesh see separate file Ingrid Hardacre</td>
<td>The SCENHIR does not carry out pure research or have laboratories; it carries out a meta-data analysis, i.e. a literature research considering relevant independent studies from all over the world, in order to draw solid conclusions. Anecdotal experiences should be part of scientific studies. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>21. Schotman Frank, <a href="mailto:frank_schotman@wxs.nl">frank_schotman@wxs.nl</a>, Netherlands</td>
<td><strong>EXECUTIVE SUMMARY</strong> Please see attached file.</td>
<td>The SCENHIR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents.</td>
</tr>
<tr>
<td>No.</td>
<td>Author</td>
<td>Email</td>
</tr>
<tr>
<td>-----</td>
<td>--------</td>
<td>-------</td>
</tr>
<tr>
<td>22.</td>
<td>Toozs-Hobson Philip, British Society of Urogynaecology, <a href="mailto:toozscompany@me.com">toozscompany@me.com</a></td>
<td></td>
</tr>
</tbody>
</table>

The SCENIHR agrees with the comments on terminology. The text has been changed accordingly.

The title of the Opinion is part of the mandate and cannot be changed.

Several comments concern risk management and policy implementation, which are outside the scope of SCENIHR. No changes to the Opinion are required.

See also response to the same comments further below.
a European nation document with guidance. There may be other national member state documents that relate to this. Some will look at efficacy, whilst others (NICE) examine efficacy within an economic model. These groups need to referenced. There are theoretical concerns with type 3 polyester mesh (even inserted abdominally) as limited data are available. The theoretical concerns suggest added caution. As with all procedures careful audit should be mandatory. There are 2 sources of information that do not seem to be included for retropubic tapes. Firstly the 17 year data on the original TVT set by Nilsson and secondly the original Austrian database on TVT. As a comment about colposuspension the results in the Ward and Hilton series did not show any inferiority with regard TVT and they do not report pain as a significant issue in their 5 year follow up. In addition the original article is referenced but the 5 year follow up is not. The document comments on work on comprehensive informing patients. We would highlight the existence of the BSUG database here. The numbers on this are now sufficient to add to the debate. There are several units who can now quote their own data and we would suggest that any new registry does this in conjunction with BSUG as it will make data comparable. We feel that mandatory registers will give more meaningful data, as the data set will be complete. Ideally each unit should have knowledge of their own outcomes. In the UK this fits into HQIPP and outcomes framework. However it needs to be appreciated that small data series form individual units may give misleading outcomes. The document states that there is a need to Establish European registries. We would respectfully suggest that there is an opportunity to work collaboratively here. We have already established the BSUG database and spent a number of years refining the
<table>
<thead>
<tr>
<th></th>
<th>Shields Charles, International Urogynecological Association, <a href="mailto:chuck@iuga.org">chuck@iuga.org</a>, USA</th>
<th>EXECUTIVE SUMMARY</th>
<th>Please see attached file.</th>
<th>No changes in the Opinion needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.</td>
<td></td>
<td>Page 8: Line 7&amp;8: Needs a reference for the failure of allografts and xenografts. Line 17 &amp; 17: This conclusion is not in line with the evidence presented later in the paper showing superior outcomes with mesh in the primary repair of POP. Line 27 Are specific meshes, in terms of designs an d/or materials, considered to be of a higher risk? If possible list and describe the risks. Why are absorbable meshes not discussed? Line 34: This document needs to reflect that the classification by Amid does not adequately cover all the available materials. For example: i) the bonded mesh in Obtape® falls outside of this classification. ii) The classification also fails to discriminate between the multiple different Type I implants all with vastly different biomechanical properties. iii) It does not include hybrid materials or polypropylene implants covered by other materials such as collagen or titanium. Line 40 to Page 9 Line 3 Why do the authors only discuss polypropylene and polyester. There are other polymer materials e.g. Polyvinylidenefluoride (PVDF) that may be considered more suitable than polypropylene. Polyester sutures are well known to cause more wound problems than monofilament sutures. It is difficult to understand how a polyester mesh can be judged safe considering that it is a multifilament mesh. Page 9 Line 13 Mesh extrusion can also be seen with xenografts</td>
<td>Executive summary_Shields Cha</td>
<td>Appropriate references are included in the rationale. No changes in the Opinion are required. They are not discussed because of time limitations. No changes in the Opinion are required. The new classification is mentioned. However, Amid classification is the one that has been cited in most reviews and meta-analyses examined. No changes in the Opinion are required. The comment was considered. The text has been changed accordingly.</td>
</tr>
<tr>
<td>Line 20:</td>
<td>A broader range of mesh exposure should be quoted – 4-12%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line 24:</td>
<td>Speculation on the type of anaesthesia irrelevant.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line 40:</td>
<td>Not sure that the higher complication rate in the vaginal procedures is attributable to the area of the mesh. It may be due to the different microbial environment, the proximity to the scar and the different wound healing mechanisms as in the abdomen.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Page 10 Line 6/7:</td>
<td>There is no confirmation that the xenograft or allograft materials have less severe side effects. There are some clinical reports that demonstrate they actually do not reduce the number of GRC (11, 12). It is theoretically possible that they may have immune mediated complications like the inducement of rheumatoid arthritis.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line 15:</td>
<td>Add smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line 24/24:</td>
<td>The Burch Colposuspension has an incidence of postoperative pain in the Pfannenstiel scar as high as 7%. It is important that this paper reflects the fact that conventional surgery has a set of complications attributable to that operations specific technique.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Page 11 Line 16:</td>
<td>How can they urge caution in the younger age groups? If so they need to be more specific about what they mean by younger. The TVT has 20 year follow up which is comparable with almost any implant in the world.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lines 25 to 37:</td>
<td>Consider using the recommendations set out by the round table IUGA conference in relation to the introduction of new materials or techniques</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We agree. No changes in the Opinion are required. No speculation made. Just options mentioned. No changes in the Opinion are required. This is a hypothesis. No changes in the Opinion are required. This is a personal Opinion on the severity of side effects not supported by evidence. No changes in the Opinion are required. We do not agree with this comment. No changes in the Opinion are required. The SCENIHR agrees with the comment and the text has changed accordingly. The text has changed. The SCENIHR agrees with the comment and the text has been changed accordingly.

25. Slack MArk, International Urogynaecology Association – IUGA, markslack@me.com, United Kingdom

EXECUTIVE SUMMARY

Please see attached file.

Please see the answers above.
In line 1, page 18, the report states 'synthetic surgical meshes are non-active' yet this has been proven to be untrue - see attached research on 100 mesh explants and 'mesh not inert'. In lines 9 and 10, page 18 the report states 'in the case of meshes no mandatory testing of the device and 10 not even a third-party test of its design dossier is requested'. This suggests a negligent attitude to a device that is designed to be permanently implanted within tissue - mesh is harder to remove safely than many other devices if they fail. As reported in http://www.europeanurology.com/article/S0302-2838%2812%2900235-7/fulltext/tension-free-vaginal-tape-and-beyond-our-challenges-and-the-future-of-anti-incontinence-therap, a 30-40% failure rate is not acceptable' - and this high rate is borne out by the more informal reporting on internet sites and petitions. In lines 21-33 (p 18) state that 'sufficient clinical data should be available for 32 surgical meshes to allow adequate risk assessment and identification of problems with 33 their design and/or their use'. My response is that in the UK a) there is no requirement for registration of adverse events relating to polypropylene (PP) mesh surgery therefore there is no record of how many adverse events there are b) there are few long term studies that track the subjective as well as objective outcomes of PP and, despite the recommendation later in the report that women are counselled to this effect, none of the hundreds of women who I know who have had adverse outcomes were informed of the risks c) there is no requirement for patients to receive full information about the potentially life altering risks d) those studies on SUI slings that have been referred to by the MHRA’s reports (UK regulatory body) do not include reference to the risks as set out in all four attached reports. These should inform The SCENIHR agrees with the comment. The text has been changed accordingly.

The European regulatory policy is described clearly in the text. The MHRA ask for an alert on every case (there is a requirement to have full information). No changes to the Opinion are required.
<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>27.</strong> Shields Charles, International Urogynecological Association, <a href="mailto:chuck@iuga.org">chuck@iuga.org</a>, USA</td>
<td>4.1. Introduction</td>
<td>Page 13 Line 12 Why have they not dealt in detail with meshes used for colorectal prolapse. This subject is as important as that used for uterovaginal prolapse. Line 14 to 21 It is true that there is a shortage of randomized controlled trials but it must be recognized that because of their cost and difficulties they may not be sufficiently robust to detect uncommon differences or complications or too short to detect remote complications.</td>
<td>This subject is not within the scope of the current mandate. No changes to the Opinion are required.</td>
<td></td>
</tr>
<tr>
<td><strong>28.</strong> Wijchers Janneke, <a href="mailto:wijchers@planet.nl">wijchers@planet.nl</a>, Netherlands</td>
<td>4.1.1. Indications for the use of surgical meshes</td>
<td>Surgical Meshes must not be used, they give too much problems and can’t be removed from the body without making more damage. Too many women are in constant pain en invalids, not able to work, or live the life they were used to. I’m a victim myself, after 6 years and several operation trying to make it better I still have severe pain every day and even special medication and operations for pain blocking, do not make any difference. When I was 51 I got the Mesh, after the operation I felt like an invalid woman of almost 100 years. That gives me not only physical pain, but it makes me also very angry and sad and also my family and friends (at least the friends I didn’t loose being an invalid :( )</td>
<td>Risk management and policy implementation do not fall within the scope of the SCENIHR. No changes to the Opinion are required.</td>
<td></td>
</tr>
<tr>
<td><strong>29.</strong> New Zealand</td>
<td>4.1.2. Regulatory framework</td>
<td>28, Surgical mesh as a medical device • have an acceptable risk/benefit ratio; How can this be determined when worldwide under-reporting is known to be a problem, lack of informed consent is an issue and misdiagnosis of surgical mesh symptoms is common?</td>
<td>Risk management is not in the remit of the SCENIHR. No changes to the Opinion are required.</td>
<td></td>
</tr>
<tr>
<td><strong>30.</strong> Hardacre Ingrid, member of the public / mesh injured patient, ingrid.hardacre @talktalk.net, United Kingdom</td>
<td>4.1.2. Regulatory framework</td>
<td>4.1.2 Regulatory framework 1-10 Notified Bodies, Patient’s safety, MHRA, lack of a national register. It makes me rather suspicious and thinking that this report, like any other from England (York Report and statements from the MHRA in England), on</td>
<td>The comment does not refer to the Opinion. Risk management is not in the remit of the SCENIHR. No changes to the Opinion are required.</td>
<td></td>
</tr>
</tbody>
</table>
their report from Nov 2014 in which the MHRA are holding on to their blinkered view that - “Benefits outweigh the risks” is weighted in favour of the mesh manufacturers by basically ignoring the huge number of mesh victims that are now emerging, who now know where and how to report their adverse incidents, by going public on Facebook and self-help support groups. Why? Due to a lack of robust data and the absence of a national register the MHRA cannot be believed in their statement. Because mesh patients are not being listened to and are not believed because medical professionals are in denial or maybe they are embarrassed to admit at having been deceived by the mesh manufacturers and notified bodies. Notified bodies contribute nothing to the reality of severe mesh complications, because notified bodies licences can be bought without any problems at all. See the RADAR Report from Holland and their undercover work in exposing the notifying bodies in England and Austria and Germany, to name but a few countries in the EU. Frankly, to use the pretext “we must not stifle innovation” is criminal and insulting to every patient that has been injured by mesh and any future patient who will also be injured by mesh, if the practise of using this “minimally invasive procedure ” is being continued. This is quite clearly the case in England under NHS and private practice. But it is morally wrong to subject another human being to undergo such an, entirely elective, dangerous, under-trialled operation and not giving full risks and long-term problems with a product that is not fit for purpose. In the US there a many litigations going on with various mesh manufacturers and patients have won their cases. Before long, patients in Europe will be successful in litigations – it is only a question of time. Dr Carl Hennighan, Oxford, has commented on the process of licensing required.
implant products through a notified body in May 2012 - even before he worked together with RADA on the “Mandarin Net” expose! See links attached. 16 Implantation techniques for SUI 17 o There is no such evidence available in England, as part of a EU nation. England has been lax in keeping any implant records and Hospital Episodes Statistics are only the tip of the iceberg. England's NHS is refusing to do any retrospective national register studies. It is further not willing to put in place a National register for mesh implants, as SCENHIR recommends. Yet England has put in place a National Register for hips and knee implants? Until we have a National Register in England of implant and explant there will never be any substantial accuracy. This means that all the evidence that exists is that of injured patients coming forward to report their failures and adverse reactions. You refer to the toxicity of mesh products in your report and yet NHS England is refusing to acknowledge the immune reactions that patients report post mesh implantation. See link: Polypropylene mesh implant and the Autoimmune connection.

31. Hardacre Ingrid, Member of the public- mesh injured patient, living in England UK, ingrid.hardacre@talktalk.net, United Kingdom

| 4.1.2. Regulatory framework | See copy of Transcript (courtesy of http://www.scottishmeshsurvivors.com/) from the Public Committee meeting in the Scottish Parliament, 24 Feb 2015 and their questions to the MHRA on their lack of rigour on putting out a warning on the dangers of mesh, as the England Regulatory Authority of the UK | Please see above. | The comment does not refer to the Opinion. No changes to the Opinion are required. |

32. Hardacre Ingrid, member of the public mesh injured patient, ingrid.hardacre@talktalk.net, United Kingdom

<p>| 4.1.2. Regulatory framework | See copy of Transcript PART 2 21 - 40 PAGES (courtesy of <a href="http://www.scottishmeshsurvivors.com/">http://www.scottishmeshsurvivors.com/</a>) from the Public Committee meeting in the Scottish Parliament, 24 Feb 2015 and their questions to the MHRA on their lack of rigour on putting out a warning as the England Regulatory Authority of the UK Thank you for the opportunity to comment. IH. | Please see above. | The comment does not refer to the Opinion. No changes to the Opinion are required. |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>33.</td>
<td>Charles Shields, International Urogynecological Association, <a href="mailto:chuck@iuga.org">chuck@iuga.org</a>, USA</td>
<td>4.1.2. Regulatory framework</td>
<td>Page 16 Lines 19 – 41 It should be recognized that the regulatory framework provided by the FDA and CE marking process is inadequate and will not prevent the complications seen with the introduction of these materials and operations. Again we should advocate that the committee take heed of the IUGA round table advice which provides a framework for the safe and ethical introduction of these materials and operations. Page 18 Line 1 – 32 Again this is probably inadequate. We should request conformity with the recommendations of the IUGA round table conference ensuring that all mesh products have had animal studies on that specific mesh as well as a significant cohort study with 12 months follow-up and the setting up of a prospective registry. This ideal would always be for a randomized trial to follow.</td>
<td>Risk management and policy implementation do not fall within the scope of the SCENIHR. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>34.</td>
<td>Schotman Frank, <a href="mailto:frank_schotman@wxs.nl">frank_schotman@wxs.nl</a>, Netherlands</td>
<td>4.2. Treatment</td>
<td>Please see attached file.</td>
<td>The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents. No changes in the Opinion needed.</td>
</tr>
<tr>
<td>35.</td>
<td>Ankorina-Stark Ieva, Contura International/Speciality European Pharma, <a href="mailto:ivas@contura.com">ivas@contura.com</a>, Denmark</td>
<td>4.2.1. Treatment without using meshes</td>
<td>Page 21, lines 7-9. Page</td>
<td>1 Comment on EU Scientific Committee preliminary Opinion on the safety of surgical meshes used in urogynecological surgery Speciality European Pharma / Contura International A/S thank the Scientific Committee on Emerging and Newly Identified Health Risks for the opportunity to comment on the preliminary Opinion on the safety of surgical meshes used in urogynecological surgery. As the Committee states, it is important to consider non-surgical options before commencing on more invasive treatment methods. In Section 4.2.1 Treatment Without</td>
</tr>
</tbody>
</table>
Using Meshes, a number of alternatives to meshes are reviewed. One of these is the use of urethral bulking agents, mentioned on page 21, lines 7 to 9. The first Cochrane report on urethral bulking from 2003 is referenced there (Error in the current text: Pickard et al., 2004). However, since then additional data on bulking has been published and it is our suggestion that this data (see below), together increasing adoption of the bulking approach across Europe, warrants more significant consideration of this treatment modality in the report. Injection of a bulking agent into the urethral submucosa improves coaptation and is proposed to work by increasing the power of the urethral sphincter (Klarskov & Lose, 2008). Different bulking materials have been used over the years and can be mainly divided into two types: the homogenous products, where the filling effect stems from the material itself (e.g. Bulkamid) (Lose et al., 2006), and combination products where the filling effect stems from the host inflammatory response to micro-particles (e.g. Macrosplastique) (Ghoniem & Miller, 2013). Biocompatibility, duration in the tissues and ease of injection are some of the features which contribute to the product clinical performance (Davis et al., 2013). Long-time observation data on older bulking agents have shown a decrease of their effect over time requiring several reinjections (Kirchin et al., 2012). Contigen has reported cure rates of 53% (Corcos et al., 2005) and very good safety profile (Davis et al., 2013), however due to its degradable nature, the efficacy is shown to decrease with time (Herschorn & Radomski, 1997) and this has influenced the overall perception of bulking having poor durability. Newer, synthetic bulking agents like Macroplastique and Bulkamid demonstrate stability over several years (Mouritsen et al., 2013; Toozs-Hobson...
et al., 2012; Ghoniem & Miller, 2013; Mohr et al., 2013). In multicenter European study including 135 patients, Bulkmid has shown that the significant reduction in leakage (89%) and incontinence episodes (83%) as well as 67% subjective cure rate at 1 year were maintained at 2 years (Toozs-Hobson et al., 2012). In a randomized controlled study with 345 patients, 76.5% of the Bulkmid® treated group and 70.6% of the Collagen treated group had an improvement in their incontinence at the 1 year follow up (Sokol et al., 2014). Two center study in 29 urodynamic stress urinary incontinence patients showed an objective success rate (negative cough test) of 79.3% and subjective response rate of 89.7% at 12-month follow up (Maggiore et al., 2012). A subjective response rate of 74.4% was reported at 12 months study including 82 women (Maggiore et al., 2013). Bulking after mid urethral sling failure in 60 patients achieved 83.7% improvement at 12 months (Zivanovic et al., 2015).

The midurethral tape procedure has mainly been used as a first line invasive treatment for stress or mixed urinary incontinence and in predominantly young women (Ward & Hilton, 2008; Ogah et al., 2011; Barber et al., 2012; Serati et al., 2013). In contrast, bulking has traditionally been studied mostly in older and frail women, who had undergone other invasive procedures (Kirchin et al., 2012; Van Kerrebroeck et al., 2006). Moreover, several authors have shown that cure rates with mid urethral tapes vary even within the same study group depending on the outcome measures reported (Ward & Hilton, 2008). Therefore, comparison of cure rates between tapes and bulking agents using the current literature is not feasible as the patient selection criteria were very different. Nonetheless recent data presented on bulking
has shown patient satisfaction to be around 80% (Zivanovic et al., 2015), which is not too
dissimilar to that of midurethral tapes (Kulseng-Hanssen et al., 2008). It
should also be noted that bulking is a less
invasive procedure than insertion of a mid
urethral tape, and is usually carried out in an
out-patient setting under local anaesthesia.
Indeed in the Sokol 2014 study all 345
patients were treated in the office setting.
In conclusion, it seems that the relative risk
benefit profiles of slings and bulking is
shifting, particularly in light of the more
recent data with the newer bulking agents
such as Bulkamid (Lose et al., 2010; Tooozs-
Hobson et al., 2012). Consequently the
prospect of offering patients the less invasive
alternative of bulking as well as slings should
in our Opinion is more prominent in the EU
report in section 4.2.1. The body of growing
evidence demonstrates its subjective
outcomes being comparative to slings, and as
such the option of bulking should be made
more aware to patients by their treating
physicians as an option alongside slings.
Whilst there is now evidence and Opinion to
support this approach, further prospective
randomized studies are required to further
eucidate the effectiveness of urethral bulking
and midurethral sling placement in particular
patient groups. July 18, 2015Eva Ankorina-
Stark, PhD Chief Scientific Officer
Contura International/Speciality European
Pharma Sydmarken 23, 2860 Soeborg
Denmark, E-mail: ivas@contura.com

References
Barber MD, Weidner AC, Sokol Ai et al;
Foundation for: female health awareness
research network. Single incision mini-sling
compared with tension-free vaginal tape for
the treatment of stress urinary incontinence:
a randomized controlled trial. Obstet Gynecol


Page | 4


incontinence Int Urogynecol J 2012; 23:1373-1378.
Ward KL, Hilton P on behalf of the UK and Ireland TVT Trial Froup*. Tension-free vaginal tape versus colposuspension or primary urodynamic stress incontinence: 5-year follow up. BJOG 2008; 115:226-33.

36. Shields Charles, International Urogynecological Association, chuck@iuga.org, USA
4.2.1. Treatment without using meshes
Page 19 Line 32/33 Don't think this is a good recommendation
Page 24 Line 5/8 I think they should separate sacrocolpopexy from sacrohysteropexy. They are very different operations, often performed in different age groups or patient profiles, and likely to have very different outcomes. While sacrocolpopexy has a low mesh complication rate it is not insignificant and shouldn’t be underestimated. Removal of the mesh in these patients is technically more challenging, and may be associated with significant morbidity. A warning needs to be made about abdominal sacrocolpopexy or we will face another mesh scandal related to ASC.

Page 19 Line 32/33. The comment has been considered and the text has been changed accordingly for clarity.
Page 24 Line 5/8. SCENIHR agrees with the comment. The text has been changed accordingly.

37. ElSheemy Mohammed, Cairo University, mohammedshemy@yahoo.com, Egypt
4.2.2. Treatment using meshes
YILDIRIM and associates compared the mesh-to-tissue attachment strength and evaluated tissue reactions to five sling materials used in TVT, intravaginal slingplasty, polypropylene mesh hernia repair, the suprapubic approach to suburethral polypropylene tape (SPARC) and cadaveric fascia lata procedures in 20 female rabbits. All five synthetic sling materials produced similar tissue reactions. When comparing the 4 polypropylene mesh materials; the attachment capacity of TVT was

This is a proposal for a treatment technique.
No changes to the text are required.
superior and that of intravaginal slingplasty was the least of the 4. TVT was statistically better than intravaginal slingplasty at all data points. SPARC and hernia mesh provided results similar to those of TVT. Based on the similar histological and biomechanical properties noted in that study, they reported that surgical hernia mesh with an affordable price may be a good alternative to prepackaged polypropylene kits. Yildirim A, Basok EK, Gulpinar T, Gurbuz C, Zemheri E, Tokuc R. Tissue reactions of 5 sling materials and tissue material detachment strength of 4 synthetic mesh materials in a rabbit model. J Urol. 2005 Nov;174(5):2037-40. Krause and associates evaluated the biocompatibility of eight different types of mesh: Atrium, Dexon, Gynemesh, intravaginal slingplasty, Prolene, SPARC, TVT and Vypro II. They were implanted into the abdominal walls of rats for 3 months duration. Explanted meshes were assessed using light microscopy, for parameters of rejection and incorporation. Inflammatory cellular response and fibrosis at the interface of mesh and host tissue was most marked with type 3 (Vypro II and intravaginal slingplasty). All type 1 meshes (Atrium, Gynemesh, Prolene, SPARC and TVT) displayed similar cellular responses. Krause HG1, Galloway SJ, Khoo SK, Lourie R, Goh JT. Biocompatible properties of surgical mesh using an animal model. Aust N Z J Obstet Gynaecol. 2006 Feb;46(1):42-5.

38. ElSheemy Mohammed, Cairo University, mohammedshemy@yahoo.com, Egypt

4.2.2. Treatment using meshes

The safety and efficacy of traditional polypropylene mesh used in hernia repair (Prolene®; Polypropylene Mesh; Ethicon Ltd; UK) was evaluated after tailoring it as a transobturator tape or Contasure-Needleless tape in different studies. ElSheemy and associates evaluated the long-term safety and efficacy of ordinary polypropylene mesh as TVT-O. Complications were vaginal discharge Please see above. See the response to the above comment.
(6%), dyspareunia (1%), groin pain (20%), UTI (3%), and obstructive symptoms (1%). They had no cases of erosions or de novo urgency. Of the 59 females, 91% cured, 5% improved while failure was detected in 3% [1]. This was followed by a cohort study comparing this surgeon-tailored mesh (79 females) versus TVT-O (66 females). No significant difference was found between both groups in complications and cure after 5-years follow-up. Again, there was no erosions or mesh exposure [2]. The safety of this surgeon-tailored mesh was confirmed again in another study after tailoring it in the form of Contasure-Needleless single incision sling in 43 females. Postoperative complications were vaginal discharge (4.65%), failure of wound healing (4.65%), dyspareunia (4.65%) and UTI (4.65%). The sling was removed in 1 (2.3%) case. Failure was detected in 1 (2.3%) patient only [3]. When compared against TVT-O, no significant difference was found in complications or cure between surgeon-tailored Contasure-Needleless single incision sling (72 females) and TVT-O (48 females). Failure of wound healing occurred in 1/72 (1%) female only in surgeon-tailored group [4].

<table>
<thead>
<tr>
<th>Page</th>
<th>Name</th>
<th>Email</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>39.</td>
<td>Balzarro Matteo, AOUI Verona, dept of Urology, <a href="mailto:matteo.balzarro@ospedaleuniverona.it">matteo.balzarro@ospedaleuniverona.it</a>, Italy</td>
<td></td>
<td>In the Terms of Reference there is a request to assess surgery techniques as well. No changes to the text are required.</td>
</tr>
<tr>
<td>40.</td>
<td>BALZARRO MATTEO, AOUI VERONA, <a href="mailto:matteo.balzarro@ospedaleuniverona.it">matteo.balzarro@ospedaleuniverona.it</a>, Italy</td>
<td></td>
<td>The references are given in the Opinion. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>41.</td>
<td>BALZARRO MATTEO, AOUI VERONA, <a href="mailto:matteo.balzarro@ospedaleuniverona.it">matteo.balzarro@ospedaleuniverona.it</a>, Italy</td>
<td></td>
<td>The comment has been considered and the text has been changed accordingly.</td>
</tr>
<tr>
<td>42.</td>
<td>Kirschner-Hermanss Ruth, University Clinic of Bonn, <a href="mailto:rkienschnerhermanns@googlemail.com">rkienschnerhermanns@googlemail.com</a>, Germany</td>
<td></td>
<td>The comment has been considered by the SCENIHR. The text in the Executive Summary and the Opinion have been changed accordingly.</td>
</tr>
</tbody>
</table>


4.2.2. Treatment using meshes page 38 line 1. At page 38 line 1 is recommended the use of laparoscopic approach for sacral colpopexy. It has been considered the clinical equivalence between open and laparoscopic sacrocolpopexy (Freeman et al. 2013) and the higher morbidity in the open surgery group (Tyson et al. 2013). But in the SCENIHR document the topic is the meshes’ complication between the open vs laparoscopic/robot approach not the surgical approach complication per se.

4.2.2. Treatment using meshes page 38 lines 7-8. At page 38 lines 7-8 is “if hysterectomy is required, it is recommended to perform a subtotal hysterectomy”. This message should be supported by randomized controlled trials (RCT) before to become a recommendation with a high Level of evidence.

The conclusions on Robotics procedures for POP are premature. page 38 line 15 Through my own research work, done in the last years (1-3) and confirmed by the work of Clavè, Klinge and Klosterhalfen (4-6) we know that polypropylene as one textile option is not inert. We strongly believe that with PES and PVDF there are better materials on the market than Polypropylene. I strongly believe that this should be already mentioned in the
abstract – see my comments
PVDF is well known for its excellent biocompatibility, its good mechanical and chemical features, its high consistency for hydrolysis and its low tendency to age. In comparison aging of Polypropylene leads to crystallization and to a reduction of stability in up to 47%, compared to 4.7% in PVDF. Implants made of PVDF benefit from these characteristics in respect to integration into the tissue, stabilization of anatomical structures and thus a reduction of arrosion, infection, fibrosis and hematoma. In comparison to Polypropylene PVDF keeps its effective pores with a median size of > 0.6mm even under tension.
The abstract should be
I want to give some additional comments to the questions asked:
Q1
Are specific meshes, in terms of designs and/or materials, considered to be of a higher risk? If possible list and describe the risks.
Discussing different materials for incontinence and prolapse surgery it is important to consider alternatives to Polypropylene (PP). PP is quite a cheap polymer which has been used as a monofilament in surgical sutures for decades. However, polypropylene shows a degree of rigidity and surface cracking after implantation into tissues as it degrades. Degradation and cracking produce a larger surface which may be the reason for an enhanced inflammatory reaction when compared to the properties of other materials such as polyvinylidenfluoride (PVDF). Monofilaments of PVDF can be made stronger than fibers of polypropylene, and they appear to degrade less when used in vivo. PVDF has already been used successfully for years in cardiac and ophthalmic surgery, whereas its use for surgical textiles started in the early 2000s.
Composite meshes use a combination of

40
materials to improve mesh-tissue interaction and reduce complications with the aim of minimizing clinical complications. For example Vypro mesh is made of polyglactin (absorbable) and polypropylene (nonabsorbable) fibres, which is said to increase increases its longevity compared to absorbable mesh. Though these meshes have very large pores in its packaged form, these pores rapidly showed a collapse if put under tension. Correspondingly, Vypro implants in the pelvic floor often form ropes with surrounding dense scar tissue. Coating of polypropylene mesh with collagen (porcine collagen Pelvitex, Avaulta plus) may improve its biocompatibility with native tissue; however, the effect is limited and cannot cover the detrimental effect of an inadequate textile construction. A greater pore size is considered advantageous, as it allows the admittance of immune cells and greater collagen ingrowth into the construct (Birch and Fynes, 2002b) (page 29 row 34,35) – but it is even more important to assess, which meshes keeps porosity after implantation. A further aspect to increase safety for mesh procedure are purpose designed mesh such as the system made of polyvinylidene fluoride (PVDF) for bilateral sacrocolpopexy (eg. Dynamesh). This specially designed mesh includes small ferro-magnetic particles making it visible on MRI. These meshes may allow checking of correct positioning, study of the impact of stress on the pelvic floor and location of the mesh, if there are complications with time. Mesh materials and design should be adjusted to the specific requirements of the pelvic floor in women and
<table>
<thead>
<tr>
<th></th>
<th>Gessel Yvonne, Meshed-up, <a href="mailto:gesje@me.com">gesje@me.com</a>, Netherlands</th>
<th>4.2.2. Treatment using meshes</th>
<th>in men with focus on risk reduction due to inflammation and scarring. I think PVDF and PVDF constructions as an alternative approved material in the market – has to be discussed within the frame of this paper.</th>
<th>No changes to the Opinion are required.</th>
</tr>
</thead>
<tbody>
<tr>
<td>44.</td>
<td>van der Salm-Kroon Riet, <a href="mailto:n.salm@upcmail.nl">n.salm@upcmail.nl</a>, Netherlands</td>
<td>4.2.2. Treatment using meshes</td>
<td>Ik heb veel last bij het vrijen, de pijn is dan niet uit te houden</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>45.</td>
<td>Verhagen Harry, <a href="mailto:Luna31ft@gmail.com">Luna31ft@gmail.com</a>, Netherlands</td>
<td>4.2.2. Treatment using meshes</td>
<td>Het implanteren van mesh voor behandeling van verzakking mag niet worden overwogen en dient te worden verboden. De risico&quot;s van mesh die niet meer verwijderbaar is zijn te gevaarlijk en veroorzaken meerdere en ernstigere lichamelijke klachten dan de eerst bestaande verzakkingklachten met alle gevolgen van dien. Door krimp van de mesh uiten deze gevolgen zich voor mijn vrouw in: 1. Recidive enterocele &quot;oplossing&quot; mesh heeft niet geleid tot opheffing eerder bestaande klacht. 2. Ondraaglijke pijn waardoor zij is veroordeeld tot herhaaldelijke pijnblokkades op OK en langdurig/levenslang gebruik sterk verdovende pijnstilling waaronder verschillende soorten opiaten. Met alle bijwerkingen en beperkingen die deze geven. (autorijden b.v. niet meer mogelijk) 3. Zenuwbeschadiging. (pudendus) waaronder verstoringen in blaas en darm waaronder pijnlijke lozing en wisseling in incontinentie en obstipatie en seksuele activiteit. 4. Sterke beperkingen in zitten, beperking in langdurig staan en lopen/ traplopen niet meer mogelijk om lichte en zware voorwerpen te tillen. 5. Beperkingen in tillen, bukken, duwen en alle bewegingen die druk geven op de buik en het bekkenbodemgebied. 6. Daarnaast nog door beperkingen kwijtraken van betaalde baan en inkomsten en beperkingen in uitoefenen eigen hobby’s en sociale activiteiten. 7. Ik als haar man, zie ook een verandering in haar mentale kracht welken steeds verder reduceert en</td>
<td>No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>
steeds meer op een Depressie beginnen te lijken als gevolg van de nu al jaren durende strijd tegen de pijn en de machteloosheid mbt de mesh en de gevolgen hier van. 8. tevens vind ik dat de betrokken partijen betere voorlichting moeten krijgen dan wel geven aan de patiënt mbt de mesh in plaats van het bekende vinger wijzen en ontkennen. Dit werkt averechts voor de patiënten en zorgt alleen maar voor meer stress en wantrouwen naar de arts en fabrikant van de mesh.

46. Wurms Daniella, Lwurms@hotmail.com, Netherlands
4.2.2. Treatment using meshes
Ater till startsidan Hi my name is daniella wurms I'm 46 years I have had surgery in 2006 to my belly my uterus has been removed and my ovaries partly after the surgery turned out to be the malicious so I have control every year 2010 I got a lot of abdominal pain after about 3 months they came out that my old surgical wound from inside was ripped in 2011 January I operated on a mat in my stomach after 6 weeks first check much pain after 3 months back still echo a lot of pain after a ct scan a lot of fluid in the abdomen there by pain complaints in april this year operated on moisture from my belly ended after 6 weeks back even pain after 3 weeks back echo much fluid with a syringe blood from my stomach sucked after 6 weeks still have an echo back pain now .in 2014 they try to remove the mesh i had a bacterie staffyokokken on the mesh a m still in pain.

47. Netherlands
No agreement to disclose personal data
4.2.2. Treatment using meshes
daily pain in back and abdomen after posting mech through the abdomen. I am about the harm that I have suffered physically and mentally. They have never told what damage I may incur.

48. Mukhopadhyay Sambit, Norfolk and Norwich University Hospital NHS
4.2.2. Treatment using meshes
Mesh materials and design should be adjusted to the specific requirements of the pelvic floor.

This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents.
with focus on risk reduction due to inflammation and scarring. The uses of meshes for vaginal prolapse surgery should not completely be dismissed as more biocompatible meshes are available. Currently, there are three polymers in use for the construction of surgical textiles. Polyester polymers are usually spun into multifilament. It is very interesting to see that the committee recommends use of polyester for abdominal repair of prolapse. Polypropylene is a cheap polymer which has been used as a monofilament for in surgical sutures for decades. However, polypropylene shows a degree of rigidity and surface cracking after implantation into tissues as it degrades. This leads to degradation and an enhanced inflammatory reaction when compared to the properties of other materials such as polyvinylidenfluoride (PVDF). Increased inflammatory reaction can lead mesh exposure or erosion. PVDF has already been used successfully for years in cardiac and ophthalmic surgery, whereas its use for surgical textiles started in the early 2000. I had been using PVDF sling for stress incontinence since early 2013. To date I have not encountered any adverse effect particularly mesh erosion. Whilst there is published evidence of PP use in prolapse surgery, PVDF being a late entry into the arena of pelvic floor surgery should not be discounted. There are good published evidence of PVDF in animal studies showing favourable outcome when inflammatory markers were measured. Due its property of less inflammatory reaction (biocompatibility), reduced bacterial adherence and structural stability when compared to Polypropylene, PVDF should be included into the recommended material for pelvic floor surgery. Complications related to abdominal use of mesh happen many years after original procedure. Polyester with microporous

<table>
<thead>
<tr>
<th>Trust, <a href="mailto:sambit.mukhopadhyay@nnuh.nhs.uk">sambit.mukhopadhyay@nnuh.nhs.uk</a>, United Kingdom</th>
</tr>
</thead>
<tbody>
<tr>
<td>with focus on risk reduction due to inflammation and scarring. The uses of meshes for vaginal prolapse surgery should not completely be dismissed as more biocompatible meshes are available. Currently, there are three polymers in use for the construction of surgical textiles. Polyester polymers are usually spun into multifilament. It is very interesting to see that the committee recommends use of polyester for abdominal repair of prolapse. Polypropylene is a cheap polymer which has been used as a monofilament for in surgical sutures for decades. However, polypropylene shows a degree of rigidity and surface cracking after implantation into tissues as it degrades. This leads to degradation and an enhanced inflammatory reaction when compared to the properties of other materials such as polyvinylidenfluoride (PVDF). Increased inflammatory reaction can lead mesh exposure or erosion. PVDF has already been used successfully for years in cardiac and ophthalmic surgery, whereas its use for surgical textiles started in the early 2000. I had been using PVDF sling for stress incontinence since early 2013. To date I have not encountered any adverse effect particularly mesh erosion. Whilst there is published evidence of PP use in prolapse surgery, PVDF being a late entry into the arena of pelvic floor surgery should not be discounted. There are good published evidence of PVDF in animal studies showing favourable outcome when inflammatory markers were measured. Due its property of less inflammatory reaction (biocompatibility), reduced bacterial adherence and structural stability when compared to Polypropylene, PVDF should be included into the recommended material for pelvic floor surgery. Complications related to abdominal use of mesh happen many years after original procedure. Polyester with microporous</td>
</tr>
</tbody>
</table>
4.2.2. Treatment using meshes

The multifilament structure is more likely to cause intense inflammation and damage to surrounding viscera.

| 49. | Dr. Obolenski Boris, FEG Textiltechnik Forschungs- und Entwicklungsgesellschaft, b.obolenski@feg-textiltechnik.de, Germany | 4.2.2. Treatment using meshes Page 26, line 12-18 (search terms for literature "polypropylene") Page 37, line 19 By using "polypropylene" as explicit search term other polymers such as PVDF are excluded in the literature search. Used since 1950 PP is obviously the most mentioned material, but this does not mean that it is technically the superior polymer. Starting already in 1987 and well described in the following publication, Laroche and his Canadian research team showed that the stability of PP decreases up to 40% over 7 years compared to less than 10% for PVDF. Laroche G et.al.: Polyvinylidene Fluoride Monofilament Sutures: Can They be Used Safely for Long-Term Anastomoses in the Thoracic Aorta? Artificial Organs19/11: 1190-9; ©Blackwell Science, Inc., Boston (12/1995) Clavé from France showed that PP is not inert used in pelvic surgery. Clavé, Arnaud, Hannah Yahi, Jean-Claude Hammou, Suzelei Montanari, Pierre Gounon, und Henri Clavé. „Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants“. International Urogynecology Journal 21, Nr. 3 (2010): 261–70. A research group from Germany showed that the biocompatibility of all synthetic polymers can be increased using a coating, however uncoated PVDF delivers better results than coated PP and all other investigated materials. Gerullis et al „IDEAL in Meshes for Prolapse, Urinary Incontinence, and Hernia Repair“. Surgical Innovation, 2013. doi:10.1177/1553350612472987. A group from Switzerland and Germany analysed already in 2007 failure reports of Alloplastic implants used for the treatment of stress urinary incontinence and postulated... | The comment has been considered and the text has been changed accordingly. |
new demands for materials and structures of textile implants. Klinge U, Binnebösel M, Kuschel S, Schuessler B: Demands and Properties of Alloplastic Implants for the Treatment of Stress Urinary Incontinence Expert Review Medical Devices 4/3: 349–59, DOI 10.1586/17434440.4.3.349; ©Future Drugs Ltd., Austria (2007) Open letter to the SCENIHR committee: To whom it may concern, FEG Textiltechnik Forschungs- und Entwicklungsgesellschaft started in 1992 as a research and development company. FEG has its own research team consisting of chemical, biological, material and textile engineering experts and has been a partner in more than 20 national and international public funded research projects. After 10 years of extensive research we decided to set up our own manufacturing line of textile implants in 2003. Our aim was (and still is) to use latest technology and knowledge to produce optimal surgical implants. Due to the technical challenges in dealing with fluoride and knowing that the PVDF raw material is approximately 20 times more expensive, we decided to follow our mission to use the most appropriate material for highest patient safety. FEG Textiltechnik is an independent fully integrated SME manufacturer of synthetic, non absorbable textile implants for hernia, incontinence and prolapse repair. Our product range consists of state-of-the-art open pore, surface minimized warp-knitted structures made from Polyvinylidene fluoride (PVDF) and/or Polypropylene (PP) monofilaments. We have no interest (especially no commercial one) in promoting any polymer material. Our company philosophy and promise to the patient is to use the actual best available polymer material, which is without a doubt, PVDF. For the future we are sure that other materials will arise and we will carefully check that all
new developments are incorporated into our product.

4.2.2. Treatment using meshes

Chapter 4.2.2. line numbers 18 ff (Comment Liedl - mesh material) Chapter 4.2.2. Implantation techniques of mid-urethral slings (MUS). Line 41 ff (Comment TFS-Liedl). Comment by Dr. Bernhard Liedl, President of International Society for Pelviperineology (ISPP) concerning chapter 4.2.2. Treatment using meshes In chapter 4.2.2. the following papers from Sivaslioglu et al. (2012), Sekiguchi et al. (2009) and Petros and Richardson (200) are not cited. So the TFS (tissue fixation system) sling which is the first published minisling has not been mentioned in the text nor have the data of Sekuguchi and Sivaslioglu been cited which show the efficacy of this mini-sling and the superiority of this sling in comparison to transobturator sling. Sivaslioglu AA, Unlubilgin E, Aydogmus S, Keskin L, DolenI. A prospective randomized controlled trial of the transobturator tape and tissue fixation mini-sling in patients with stress urinary incontinence: 5 year results. J Urol 2012; 188:194-199

Quote from SCENIHR Mesh size and Clinical Outcomes (p4)“Clinical outcome following mesh implantation is influenced by material properties, product design, overall mesh size, route of implantation, patient characteristics, associated procedures (e.g. hysterectomy) and the surgeon’s experience. The SCENIHR
recommends that such aspects should be taken into account when choosing an appropriate therapy.” We agree totally with this statement, in particular the mesh material, size and surface being a major factor in complications. Thus it is important to consider alternatives to Polypropylene (PP) as a mesh material which is known to show a degree of rigidity and surface cracking after implantation into tissues as it degrades. Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants Arnaud Clavé & Hannah Yahi & Jean-Claude Hammou & Suzelei Montanari & Pierre Gounon & Henri Clavé Int Urogynecol J DOI 10.1007/s00192-009-1021-8 E.g. Polyvinylidenfluoride (PVDF) has already been used successfully for surgical textiles since the early 2000s and shows a higher biocompatibility and biostability when compared to the properties of PP. Comparison of Long-Term Biocompatibility of PVDF and PP Meshes C. D. Klink, K. Junge, M. Binnebosel, H. P. Alizai, J. Otto, U. P. Neumann, U. Klinge Journal of Investigative Surgery, 24, 292–299, 2011 Copyright © Informa Healthcare USA, Inc. ISSN: 0894-1939 print / 1521-0553 online DOI: 10.3109/08941939.2011.589883 Next to the material properties the mesh design, best described by the porosity and the dynamometric properties, are of utmost importance. The design should always be adjusted to the specific requirements of the pelvic floor in women and in men with focus on reduced material/surface by sufficient strength and stability. Elongation of textile pelvic floor implants under load is related to complete loss of effective porosity, thereby favoring incorporation in scar plates. Otto J, Kaldenhoff E, Kirschner-Hermanns R, Mühl T, Klinge U. J Biomed Mater Res A. 2014 Apr;102(4):1079-84. doi: The comment has been considered by SCENIHR. The text has been changed accordingly.
In this context, the midurethral sling in an optimized textile construction has the least mesh-related complications as it uses only a thin strip of mesh.

| 51. | Charles Shields, International Urogynecological Association, chuck@iuga.org, USA | 4.2.2. Treatment using meshes | Page 26 Lines 31/38 Although autologous graphs degrade the results of the autologous fascial sling match anything else in the literature. Page 27 Line 11/25 They should not refer to allografts as non-immunogenic. The host response with subsequent degradation confirms that they are immunogenic. At the most they can be referred to as relatively non-immunogenic. Page 28 Line 8 / 19 Similar point to above Page 29 Line 31/33 The authors acknowledge that Mersilene(Polyester) is associated with high erosion rates and complication rates. This should dictate against proposing Polyester as a suitable mesh. Page 32 Line 9/13 Difference in inflammatory response noted. Line 19/21 SPARC and TVT are identical meshes. These studies are not relevant Page 34 Line 32 The authors seem to gloss over the 10% groin pain complication rate associated with the Transobturator techniques. This should be highlighted, as it is almost impossible to resolve. All the papers compare absolute complication rates between TOT and TVT. They fail to stratify according to severity. Thus a higher incidence of bladder injury is not important as it is resolved at the time of surgery whereas a groin complication has a chronic nature. NO COMMENT ON THE MALE SLINGS Page 37 Line 18 I am not sure that there is sufficient justification in the international literature to recommend only two meshes. There are both theoretical and published reasons to avoid the use of Polyester. There | Please see the answer to comment 35 |
has to be provision in this report to recommend a strategy introduce new materials. Again we refer to the IUGA round table recommendation on the introduction of new materials and operations. Line 31/35 In posterior mesh placement the mesh is not always attached to the levator ani muscles. Some surgeons limit attachment of the mesh to the posterior wall of the vagina alone and avoid attachment to the levator ani muscles. There is no consensus on the type of suture used to attach the mesh to the vagina or levator ani. There are reports of the use of non-absorbable, absorbable and delayed absorbable sutures. It is important that the document recognizes these differences and that the clinical consequences at present are unknown. No technique can be promoted or discontinued with the current knowledge.

Page 38 Line 1/3 We do not think there is sufficient justification to recommend a laparoscopic approach over an open laparotomy for sacral colpopexy. Either approach is justified and the decision made according to the skill mix of the surgical team. Likewise there is equal justification to perform the procedure robotically from a surgical point of view. It is the responsibility of individual organisations to make a decision on the cost effectiveness of the robotic approach. We do not believe that this committee has the expertise or knowledge base to make this decision, neither is that now the priority.

This point in more about the technique than the material and for this reason we refer to the review made by Cochrane in 2015.

| 52. | Zuidervaart Agnete, Zuidervaart@xs4all.nl, Netherlands | 4.2.3. Results of treatment using meshes | After anus amputation, rectum cancer a mesh was used to repair the bottom of my pelvis. It didn't work. Had three ruptu reoperations and one operation because of too much pain. The mesh causes problems also for other uses than urogenital use. I cannot sit for longer than 20 minutes. And having a social life became impossible | This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents. |
| 53. | Smeets Truus, | 4.2.3. Results of I am a victim of the mesh, It is removed, but | This is a report of a personal |
| 54. | Thorig Edwina, edwientje@msn.com, Netherlands | 4.2.3. Results of treatment using meshes | I had a vaginal mesh in 2009, after this surgery I had a lot of complaints that I couldn't explain. One of the complaints I have had is sitting, riding a bike, too long walk and sexual problems. After 4 years I became aware that the problems I suffered were because of shrinking of the mesh. Now I had to have another operation to remove the mesh. My problems are not over yet. Still there is some mesh in my body. I will not advise people to do this operation! | This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents. |
| 55. | Urban Janis, janishietala@yahoo.com, United States | 4.2.3. Results of treatment using meshes | As a physically active healthy woman at the age of 58 my life was about to change forever. On December 15, 2011 I walked into the Same Day Surgery Center to have what was explained to me a procedure to help with SUI, noninvasive in an out. I was told nothing more. Just before I was wheeled to the OR I asked the Doctor if it was mesh that he was going to place inside me. "Yes, he replied" I said "NO, Doctor Borth a general surgeon told me and my husband to never put mesh in your bodies". Husband saw him for a belly button hernia. His reply "Oh nonsense, I have been placing mesh for 2 years and have had no problems". And away I went. I was implanted with a Gynecare TVT Exact retropubic sling manufactured by Ethicon. When I woke up I had so much pressure in my pelvic area, it felt like pelvic area was tied around my neck. I could not urinate and was sent home with a catheter for 6 days. A short time after arriving home and sitting at the computer my lower back began to hurt, the pain was deep and I could not get up, stand up | This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents. |
straight or walk, sitting or laying down was excruciating bending leaning over or crawling was the only position that relieved the pain. It took several weeks to straighten out. Within 6 weeks I became totally incontinent, when I laid down the radiating pain started in my pelvic and hips, down both legs to my feet. There was no position I could use to be comfortable, if I laid there suffering I could not move my legs at all. The pain was severe. I feel ill all the time. Husband would help me get them to move. Then my toe nails all turned black, developed Lichen Sclerosus of the vulvar, skin lesions, itchy, scaly, dry, cracked skin issues, sores that have still not healed, hair loss, teeth at the gum line turned black, and break off, abdomen, legs, ankles, feet severely swell. I can not stand or walk for more then a few minutes, the pain overwhelms my whole body that begins at the pelvic and lower back. I have never had a weight problem; I have gained 80 pounds since my mesh implant. I've been told by many Doctor's and Nurses that mesh could not cause any of these issues. Time will tell.

4.2.3. Results of treatment using meshes

Page 39 Lines 13 onwards We are not sure that this committee is in a position to make recommendations about the effectiveness of the various types of sling procedures for incontinence. Bodies such as NICE and the various specialist societies are far better placed to perform this function.

Page 41 Line 22 /41 We agree with the overall conclusion. This section should include a comment on the occurrence of groin pain which is specific to the transobturator route.

Page 45 These tables seem to have been lifted directly out of the original paper by Milani.

Page 51 Line 3/11 In keeping with the conclusion in the Cochrane review of surgery for POP the authors have agreed that the anatomical results of a mesh based repair are
superior to a native tissue repair but conclude that for primary cases the long term benefits remain unproven and therefore the techniques utilizing mesh should not be used for primary surgery. We are unsure about the conclusion that surgery involving mesh is associated with higher rates of new onset stress urinary incontinence. Similar rates are reported with a range of operations for the treatment of POP. These range from transabominal procedures using mesh to transvaginal procedures using mesh as well as transvaginal native tissue repairs. This statement is confusing and should be removed. We do not agree that there is any evidence that the use of mesh in posterior wall surgery results in higher rates of objective cure. The Cochrane review on posterior wall surgery concluded that there was no evidence that mesh augmented surgery conferred any advantages...

Line 16/21 The conclusion that the use of mesh results in significantly higher rates of de novo POP of the untreated vaginal compartments is misleading. A review of a lot of the articles that conclude that the untreated compartments demonstrate higher rates of subsequent prolapse shows that these patients had significant prolapse in these compartments demonstrable at the end of surgery. I.e. they should have had that compartment operated on at the time of the initial surgery! This more likely reflects the fact that increasingly naive surgeons were using mesh and failing to appreciate the degree of prolapse in other compartments.

Page 52 Line 14/22 We do not believe there is scientific evidence of post operative pain specific to the presence of mesh. We agree that the incidence of pain is similar after native tissue repair. This point needs to be emphasized as well as the point that removal of mesh will not necessarily result in...
<table>
<thead>
<tr>
<th>Page</th>
<th>Name</th>
<th>Email</th>
<th>Role</th>
<th>Paragraph</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>Shields Charles, International Urogynecological Association, <a href="mailto:chuck@iuga.org">chuck@iuga.org</a>, USA</td>
<td></td>
<td>4.2.5. Mitigating risks through patient selection and counselling</td>
<td>We agree with these conclusions.</td>
<td>No changes to the text are required.</td>
</tr>
<tr>
<td>58</td>
<td>Somerfield Michelle, <a href="mailto:Shellys125@yahoo.co.uk">Shellys125@yahoo.co.uk</a>, United Kingdom</td>
<td></td>
<td>4.2.6. Patient counselling</td>
<td>After undergoing surgery for SUI in February 2014 for a TVT my life has completely changed due to not being given the full facts as noted in the report by the surgeon. The operation was done via day surgery as explained and would be a simple operation, you are then discharged with no follow up appointment. Although no pain in the first few months I knew something was not right in the vaginal area and I was still suffering with SUI, I spoke with the original surgeon who would see me again however I needed to go back through my doctor to be referred. September 2014 I saw the original consultant who confirmed I had vaginal mesh erosion and I had an operation to correct this 2 weeks later, this is when severe pain started. 6 weeks later in November I had a follow up appointment and the mesh was still eroded I had corrective surgery there and then and also steroid injections in an attempt to stop pain in the pubic area. I am still suffering debilitating pain in the pelvic area and vaginally. Following a follow up appointment I was advised I had no mesh erosion, different creams and antibiotics were given in an attempt to help with the pain and the tender area, Still with no conclusion after another hospital appointment I had an MRI scan to ensure there was no further issues before I agreed for a removal of the tape as the pain seemed to be unexplained, I had a second Opinion privately where I was told the mesh was still eroded and I would need to see a urogynaecologist who was specialised in Tvt, POP. After the private consultation with the urogynaecologist I had another operation to</td>
<td>This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents.</td>
</tr>
</tbody>
</table>
remove part of the mesh and repair the erosion. Following the histology report I was diagnosed with vaginal adenosis. I was also referred to a professor regarding the pain who confirmed that I had pudendal neuralgia due to the nerve being damaged at some point during my care. I then self-referred privately to one of only two surgeons in the UK who can competently remove the mesh Laparoscopically who agreed the best way forward was for complete removal of the mesh. Following removal of this mesh it was confirmed to me that the mesh was eroded vaginally again and also in my muscle. When patients are being offered this as a final resort to help SUI it must be made perfectly clear that the complications and life changing pain can outway the benefits as it was certainly not made clear to me and other woman found via groups that this could be the case. This is a permanent device not one that should be removed and it is more complicated to remove than to put in. I believe only competent Urogynaecologists should offer this surgery who are also competent to remove fully if there are complications.

| 59. | Shields Charles, International Urogynecological Association, chuck@iuga.org, USA | 4.2.6. Patient counselling | Page 55 line 25 to Page 58 line 31 We agree with these conclusions. | No changes to the Opinion are required. |
| 60. | Shields Charles, International Urogynecological Association, chuck@iuga.org, USA | 4.2.6. Patient counselling | Page 57 Line 25/ Surgeons in the UK need to be aware of the Montgomery ruling. As a result of this all patients need to be made aware of all the options including the option of doing nothing. They need to inform patients of all possible complications. | No changes to the Opinion are required. |
| 61. | Mann Suki, Mesh injured, suki.mann@ntlworld.com, United Kingdom, | 4.2.7. Risk assessment and recommendations by National Associations | Public consultation on the Preliminary Opinion on the safety of surgical meshes used in urogynaecological surgery - Directorate General for Health and Food Safety This report was done by a known pharma paid consultant and we were not expecting much this report. There are 2 alarmed things that | The rules for the composition of the working group and the public consultation are described in the Rules of Procedures of the Scientific Committees. These are personal |
stick out 1) they are saying the SUI slings have less complications - SUI slings are the TVT-O and goes through the leg. I have sent you articles where the report says tvt-o are more harmful from consultants and there is a medical study that shows the % of complications is higher in tvt-o and the complications more serious because if goes close to the leg nerves and arteries. This sling can only be inserted vaginally - and they say that should be avoided in the pop - that is because bacteria picked up and sitting on the mesh - causes massive health problems going into the tissue of women and on removal - infections are great. So SUI slings should be stopped . 2) it says only trained surgeons to put in - how long have we been trying to get the message across that surgeons are not trained to take them out! A half day course to put in and then the protocol that this report suggests surgeons follow is to leave women 6 months under observation and then offer pain. Management - I have seen the training notes!! England does not have an effective method of taking these out, does not react quick enough so permanent damage is avoided AND does not tell any women this is a permanent fixture and is not supposed to ever be removed - and in removal can damage more nerves and arteries- You don't to be a surgeon to see this pelvic area in women has thousands of nerve endings - you just have to google on YouTube and look at a SUI insertion and Google an anatomy page - anyone can see what dangers there are! Next the toxic plastic chemical material was not addressed - nor that the plastic shrinks and we are not wearing the implant bracelets that should alert emergency crew in hospitals that we have a plastic mesh implant that melts near heat!!!! I don't know how many times I have written about all this to all bodies involved and have spoken so many times about the considerations, not providing scientific evidence to improve the scientific basis of the opinion.

No changes to the text are required.
consent form where surgeons don't show you what is implanted only tell you it's tape... We are going round in circles and these reports are taking forever and saying the same thing over and over again - without looking at us - the flesh and blood - the physical evidence that this is hurting women . I plead with you to be harder in the regulatory bodies and have more in depth questions and get people who are NOT connected to pharma companies to do them!! This report is a disgrace for the time it took!! Suki mann Sent from my iPhone

This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents.

I got a Mesh in 2010, I'm an invalid ever since, 7 operations trying to remove the plastic later its growing worse and worse. The plastic is hurting my belly en growing into my muscles and organs. Bringing severe pain every moment of the day. Can't sit, cant bike, can't sleep, lost my job, lost my social life. It's becoming not only a fysical problem but even a financial problem, where is the end of this trouble ??? Please don't do this to more people !!!

This comment has been considered by the SCENIHR. The text has been changed accordingly. The Amid classification has been used because this is cited in most clinical guidelines.

Polyvinylidene Fluoride (PVDF) is definitely a proofed alternative to common Polypropylen (PP) surgical meshes. Especially in the light of the mentioned aspects in line 2 - 11 PVDF shows clear advantages to PP. Otto, Jens, E. Kaldenhoff, R. Kirschner-Hermanns, Thomas Mühl, und Uwe Klinge. „Elongation of textile pelvic floor implants under load is related to complete loss of effective porosity, thereby favouring...
the mesh pores and reflecting the state of the art of modern lightweight open-porous surgical meshes. As most of these meshes showed pores far larger than 75 µm, a revised classification was necessary. Currently the most appropriate proposal for a surgical mesh classification was given by Klinge und Klosterhalfen. I suggest to SCENIHR that it should use these updated classification for the current Opinion. Klinge, U., und B. Klosterhalfen. „Modified classification of surgical meshes for hernia repair based on the analyses of 1,000 explanted meshes.” Hernia 16, Nr. 3 (5. Mai 2012): 251–58. doi:10.1007/s10029-012-0913-6.

Shields Charles, International Urogynecological Association, chuck@iuga.org, USA

5.1.1. Risks associated with the use of mesh in urogenital surgery

Page 61 Line 30/33 This report cannot endorse the use of type III microporous multifilament polyester. This flies in the face of current knowledge/ Any recommendations must also make provision for the introduction of new materials in the future. Once again we would recommend the use of the guidelines produced by the round table conference on the IUGA in 2012. Blanket endorsement of two specific products is biased and unfair on other products. There is no certainty that Type I polypropylene is without problems and therefore research in the use of this substance should be ongoing.

The text of the Opinion was changed accordingly

65. Dowdall Jane, dowdalls@rogers.com, Canada

5.1.2. Identification of high risk patient groups

It was suggested that limiting the amount of mesh could improve the outcome. That is certainly not true in my case, as well as thousands of other women. The side effects of the TVT-O (very small amount of mesh) that I had implanted, has caused continual pain and forced me to be on disability. Partial mesh removal, since the arms of the mesh are extremely difficult (if not impossible) to remove, has not solved the problem. Polypropylene, the material used for mesh, is not inert as the manufacturers claim, and is causing a myriad of health issues. Court cases

This is a report of a personal case. The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents.
in the USA have ruled against mesh manufacturers time and time again, and ruled that these products are defective. How many women must suffer before something is done?

<table>
<thead>
<tr>
<th>67.</th>
<th>Netherlands</th>
<th>5.2. Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>No agreement to disclose personal data</td>
<td>Whereas the complications erosion, shrinkage, inflammatory reaction, increasing stiffness of the mesh, tissue thinning around mesh and infection are directly related to the material mesh in the pelvic area also colorectal mesh surgery should be researched. In case complications occur these consequences are also debilitating including severe pain and serious functional problems. Even if the risk rate in abdominal colorectal or urogynecological mesh surgery and sling surgery are less than in transvaginal surgery, the complications can be extremely serious and therefore in all cases other solutions or surgery without mesh in the pelvic area should be considered first. It does not make sense to conclude that mesh used for colorectal procedures can be offered to patients as an appropriate procedure when this assumption is based on literature and research where mesh complications were not specifically included as part of the investigation. New information about mesh complications in the pelvic area has to be taken into account also for colorectal surgery. From an ethical point of view research should be done on mesh complications to help patients who already suffer from complications and for specialists to learn about the early signals and to understand the serious consequences of complications. Based on the research it should be concluded that mesh in the pelvic area only should be used if there are no other suitable possibilities. Patients have to be informed comprehensively about the possible complications.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>68.</th>
<th>Noé Guenter, Comunal Clinics Rhein-Kreis Neuss</th>
<th>5.2. Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>The gold-standard in apical defect repair is still the sacro-colpo-pexy. In the last decade</td>
<td>The comment on new materials has been considered. The text</td>
<td></td>
</tr>
</tbody>
</table>
we have high experience in laparoscopic apical defect repair in two different approaches (sacropexy and pectopexy). (Approx. 1000 Surgeries) Since 2007 we use PVDF structures for these approaches with great success. The benefit of the material is on one hand the optimal manageability and the high form stability in long term. On the other hand the slow reaction of the tissue leads to an optimal fibrosis with a low risk of adhesions. Due to the high amount of surgeries we had the opportunity to perform laparoscopy short- and long-term after the approaches. Therefore we have experience in the long-term stability and adhesions outcome of the material. Not in a single case we had to explant the PVDF-structure and the infection – rate is very low. To our point of view the material can be recommended for the apical defect repair of bowel prolapse. Ref. Laparoscopic pectopexy: A randomised comparative clinical trial of standard laparoscopic sacral colpo-cervicopexy to the new laparoscopic pectopexy – short-term postoperative results Archiv of Gyna Obst 2012 DOI 10.1007/s00404-012-2536-7 G.K. Noé; C.Spüntrup; M.Anapolski , Value of clinical and laboratory inflammation factors in the postoperative period after laparoscopic urogynecological surgery Gynecologic and Obstetric Investigation Vol. 79, No. 1, 2015 DOI: 10.1159/000364868 G.K. Noé, M.Anapolski, M Soltész, C. Spüntrup, T.Schollmeyer, I. Alkatut Pain medication requirements after sacropexy and combination interventions A cohort study JSLS. 2014 Jul-Sep; 18(3): e2014.00036 JSLS DOI: 10.4293/108680814X13938810111666 G.K. Noé, S. Soltész, S Schiermeier; W. Hatzmann, C. Spüntrup M. Anapolski Laparoscopic Sacropexy - An Underestimated
<table>
<thead>
<tr>
<th>69. de TAYRAC Renaud, Nîmes University Hospital, <a href="mailto:renaud.detayrac@chu-nimes.fr">renaud.detayrac@chu-nimes.fr</a>, France</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2. Recommendations</td>
</tr>
<tr>
<td>It seems not logical to recommend mesh in recurrent prolapse only (or mainly), knowing that only one RCT has been done in recurrent cases (Withagen M et al.), and many others in</td>
</tr>
<tr>
<td>The scientific rationale is clearly written in the text. No changes to the Opinion are required.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>70.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>71.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>72.</td>
</tr>
</tbody>
</table>

Primary cases ... which means that based on literature mesh surgery for vaginal cases should be recommend mainly for primary cases!
the terminology firstly the term erosion is
used and according to the current IUGA
classification this is not correct. The correct
term extrusion (see Haylen et al IUJ
terminology). Secondly the term mesh
shrinkage should be used in conjunction with
the scar tissue that contracts around the
mesh.
Broadly speaking we welcome the suggestions
in terms of introduction of a certification
system based on international guidelines and
established in co-operation with relevant
European Surgical associations and registries
but have some specific points and feel that
there are important messages about
standards in training and practice. Exec
summary Continues to use erosion as a term
Line 8 page 8 Explore surgical solutions. We
would have referenced NICE guidance here as
a European nation document with guidance.
There may be other national member state
documents that relate to this. Some will look
at efficacy, whilst others (NICE) examine
efficacy within an economic model. These
groups need to referenced. There are
theoretical concerns with type 3 polyester
mesh (even inserted abdominally) as limited
data are available. The theoretical concerns
suggest added caution. As with all procedures
careful audit should be mandatory.
There are 2 sources of information that do not
seem to be included for retropubic tapes.
Firstly the 17 year data on the original TVT set
by Nilsson and secondly the original Austrian
database on TVT.
As a comment about colposuspension the
results in the Ward and Hilton series did not
show any inferiority with regard TVT and they
do not report pain as a significant issue in
their 5 year follow up. In addition the original
article is referenced but the 5 year follow up is
not.
The document comments on work on
comprehensive informing patients. We would highlight the existence of the BSUG database here. The numbers on this are now sufficient to add to the debate. There are several units who can now quote their own data and we would suggest that any new registry does this in conjunction with BSUG as it will make data comparable. We feel that mandatory registers will give more meaningful data, as the data set will be complete. Ideally each unit should have knowledge of their own outcomes. In the UK this fits into HQIPP and outcomes framework. However it needs to be appreciated that small data series form individual units may give misleading outcomes. The document states that there is a need to Establish European registries. We would respectfully suggest that there is an opportunity to work collaboratively here. We have already established the BSUG database and spent a number of years refining the dataset and database. There is an opportunity to standardise this across Europe, which will strengthen the utility of other systems. There remain important questions as to how are these to be policed to how ensure that mandatory which presumably requires European law? There are also issues as how they would be funded and there needs to be further direction if this document is to truly move this issue forwards. The document could also give endorsement to other relevant documents e.g. the mandating of adoption of the outcome measure documents of IUGA for prolapse surgery ensuring all registered studies have built in follow up for 5 years (IUGA standardisation of outcome for prolapse surgery) There are references to training and the need to be trained. In the UK there are established RCOG training programmes at 2 levels Advanced Training Skills Module and Subspecialty training. There is also an established training programme in Holland.
There needs to be more guidance about what training should constitute and the minimum standards required. There will need to be narrative when this training occurs. Such this be prior to or post CCT. There may be variations to timing of training across Europe. Likewise is there a role for specialist centres and how would these develop?

Page 12 line 29 Olsen data needs correcting as this refers to all surgery not recurrence (several subsequent studies have reinterpreted these data and redefined the recurrence rates)

Page 16 possibly the most useful reference on the incidence of prolapse is the Swift. In the UK Nadia Ali Ross published her thesis looking at the natural history of prolapse. The report mentions that procedures and materials must have an acceptable risk/benefit ratio; but this is not defined and there needs to be some guidance on how this is assessed. It is also important to mention that these will change as techniques are refined. Likewise they state that these be designed based on state-of-the-art knowledge by observing the principles of inherent safety; which need to be described or defined Similarly; have been proven safe and effective by clinical evidence then this should ideally quote the IUGA outcomes document. However, in the case of meshes no mandatory testing of the device and not even a third-party test of its design dossier is requested. We would hope that a recommendation would be made here.

P 20 line 31 space needed after Pereyra

P21 urethral injection data line 7 well out of date an there is much more data on Bulkamid

P22 L 28 doesn't mention Duloxetine

P23 L21 colposcisis up to 25% SUI rate

P30 LINE 27 Bazi et al showing how similar Advantage and TVT are (missing word Boston)

Diagram fig 1

P 31 advantage no degradation

The text is clear. No changes are required.

Policy making and risk management do not fall into the scope of SCENIHR.

Text changed.

The Opinion focuses on mesh use.
P 34 L 15 incomplete? L 24 spelling injury...
Line 25 quotes a lower extrusion rate 1% L 41
SIS term should be SIMS not SIS as this
confuses mesh
P 36 should include information on SIMS trial
P37 the use of polyester (mersilene). See
earlier comment L 38
P37 there is no discussion about suture type
and this is potentially a missed opportunity.
The UK experience has shown a significant
extrusion rate using braided sutures (ethibond) but this has disappeared since
stopping using these about 7 years ago. There
is one publication in the orange journal about
suture type from the UK.
P 39 use term SIS which should be SIMS. It is
important to have consistency as SIS is a type
of biological graft. However we appreciate that
different biological meshes do not necessarily
behave in the same manner in terms of
efficacy and side-effects.

P50 The outcome data for mesh repair
appears to be worse with mesh in posterior
compartment with combined repair. This
should be highlighted. P51 conclusion
Evidence superior for anterior (no or very
limited role posteriorly) but subjective and re-
op rates not sig different P52 Dyspareunia
may not be right end point composite absolute
rates (apareunia as well as dyspareunia
important)
P55 trainers need to be vetted? More details
are suggested, so potential to put peer review
into training. A competency model would be
ideal.
P 55 L30 mistake
P 57 L16 if can't be used in primary cases how
can previous vaginal surgery be a risk? This
needs additional comment.
P 57 L22 grade of prolapse requires
clarification as have said grade 2 or less
unlikely to be of benefit

Reference not given.
No changes in the Opinion are
required.

Comment not clear.
Text corrected.
The difference between SIS and
SIMS is given in the glossary.

Comment not clear.
No changes in the Opinion are
required.
No RCTs cited. No changes in
the Opinion are required.

An question of terminology. No
changes in the Opinion are
required.

No changes in the text are
required.
Opinion Are specific meshes, in terms of designs and/or materials, considered to be of a higher risk? If possible list and describe the risks. (Q1) In this Opinion, the SCENIHR considers the uses of synthetic non-absorbable meshes. Current consensus is that Type 2 (microporous, less than 10 microns, mono and multifilament) and sub-micronic and monofilament are not appropriate for use in this clinical context. If this is the Opinion then surely the report shouldn’t approve polyester abdominally. Currently, there is no sufficient evidence for other materials. We would agree. Are certain surgery techniques of higher risk? If possible list and describe the risks. (Q2) All synthetic materials are associated with the risk of mesh exposure. The correct term is extrusion. The SCENIHR acknowledges the efficacy and use of implanted meshes for SUI but recognising the absence of long-term data, This should read limited L-T data. The SCENIHR acknowledges that vaginally implanted mesh for POP is associated with increased risks compared to mesh implantation for SUI. Its use should be restricted to patients defined according to established evidence-based clinical guidelines. SCENIHR acknowledges the importance of established guidelines, clinical experience and adequate training of the surgeon but there are no descriptives here which we would hope would be included. In the light of the above, identify risks associated with use(s) of meshes other than for urogynecological surgery and advise if further assessment in this field(s) is needed. (Q8) Such as? Three needs to be more detail in this recommendation. Overall broadly speaking BSUG welcomes this provisional report and the emphasis on better research using established methodologies; the recognition that new methodologies may need to evolve and be defined. The document

<table>
<thead>
<tr>
<th>Outside the scope of SCENIHR. No changes in the Opinion are required.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Text corrected.</td>
</tr>
<tr>
<td>Text is clear. No changes are required.</td>
</tr>
<tr>
<td>No specific recommendation is made. No changes are required.</td>
</tr>
<tr>
<td>No changes in the Opinion are required.</td>
</tr>
</tbody>
</table>
focuses on what evidence is available rather than where are the gaps in out knowledge (e.g. reference to suture type as well as mesh type). BSUG also welcomes the emphasis on training and data collection, but would hope the final report would be able to give more data and incorporate more emphasis on the existing standardisation and standards documents from IUGA and UKCS minimum standards documents. We would hope that the development of databases should be based on the BSUG database, which has spent 10 years developing and refining the data to capture. Using this as a template would shorten the curve for other societies/national bodies in developing a system. We would support a move to legislation to mandate the collection of data in its most complete form possible and it is only then that we will be able to truly accurately know the incidence of problems. BSUG would welcome the opportunity to work with SCENIHR on the review and finalisation of the document.

| 73. Shields Charles, International Urogynecological Association, chuck@iuga.org, USA |

Federal Agency for Medicines and Health Products, meddev@fagg.be, Belgium

Opinion

Summary of the Evaluation by two Belgian experts of the preliminary SCENIHR Opinion on the safety of surgical meshes used in urogynecological surgery: Stress Urinary Incontinence (SUI): Currently we opt for a mesh treatment when lifestyle changes and pelvic floor rehabilitation do not offer improvement. The polypropylene mesh has shown its effectiveness and improves the quality of life of the patients. Moreover, the benefits and risks of synthetic mid-urethral sling surgery are well documented. In agreement with the SCENIHR report, the risks associated with the use of mesh material for the treatment of urinary stress incontinence are indeed of a smaller order of magnitude than those associated with the use of mesh material for pelvic organ prolapsed (POP) treatment. However, as stated in the report few long-term data are available on the safety and performance of synthetic non-absorbable meshes.

Pelvic Organ Prolapse (POP): Transabdominal implantation of meshes for prolapse repair is well documented. It consists

No changes to the Opinion are required.
of a technique with good results but it is more difficult, more invasive and more expensive than vaginal implantation. The rates of complications are however much lower for abdominally placed mesh compared to transvaginal placement of the mesh. The vaginal route was originally favored as it is easier to apprehend the surgical technique, however the risks associated with the use of mesh for the treatment of POP via the vaginal route are bigger than originally thought. This reveals itself in a higher exposure ratio but also more reoccurring prolapse in other compartments and in a higher risk for the development of de novo stress urinary incontinence. The exact determinants for these complications are not known yet which entangles adequate and selective offering of the technique. However the report does not state that vaginal meshes are obsolete but rather underlines the importance to limit the conditions for use of the technique with regard to the patient, surgeon and mesh. By all means patient counseling is of great importance, patients should be clearly informed of the risks associated with mesh surgery.

Regarding the patient, the technique should indeed be restricted to patients defined according to established evidence-based clinical guidelines. For instance vaginally implanted mesh for POP could be offered for those patients suffering from recurrence of pelvic organ prolapse without associated procedures (e.g. hysterectomy) and when implantation via the abdominal route would impose to many risks (e.g. history of extensive surgery or preceding sacrocolpopexy, no possibility for general anesthesia, ...) and those with potentially other risk factors (severe prolapse, co-morbidities, genetic predisposition, ...). These indications for use could be recorded in a
guideline whether or not multidisciplinary. Regarding the surgeon, he/she indeed needs to be considered an ‘expert’. The consulted experts fully agree upon the recommendation in the SCENIHR report to train the surgeons and introduce a certification system for surgeons. However such a European certification system still needs to be developed and other potential indicators of expertise which could be used are participation in international studies/registries, international publications with citation index and H index and/or offering multidisciplinary consultations.

Regarding the mesh, one should indeed use type 1 polypropylene meshes with the smallest surface area possible. The experts also agree that the establishment of European implant registries is an urgent prerequisite. Upon the expert’s Opinion it is feasible to define a selective group of patients for whom the benefits of vaginal meshes outweigh the risks. By strict regulation and adequate documented decision-making it should remain possible for these patients to offer such an option. All further use should indeed be registered to fulfill the question to gather more data.

Conclusion
Both experts described the SCENIHR report as being a detailed and accurate report that well assembled the existing evidence. The formulations are nuanced and different gaps in literature have been identified. Both experts agree with the conclusions and recommendations in the report. In line with the report the experts acknowledge and emphasize the importance of established guidelines, clinical experience and adequate training of the surgeon as well as the importance of further clinical research to gather evidence and establish these evidence-based European guidelines.
| 75. | **CONNELL ROWAN**, Benenden Hospital, Kent UK, rowan.connell@nhs.net, United Kingdom |
| Opinion | I am writing as a Consultant Urogynaecologist, of 12 years. I have been using mesh for POP and incontinence for 15 years. I used to perform Lap SCC but have not for 8 years as the anatomical results are less good, and I do feel it should be treated as research as it is not the same operation in the UK as an open SCC of the past (anatomically) I am still using polypropylene mesh for incontinence, rarely uphold for recurrent prolapse or in women with short vaginas after hysterectomy, and for a year I have been using PVDF abdominally for prolapse. We must be careful about the use of mesh |
| 76. | **De Wilde Isidora**, Patients organisation www.meshedup.eu, Doradw@hotmail.com, Belgium |
| Opinion | The TVM’s are used too soon. More study’s have to be done before the widespread and use in patients. Women don't have a clue where to report the complications, doctors don't report...how can records off the few reported complications been reliable? Why here is no place for patient groups to discuss the real and very important health concerns after POP-operations with mesh. +600 women in the Netherlands and Belgium are terrible hurt by those meshes. Only 1% in Belgium is reported by a gynaecologe to the FAGG (federal agency for health :medicine and medical devices) and only 10% of the women have make notice to FAGG...what with the other 89% ? There is a loophole in the whole regulation, registration, information and control system. What's our concern? What with the women who suffer from the injures, what is the best solution to relieve those women from there pain and complications? Mesh out, or leave the mesh in place? Which operation after a mesh failure?.... Women in our groupe have a lot off unanswered questions. There is also a worldwide inquiry and mesh hurted people are organising themselves to exchange information. Facebook groups, and websites with |

<p>| 74 | No changes to the Opinion are required. | No changes to the Opinion are required. |</p>
<table>
<thead>
<tr>
<th>77.</th>
<th>cosson michel, university hospital Lille France, <a href="mailto:michel.cosson@chru-lille.fr">michel.cosson@chru-lille.fr</a>, France</th>
<th>SCIENTIFIC RATIONALE</th>
<th>No changes of the Opinion requested</th>
</tr>
</thead>
</table>
| | | Scenihr Michel Cosson  
Professor of obstetrics and gynecology  
University hospital Lille France  
Disclosures: Member of the prolift French group who developed and used many years Prolift  
I have disclosures with industry as an owner of patents, one on technique and kits in incontinence female surgery and one in pop vaginal surgery without any products available on the market  
We develop with our team a scientific project founded by the French government on a new physiological mesh for incontinence or POP surgery in collaboration with Abyss (French company)  
I have collaborations and sometime fees from teaching sessions for Olympus, AMS, Boston scientific and have expert work with fees for Astellas, Allergan, Ams, Boston scientific  
Dear members of the scientific committee  
I want to thank you for the large work done for this preliminary Opinion on the safety of surgical meshes used in uro gynecological surgery  
This a very complete overview and precise analysis of the publications  
The safety of surgical meshes in uro gynecology surgery is certainly a main concern in our field of activity. However it is always surprising for us that it is possible to address safety of vaginal meshes and therefore make recommendations about the use of synthetic meshes without addressing in the same work the main alternative of « native » surgery.  
1- Quality of mesh: About the mesh itself the classification of Hamid is not of interest | Alternatives are discussed. No changes of the Opinion required |
anymore as the only vaginal meshes proposed are PP large pore meshes. Most of the mesh used have not been designed for vagina use and are coming from developments in the field of hernia and we do agree with committee that further development and specific research are necessary for vaginal meshes for prolapse.

2- Size of mesh: The focus on the size of meshes in relation with the rate of complications and especially mesh erosions is not clearly proved, it is coming from old studies on old meshes and it is not proved with the current meshes. However if size is an issue, most of the current meshes used for vaginal surgery of prolapse are much smaller and therefore there rate of complication is lower than the meshes assessed in randomized studies. Perhaps it is a mistake and you talk about the pore size of the mesh rather than the mesh size??

3- Mesh surgeries in randomized studies Even if for questions of simplifications some publications are not detailed and no criticism addressed, some of them with poor anatomical results or high rates of complications should be detailed (I will come back to these differences between publications later) Publications with different techniques; single mesh, 2 or 4 arms in the obturator all are not individualized, it could be important for results or complications Often complications as mesh erosion or recurrence of prolapse are compared in the analysis, however most of the mesh erosions are not difficult to address, and at least much less then prolapse recurrence Randomized studies show no differences in rates of re interventions at one year follow up, but analysis looking at 2, 3 and more follow up show that traditional repairs have increasing rates of re interventions for recurrence and this should be stated, more
follow up is needed before concluding Randomized studies are not the only interesting studies scientifically and variability of results, evolution with follow up are available from these studies too, randomized studies are often on smaller numbers and less follow up  
Asking surgeons to use synthetic meshes for vaginal repairs means that you recommend traditional repairs that are poorly evaluated and standardized. Most of the randomized studies you analyze do not use current meshes and new techniques: smaller meshes, anterior sacrospinous suspension, uterine conservation  
4- Native surgery: The only native surgery assessed in the work is the colporraphy colpectomy. It should be stated that this technique is not used in all countries and not considered as a gold standard of vaginal surgery for prolapse. This technique has never been evaluated in large prospective or randomized studies. Its technique is not clearly standardized and the number of sutures, the exact amount of colpectomy, the sutures types resorbable or not and there exact placement are not assessed. Therefore recommending not using meshes vaginally sends the surgeon and patient back to not evaluated, not standardized techniques. The only interest of the technique is therefore that it has less mesh erosion rates with no benefit in term of dyspareunia, anatomic functional or symptoms outcomes...  
In some European countries as France, Italy for example vaginal surgeries for cystocele use other techniques as « plastron », « paletot » which suppose a superposition of vaginal fascia under the bladder, manchester, campbell with tensioning of utero sacral ligaments, or even vaginal paravaginal suspensions which are not clearly standardized and not evaluated  

| | 4– The Opinion focuses on surgical meshes and only briefly mentions other treatment techniques. No changes in the Opinion are required. |
| 5- | Variability of published results: all randomized and prospective studies show high variability of anatomical results, and it should be shown in this review and conclusions should be made from these data too. Especially mesh complications from 2 to nearly 40%. These figures are rarely studied in the analysis of literature but they highlight the major importance of surgical technique and therefore surgical training. This factor is more important in these studies and in randomized studies than the size of the mesh, the obturator arms or not or even neither the commercial product nor the quality of the mesh, the incision type, the condition of the patient smoking or not. Anatomical results and their re intervention rates are highly variables too. Therefore we have the choice to act the variability and emphasize the importance of the training of the surgeon and part of the recommendations should be on the importance of the training, of the auto evaluation of the complications rates for every surgeon using meshes. The other option is to exclude all the extremes of the randomized studies publications and do the evaluation only on for example studies with less then 15% exposition rates and recommend that a surgeon with more complications should go back to training and stop vaginal meshes surgeries. To conclude At one year follow up after mesh implantation for cystocele repair there is a significant anatomical benefit, found for symptoms too. The poor follow up available do not authorize to conclude for re intervention rates and quality of life comparing traditional and mesh repairs. Most of the vaginal non meshes techniques are not standardized and very poorly evaluated. It will take a few years to get enough information to be able to precise the | 5- | This is a general comment. No changes in the Opinion are required. |
| respective indications of vaginal traditional surgeries and of different vaginal mesh surgeries for prolapse. It is not possible to recommend specific indications for traditional repairs or mesh implantation for prolapse surgeries. Surgeons doing prolapse surgeries vaginal or laparoscopic should benefit of specific training. When using vaginal meshes surgeons should evaluate their specific results and rates of complications and give this information to the patients. Over 5 to 10% of mesh erosions with the current products on the market, they should stop or go for more training. In recurrent cases patients cases should be discussed in multidisciplinary clinics or staffs to state on the best technique for a specific patient. |
### OBSERVATIONS AND COMMENT FROM MESH INJURED PATIENT - ON SCENHIR REPORT

Submitted to SCENHIR by Ingrid Hardacre. Email: ingrid.hardacre@talktalk.net

Dear Sirs

Having read your report and trying to understand it to the best of my ability allow me to respond to your above mentioned SCENHIR report, in the form of jottings with references to the page numbers. My comments corresponding to some paragraphs are in italics. Although you mention that overall there is a lack of evidence and long term studies, especially long term outcomes on mesh surgeries you condone the use of mesh.

Page 4
SCENHIR supports the use of sling mesh
29.6.2015 Consumer safety: Is not taken into consideration since all medics have ignored the plight of mesh injured patients. Emerging and newly identified health risks. Mesh problems/health risks have been known about since the introduction to the market in the med nineties in the UK. Page 32 & 14-16 body responses + 21 –32 body responses pull on adjacent tissues – mesh exposure – fibrosis: - Are all well explained.
External experts. - PROF C. CHAPPLE has written many papers on mesh complications including research below which you have considered. In this paper the author is questioning the use of mesh. 1 Chapple CR, Raz S, Brubaker L, Zimmern PE. Mesh Sling in an Era of Uncertainty: 2 Lessons Learned and the Way Forward. European Urology, 2013; 64, 525-529.
3 Chmielewski L, Walters MD, Weber AM, Barber MD. Reanalysis of a randomized trial of Although some US research has been listed. You have not taken into consideration the very frank and clear warnings from the eminent doctors in the US who remove mesh. These are:- Prof Shlomo Raz and Mr Thomas Margolis on the dangers of mesh and their experience in removing mesh. See

<table>
<thead>
<tr>
<th>Nr.</th>
<th>Name of individual/organisation</th>
<th>Comment</th>
<th>Additional documents submitted by a contributor</th>
<th>SCENIHR Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>78</td>
<td>Ingrid Hardacre, <a href="mailto:ingrid.hardacre@talktalk.net">ingrid.hardacre@talktalk.net</a></td>
<td>OBSERVATIONS AND COMMENT FROM MESH INJURED PATIENT - ON SCENHIR REPORT Submitted to SCENHIR by Ingrid Hardacre. Email: <a href="mailto:ingrid.hardacre@talktalk.net">ingrid.hardacre@talktalk.net</a> Dear Sirs Having read your report and trying to understand it to the best of my ability allow me to respond to your above mentioned SCENHIR report, in the form of jottings with references to the page numbers. My comments corresponding to some paragraphs are in italics. Although you mention that overall there is a lack of evidence and long term studies, especially long term outcomes on mesh surgeries you condone the use of mesh. Page 4 SCENHIR supports the use of sling mesh 29.6.2015 Consumer safety: Is not taken into consideration since all medics have ignored the plight of mesh injured patients. Emerging and newly identified health risks. Mesh problems/health risks have been known about since the introduction to the market in the med nineties in the UK. Page 32 &amp; 14-16 body responses + 21 –32 body responses pull on adjacent tissues – mesh exposure – fibrosis: - Are all well explained. External experts. - PROF C. CHAPPLE has written many papers on mesh complications including research below which you have considered. In this paper the author is questioning the use of mesh. 1 Chapple CR, Raz S, Brubaker L, Zimmern PE. Mesh Sling in an Era of Uncertainty: 2 Lessons Learned and the Way Forward. European Urology, 2013; 64, 525-529. 3 Chmielewski L, Walters MD, Weber AM, Barber MD. Reanalysis of a randomized trial of Although some US research has been listed. You have not taken into consideration the very frank and clear warnings from the eminent doctors in the US who remove mesh. These are:- Prof Shlomo Raz and Mr Thomas Margolis on the dangers of mesh and their experience in removing mesh. See</td>
<td></td>
<td>The SCENIHR appreciates patient involvement and the helpful comment which the committee has taken on board but which doesn't necessitate a change in the documents.</td>
</tr>
</tbody>
</table>
links below; including comments from Professor Tom Joyce, UK
Written Submissions to the Scottish Parliament in April 2015:
- PE1517/A: Professor Tom Joyce Email of 23 March 2014 (38KB pdf)
- PE1517/B: Dr Michael Margolis Letter to the Cabinet Secretary for Health and Wellbeing of 8 September 2013 (141KB pdf)
PLEASE NOTE THAT ENGLISH IS NOT DR RAZ’S FIRST LANGUAGE
Email from Dr. Schlomo Raz, UCLA to present to NHS England Working Group on Mesh and Tape on 3rd November 2014. On Tuesday, 15 July 2014, 14:36, "Raz, Shlomo M.D."<SRaz@mednet.ucla.edu> wrote:
I have removed now more than 1000 mesh for complications.
We can cure or improve 75-80% after mesh removal but 20% of the patient may be permanent disabled.
Mesh is inserted to improve anatomical results at the cost of 5-20% complications (minor and major). Quality of life is what counts. Traditional surgery (no mesh) compared with the use of mesh gives the same results of improving quality of life and bother scores. We are looking at why is happening that a few years later patient develop these complications. The vagina has bacteria even after the surgical scrub at the time of surgery. The mesh is inserted through a contaminated area. The mesh is infected at the time of the implant creating a biofilm (a colony of bacteria inside a protein envelope). Antibiotic cannot cure mesh infection. Bacteria can be dormant in the mesh for a long time but can be activating itself, expand and create the late complications of mesh.
Shlomo Raz, M.D. Professor of Urology Chief, Division of Pelvic Medicine and Reconstructive Surgery Department of Urology, David Geffen School of Medicine at UCLA
200 UCLA Medical Plaza, Suite 140
Los Angeles, California 90095-7366
Phone 310-794-0208 Fax 310-794-0211
It makes me rather suspicious and thinking that this report, like any other from England (York Report and statements from the MHRA in England), is weighted in favour of the mesh manufacturers by basically ignoring the huge number of mesh victims that are now emerging, who now know where and how to report their adverse incidents, by going public on Facebook and self help support groups. Why? Because mesh patients are not being listened to and are not believed because medical professionals are in denial or maybe they are embarrassed to
admit at having been deceived by the mesh manufacturers and notified bodies. Notified bodies contribute nothing to the reality of severe mesh complications, because notified bodies licences can be bought without any problems at all. See the RADAR Report from Holland and their undercover work in exposing the notifying bodies in England and Austria and Germany, to name but a few countries in the EU. Frankly, to use the pretext “we must not stifle innovation” is criminal and insulting to every patient that has been injured by mesh and any future patient who will also be injured by mesh, if the practise of using this “minimally invasive procedure” is being continued. This is quite clearly the case in England under NHS and private practice. But it is morally wrong to subject another human being to such a dangerous, under-trialled operation and not giving full risks and long-term problems with a product that is not fit for purpose.

In the US there a many litigations going on with various mesh manufacturers and patients have won their cases. Before long, patients in Europe will be successful in litigations – it is only a question of time.

Dr Carl Hennighan, Oxford, has commented on the process of licensing implant products through a notified body in May 2012 - even before he worked together with RADAR on the "Mandarin Net" expose! German Article cautions on should we stil offer implant mesh products? 20 Prof. Sheila MacNeil, University of Sheffield, Sheffield, United Kingdom, for the in-depth review of the report and for the contribution to the section on 'aging of the material of 22 surgical meshes' and its influence on the performance of these medical devices. When assessing synthetic mesh risks there is a need to clearly separate the smaller risks associated with SUI sling surgery from those of POP mesh surgery. rate while sling surgery with non-absorbable synthetic mesh was effective with an approximately 4% mesh exposure rate at 5 years.

However, synthetic sling SUI surgery is an accepted procedure with proven efficacy and safety in the majority of patients with moderate to severe SUI, when used by an experienced and appropriately qualified surgeon. Therefore, the SCENIHR supports continuing its use for SUI, but emphasises the importance of appropriately trained surgeons and detailed counselling of patients about the associated risk/benefits.

The SCENIHR recommends the introduction of a certification system for surgeons based on existing international guidelines and established in cooperation with the relevant European
Surgical Associations. No national register of mesh implantation for SUI or POP in England – how can there be any true assessment on the horrific devastation that mesh tapes cause – without national registration for both implantation and explantation?

Appropriate patient selection and counselling has not been practiced in any shape or form in any of the EU countries – so that any surgical team can profess that patient’s safety is the primary concern for any mesh inputting team. Sadly profit before patient’s safety is the order of the day!!

Appropriate patient selection and counselling is of paramount importance for the optimal outcome for all surgical procedures, particularly for the indications discussed. This should be based on the results of further clinical evidence, which should be collected in a systematic fashion for all of these devices. If no national registers are being produced how can clinical evidence be ever produced to reflect the true and honest account of any implantation - if adverse reactions and failed outcomes are not recorded and if they do exist but not available to the public – how can that be a transparent way of dealing with a new problem, which did not exist when traditional surgery was used, before the widely adopted “quick fix kits” for mesh surgery? In a shared decision process the surgeon and the patient must determine whether to use a surgical approach with or without mesh. 13 Meshes are not the first choice for any indication, but are considered as a primary surgical solution in many cases of SUI, despite reported adverse events.

Patients were not and still are not informed fully on all risks of mesh adverse reactions in the short or long term outcomes. Recent social media influence has shown that if prospective patients know all risks and life changing, long term adverse reactions – there has been indications that patients have rethought their decision regarding this elective surgery, for SUI – a condition which is not life threatening in itself, but having mesh inside your body, can have serious, long term and lifelong ill effects on health and family life as mesh injured patients have a deteriorating quality of life!

The choice to use synthetic meshes may influence the outcome of surgery and need to 25 be discussed in detail with patients before carrying out surgery. This has not happened over the past 15 years since mesh has been used and is still not been practiced NOW!! All synthetic meshes are associated with the risk of mesh exposure as demonstrated by 20 numerous animal studies. At
two-year follow up it is also evident in 4% of patients. Overall the adverse reactions are much higher than any studies which you have taken into account, and these studies are really quite old some over 10 years old. Since the arrival of Self help online patients groups (some have been started as far back as 2007) the true mesh mess horror is only now coming to the surface, as patients are coming forward to report their long and painful mesh injured journeys. Nobody seems to believe patients, citing that we are all individuals and such react in individual ways. Since the product is a standard production “one size fits all” – it is a fallacy to maintain that adverse incidents are rare and vary in each individual; because research shows that all adverse reactions follow a particular pattern, which can start with pain, due to shrinkage (According to ETHICON RECORDS 19% in the first few months of implantation!) Infection, inflammation and degradation leading to erosion, repeated urinary infection, outlet obstructions, damaged organs; such as destroyed urethras through mesh exposure...the list goes on and on de novo urgency is as distressing as SUI, because it is a different form of incontinence! Increased risks compared to mesh implantation for SUI. Its use should be restricted to 34 patients selected according to established evidence based clinical guidelines. Clinical guidelines are limited and inaccurate and in most cases conflicted, as most research has been sponsored by mesh manufacturers who had a hand in how much evidence is to be reported. Patient characteristics, such as obesity will have an influence on efficacy and 16 potential complications. There are plenty mesh injured patients were active in sports, who are not obese and yet have the same reactions to mesh – so it is not the patients – but the product and even a small TVT tape has the same debilitating effect and it is upsetting to classify a SUI tape (TVT, TOT, TVTo) as not so problematic as a larger piece of mesh. Such a statement is ludicrous! In case a medical device compromises the health and/or safety of patients or other 12 persons in spite of its correct installation, maintenance and use, adequate measures need to be taken by manufacturers, Member States and the Commission to remedy 14 existing non-compliances. The Manufacturers have not been accountable enough with regards to the points raised in the above observation. If fact, manufacturers are quite callously blaming surgeons for adverse reactions or failed and unexpected outcomes. Still commissioning services are still making provisions to supply these products which are not fit
for purpose as they quite clearly damage and injure patients at a rate up to 33% according to some very recent research! Would anyone purchase a car with a failure rate of between 4-33%? Post market surveillance must include both monitoring of complaints and adverse events, in addition to a regular 21 review and updates to the body of clinical evidence for the performance of the device. 22 The results of this regular surveillance must be assessed for potential subsequent 23 application of routine risk reduction activities (e.g. improved instructions for use) and 24 additional risk reduction activities (e.g. design changes, physician’s education and 25 training). Evidence of this process is essential to ensure that the risk to benefit ratio for 26 the device can be justified by a manufacturer. The immune response to a foreign material may be complex, dynamic and patient specific. Polypropylene meshes provoke minimal adverse reaction when implanted in the 5 abdominal wall for hernia repair, but are associated with complications in the pelvic floor 6 and suggests a site-specific host response to biomechanical exposure (Patel et al., 7 2012), which was confirmed in ewes (Manodoro et al., 2013) and emphasises the need 8 for relevant animal models and in long-term studies (Deprest and Feola, 2013). 9 Synthetic material such as polypropylene includes additives such as softeners like 10 Bisphenyl-A (BPA), which may leak into tissue and cause adverse health effects (see 11 SCENIHR Opinion on BPA), but since quantitative data on exposure are lacking, it is not 12 possible to do a risk assessment. However, data on polypropylene implants for 13 abdominal hernia repair suggest that there is no such safety concern (e.g. Henniford et 14 al. 2000). In this study of 407 patients a satisfactory hernia repair was achieved in 15 98.1% of patients and the complication rate (mostly. 16 Implantation techniques for SUI 17 o There is no such evidence available in England, as part of a EU nation. The SCENIHR acknowledges the efficacy and use of implanted meshes for SUI but 21 recognising the absence of long-term data, it considers that associated risk to be limited. 22 The complications associated with mesh insertion are related to the route of insertion. 23 The SCENIHR acknowledges that vaginally implanted mesh for POP is associated with What factors could affect the outcome of the surgical interventions? (Q6) 17 The factors influencing the surgical outcomes are: 18 • Material (biocompatibility, -tissue integration, long-term stability and mechanical 19 responses over time (flexibility, elasticity and resistance to
deformation
20 • Product design (e.g. physical characteristics of the mesh, size of the pore as a predisposing factor to infection in particular with a pore size less than 75 microns)
21 • Overall mesh size (surface area) of material used (which is greater for POP than SUI)
22 • Route of implantation, (e.g., vaginal or trans abdominal)
23 • Patient characteristics (e.g., obesity, smoking)
24 • Associated procedures (e.g., hysterectomy)
25 • Surgeon’s experience
26 SCENIHR acknowledges the importance of established guidelines, clinical experience and adequate training of the surgeon as well as the need to improve the design of the device
27 to be suitable for use in the pelvic floor which appears to be a more demanding environment than the abdomen (where the same non-degradable meshes have a low performance and risks associated with synthetic non-absorbable meshes
28 • Establish European implant registries: NHS England has refused to implement a national register on mesh implant and removal. It also has refused to carry out retrospective studies on information available in conjunction with Hospital Statistics.
29 • Establish scientific studies to assess the long-term (at least 5 years) safety and performance of the synthetic non-absorbable meshes
30 • Support further research into novel new materials, in particular absorbable meshes
31 • Support further research into the application of regenerative medicine, such as the cellular seeding of graft materials
32 • Establish evidence based European Guidelines
33 • Develop training programs for surgeons in association with European medical associations
These are my observations
Kind regards
Ingrid Hardacre
To:
European Commission
DG Health and Food Safety
Directorate C Public Health
Unit C2- Health Information and Scientific Committees
Office: HTC 03/073 L-2920 Luxembour
SANTE-C2-SCENIHR@ec.europa.eu

79. R Bendavid MD, FRCSC, FACS, AFC (Hon.). Departments of Surgery Shouldice Hospital & University of Toronto 7750 Bayview Avenue Thornhill Ontario L3T 4A3 Canada

The SCENIHR thanks the submitters for sharing these experiences. No changes to the Opinion are required in relation to the comments.

80. Mark Slack Lead Clinician Department of Urogynaecology and Pelvic Reconstructive Surgery Addenbrooke’s Hospital Univ. of Cambridge Teaching Hospital Trust Cambridge CB2 2QQ United Kingdom 01223 586740 (Sec) mark.slack@addenbrookes.nhs.uk

Dear Sirs, On behalf of the board of the International Urogynaecological Association I would like to submit our official report on the above document. The report does not fit the format of your website so I am submitting it in its complete form. We represent a large majority of urogynaecologists internationally and believe it is important for the committee to be aware of our comments.

Yours Sincerely,
<table>
<thead>
<tr>
<th></th>
<th>Name</th>
<th>Comment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>81.</td>
<td>Lise Christensen, MD. DMSc. Department of Pathology Herlev Hospital University of Copenhagen Denmark.</td>
<td>I apologize for having referred to an Email address of mine, which is not valid. Instead it should be: <a href="mailto:Lise.Christensen.01@regionh.dk">Lise.Christensen.01@regionh.dk</a> Please find enclosed the resubmitted commentary</td>
<td>No changes to the Opinion are required in relation to the comment</td>
</tr>
<tr>
<td>82.</td>
<td>Ann Boni Ann Boni <a href="mailto:annboni@yahoo.co.uk">annboni@yahoo.co.uk</a></td>
<td>I intend to write an Opinion for a facebook group set up to support mesh injured patients. Please advise if we can gather thoughts together on paper and then send one report collectively, as a group, with all the signatures of our members who agree with the report. Yours Sincerely</td>
<td>The SCENIHR appreciates patient involvement. However, only scientific studies are taken as basis for forming their opinions. No changes to the Opinion are required in relation to the comment</td>
</tr>
<tr>
<td>83.</td>
<td>Agneet Zuidervaart <a href="mailto:Zuidervaartadam@gmail.com">Zuidervaartadam@gmail.com</a> <a href="mailto:Zuidervaart@xs4all.nl">Zuidervaart@xs4all.nl</a> (31)(0)20 6258976 (31) (0) 6 2558109</td>
<td>Dear sir, madam, I found the enquiry about surgical meshes used in uro, genital operations on facebook. There is another category of operations in which surgical meshes are used. And they are causing the same kinds of problems. They are used to repair hernia's. They are also used for problems arising from rectal cancer treatment, stoma's. There are plans to use surgical meshes around every stoma. And it is to be expected that they will cause the same problems as uro genital use. I have a stoma. And have had four operations to correct problems with the surgical mesh that they used. This category of this group of mesh problems is not included in the enquiry. I would appreciate it if you could mention this and signal the possibility of a new group of possible big mesh problems. Sorry for my english, it isn't at the best at this moment</td>
<td>These are personal consideration. No changes to the Opinion are required in relation to the comment</td>
</tr>
</tbody>
</table>
Dear sir / madam,

Please find enclosed documents. If you have any further questions, please do not hesitate to contact me.

ESFU comments on ESFFU Letter of Support NIH Grant Application.pdf

ESFU comments on SCENIHR report 2015.docx

The SCENIHR agrees that the abdominal route is less well documented and more invasive, but there are less mesh-related complications. With regard to recommendations, the SCENIHR agrees that there should be adequate patient information and adequately trained surgeons. The SCENIHR agrees on the need of long term data being accrued and further research into new approaches, looking into regenerative medicine, establishing evidence based European guidelines. No changes to the Opinion are required in relation to the comment.

ESFFU Letter of Support NIH Grant Application.pdf

The SCENIHR sympathises with the patients suffering of side effects due to different types of surgery. It is not in the mandate of the SCENIHR to consider issues such as the one mentioned in the comment. No changes to the Opinion are required in relation to the comment.

ESFU comments on SCENIHR report 2015.docx

The literature search is described in the methods section. No changes to the Opinion are required.
1. Describe and list search terms used so that an independent entity would be able to use the same methodology and reproduce the outputs of the search
2. Medline was the only search database used. Consider using others to ensure the most thorough search for appropriate articles
3. Define how literature was selected. What were the inclusion and exclusion criteria?
4. What was the Level of Evidence of the articles selected?
5. Provide a flow diagram of articles obtain with the selected search terms and then the decisions made to eliminate articles down to the final bibliography

Consideration on surgical techniques should also be considered throughout the Opinion as this could have an impact on the potential health risks of meshes used in urogynaecological surgery. To provide a balanced Opinion, we would also welcome an analysis of the benefits associated with the use of meshes, including the benefits of POP repair, in urogynaecological surgery and not only to the risks associated with these devices. It would appear that the abstract bears the hallmark of British, French and Australian surgeons and often stands in contradiction to the interdisciplinary D-A-CH guidelines. As a result, relationships that can still be found in detail in the text will be scored differently in the summary. In the abstract, therefore, conclusions are sometimes drawn which are not always related to the data. It is also not worked out that there are a variety of meshes and technologies, which are / were used by different surgeons on different patients, resulting in differences in the results. The advantages of modern mesh surgery, which can be found in the latest D-A-CH-guideline as well as the view that in certain situations not implanting a surgical mesh would be far more detrimental to the health of the patient in certain situations, is not included.

Lastly, we believe that the MHRA’s guidelines on the benefits and risks of vaginal mesh implants may be a useful source of information as it provides a good overview.

Reference to additional guidelines has been included.
<p>| 87. | # | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | General We would recommend specifying that surgical meshes may differ on the aspects mentioned in the document which in turn could impact the determination of risk for complications. The outcome and especially risks for complications from conventional surgery should be mentioned since they may be more severe than TVM complications. The emphasis is put on the device whereas several other reports (MHRA, IGZ, DGU etc.) put physician experience and training as a significant contributing factor to reducing risk. The competence and position on the learning curve of an implanter impacts clinical outcome. Although the discussion on the AMS800 AUS may appear out of place as it is not a mesh product as such, it may be understandable if it is to be considered a good and proven alternative (&gt;150,000 patients (Van der Aa et al. 2013) for mesh products for SUI. It is unclear whether the methodology used for the clinical data review complies with state-of-the-art methods for clinical evaluations (e.g. European Commission guideline MEDDEV 2.7/1 rev.3). In particular, the literature review methods, such as articles selection method, are not described. The draft Opinion fails to mention several recent quality peer-reviewed articles, which suggests that the literature search may not be complete. | The work was performed according to the Rules of Procedures for the Scientific Committees. It was based mainly on reviews and meta-analyses of RCT’s and not on single peer-reviewed articles. |
| 88. | # | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Section 4, Page 4 It is important to distinguish between mesh size and pore size. | The text is clear. No changes are required. |
| 89. | # | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Abstract Section 2, pg. 4. 1. Mesh erosion, pain, infection, bleeding, pain during intercourse, organ perforation, and urinary problems. With the exception of mesh erosion, these are all risks of traditional non-mesh surgery as well. This is also supported by Milani et al. (2013). 2. More than half of most mesh exposures from TVM are asymptomatic and only one third need minor outpatient operative intervention. However, a small bowel obstruction following an open abdominal sacral colpopexy may require a second laparotomy and a prolonged in-patient admission. Thus while the rates of “complication” may be higher with TVM, the severity of the complications associated with ASC may be greater. | 1. The Opinion is on surgical meshes. 2. This is already taken into account in the Opinion. No changes to the Opinion are required. |</p>
<table>
<thead>
<tr>
<th>Page</th>
<th>Reference</th>
<th>Section</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>90.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Abstract Section 1, pg. 5</td>
<td>We have concerns that the SCENIHR is recommending surgical procedures, such as some NTR procedures, that have a higher rate of failure (high rate of recurrent prolapse symptoms in anterior compartment; questionable conclusion in posterior as denominators are very low) over the use of mesh. The recommendation will likely require many women to seek a second surgery rather than have mesh implanted during the initial surgery. Mesh in the anterior and when multiple compartments are treated results in less recurrent prolapse symptoms (bulge); posterior recurrent prolapse symptoms show no difference but the data is scant.</td>
</tr>
<tr>
<td>91.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Abstract, Page 5 Section 10</td>
<td>This is a very true statement and is as valid for the use of mesh products for SUI as for POP</td>
</tr>
</tbody>
</table>

The rationale is clearly given in the text. No changes to the Opinion are required.

No changes to the Opinion are requested.

It is pointed out again that the evidence is not based on single peer-reviewed articles. No changes to the Opinion are required.
<table>
<thead>
<tr>
<th>93.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section 1, Executive Summary, Page 7, lines 20-28</strong></td>
<td>It should be mentioned here that except for mesh erosion and extrusion other complications are shared by Native Tissue Repair and that complications from alternative surgical approaches (SCP) may have fewer though more severe complications. Although this is mentioned elsewhere we recommend mentioning this also in the Executive Summary.</td>
<td>This point is made in the Opinion, therefore, no changes are required.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>94.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section I, Executive Summary, p. 7</strong></td>
<td>The Opinion only refers to synthetic mesh implants. This excludes mesh implants incorporating and/or being processed from animal origin components (e.g. biological mesh implants). It is unclear why these implants were not considered in the review, while the European Commission Mandate was broader and not specific to any specific mesh material. We believe this gap creates a disconnection between the current surgical practice, available surgical options and the SCENIHR Opinion.</td>
<td>This was decided for reasons of time and clinical evidence available. No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>
1.0 Executive Summary, Page 8

16 In the context of POP, the use of mesh placed by the vaginal route is only 17 recommended as a secondary choice after failed primary surgery. This statement is in conflict with other sections of the report where the SCENIHR indicates that conservative treatments should be used prior to treatment with mesh; such as, Section 4.1.1, page 15, line 7; Section 4.1.1, page 16, line 5, 9; Section 4.2.5, page 57, line 34. As such, the term “surgery” should be replaced with “treatment”; thereby, supporting the use of conservative treatment and aligning the statement with other sections within the SCENIHR document.

The text has been changed for clarity.

Allografts are not evaluated in the Opinion. No changes to the Opinion are required.
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>98.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td></td>
<td>Section I, Executive Summary, p. 8-9 It is suggested that only Type 1 (macroporous, monofilament) polypropylene are the most appropriate synthetic meshes for implantation via the transvaginal route, while other mesh materials have insufficient evidence. We believe this statement should be reconsidered while including literature references that were not considered by the SCENIHR. In addition, the classification used (Amid, 1997) may be too limited in that porosity is not well defined in the scientific literature and dependent on the test methods that are non-standardized to date (Klinge, 2013). Amid P. Classification of biomaterials and their related complications in abdominal wall surgery. Hernia. 1997;1(1):15–21. Klinge U, Park JK, Klosterhalfen B 'The ideal mesh?'. Pathobiology. 2013;80(4):169-75.</td>
<td>The recommendation is based on currently available data. The existence of new materials is now acknowledged in the Opinion. The Amid classification is the one referred to in clinical guidelines so far. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>99.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td></td>
<td>Section I, Executive Summary, p. 8-9 It is suggested that only Type 1 (macroporous, monofilament) polypropylene and Type 3 (microporous, multifilament) polyester are the most appropriate synthetic meshes for implantation via the abdominal route, while other mesh materials have insufficient evidence. We believe this statement should be reconsidered while including literature references that were not considered by the SCENIHR. In addition, the classification used (Amid, 1997) may be too limited in that porosity is not well defined in the scientific literature and dependent on the test methods that are non-standardized to date (Klinge, 2013). Amid P. Classification of biomaterials and their related complications in abdominal wall surgery. Hernia. 1997;1(1):15–21. Klinge U, Park JK, Klosterhalfen B 'The ideal mesh?'. Pathobiology. 2013;80(4):169-75.</td>
<td>See response above.</td>
</tr>
<tr>
<td>Page</td>
<td>Source</td>
<td>Text</td>
</tr>
<tr>
<td>------</td>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>96</td>
<td>Eucomed, Thecla Sterk</td>
<td>These statements should be accompanied that as a consequence the risk profile is based on device features which differ per product. This also substantiates that risk are not generalizable over all mesh products.</td>
</tr>
<tr>
<td>101</td>
<td>Eucomed, Thecla Sterk</td>
<td>Executive Summary, Page 7, 10, 13 Published until now. The use of such mesh in repair surgery may lead to various complications of poor tissue integration, such as tissue erosion, exposure of the mesh and shrinkage of the mesh. The success of mesh interventions varies depending on the type of anatomical defect, its severity, the presence of risk factors, the rationale for the use of mesh and the skill and experience of surgeons. The risk of severe side effects (e.g. mesh exposure, shrinkage, pain) increases with the surface area of used synthetic non-absorbable meshes. There are few published randomised controlled trials. The use of mesh in repair surgery may lead to various complications, such as rejection, tissue erosion, mesh exposure and shrinkage. The rate of success of treatment with mesh implantation varies. Although Manodoro et al. (2013) has shown mesh contraction in an animal model there are studies that show contradictory evidence. Dietz AJOG (2011) suggests that this is because the study only measured mesh dimensions at a single time point and that multiple time points are needed to determine mesh contraction. Dietz showed stable mesh dimensions as a function of time from two (early and late) visits post operatively and was unable to support the conclusion that mesh contraction occurs in female patients. Further, Svabik IUGA 2010, suggests that “Intraoperative folding seems to be responsible for a large part of the difference between preoperative (in vitro) and postoperative (US) measurements of mesh dimensions, suggesting that surgical techniques may require adjustment.”</td>
</tr>
<tr>
<td>No.</td>
<td>Author(s)</td>
<td>Source</td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
<td>--------</td>
</tr>
<tr>
<td>102.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td>103.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td>104.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td>105.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td>106.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
<tr>
<td>107.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
</tr>
</tbody>
</table>
addition, numerous published peer-reviewed studies, including randomized clinical trials comparing biological mesh materials versus synthetic mesh implants with conclusive outcomes, were found and not considered in the SCENIHR Opinion. This statement should either be removed, or the Opinion should be reconsidered to include non-synthetic mesh in its scope. It is also unclear why this statement does not distinguish between the surgical approach, clinical indications and type of materials.

<table>
<thead>
<tr>
<th>Page</th>
<th>Author</th>
<th>Line</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>108.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p11 9.</td>
<td>The impact of age is clear for many risks. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>109.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p11 33.</td>
<td>These refer to technological procedures. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>110.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p11 36.</td>
<td>The text has been changed to “general European guidelines” for clarity</td>
</tr>
<tr>
<td>111.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Section 1, Executive Summary</td>
<td>This is standard clinical research practice. No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>
mesh products to treat POP and SUI. The studies evaluating transvaginal POP repair are conducted within a registry database platform managed by AUGS. Industry suggests establishing a working group in collaboration with AUGS and European medical societies, regulatory bodies, and Industry to proactively leverage ongoing collaboration between AUGS, FDA, and Industry partners in US.

| 112. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section I, Executive Summary, p. 11. Encouraging technological development to enhance patient’s outcomes and restore health is welcome. However, it is unclear why technologies such as electrospinning are cited in this Opinion, in that it is not based on available clinical evidence. It is besides reminded that technologies may be subjected to industrial protection. | Please remember that the list is indicative ("such as"), not conclusive. | No changes to the Opinion are required |
| 113. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | p15 line 6. It is stated that a mesh can be used when all conservative treatments were unsuccessful. This statement contradicts other parts of the Opinion especially the abstract. | This is not a contradiction. Mesh is not recommended for primary treatment. | No changes to the Opinion are required. |
| 114. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | p16 line 6. While the Dutch Multidisciplinary Guidelines on Prolapse were considered, we would also recommend considering the latest interdisciplinary D-A-CH guidelines dealing with incontinence and descensus. | Reference to D-A-CH guidelines has been included |
| 115. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | 4.1.2 Treatment using meshes, Page 17 19 – degradation Statements and studies in the SCENIHR preliminary Opinion present conflicting results regarding degradation in polypropylene mesh strength. As an example, Spiess (2013) and Bazi (2007) shows no degradation, while Melman (2011) shows degradation. Zorn (2007) shows conflicting results between two different polypropylene meshes. It is our Opinion that these conflicting results within the literature prevent reliable conclusions to be drawn that mesh degrades over time. | But it does, as studies have shown. | No changes to the Opinion are required. |
### 116. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

Section 4.1.2, Regulatory framework, p. 17. The list of surgical meshes characteristics include "material (artificial or biologic)". The term "synthetic" is preferred to "artificial", as it corresponds to the sate-of-the-art terminology for mesh implants.

- The text has been changed accordingly.

### 117. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

Section 4.1.2, Regulatory framework, p. 17. The list of surgical meshes characteristics include "erosion/exposure" among technical characteristics. Erosion/exposure relates to a side-effect and not a technical characteristic. We would therefore recommend removing this from this list.

- Not “technical” but “performance” characteristics.
- No changes to the Opinion are required.

### 118. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

Section 4.1.2, Regulatory framework, p. 17. The absence of a preclinical model for characterizing urogynaecological mesh implants is noted in the Opinion. Such published models exist for other therapeutic areas when mesh implants are used, such as abdominal wall repair. It should therefore be clarified that this statement is only valid for functional models applicable to stress urinary incontinence and/or prolapse repair. In addition, the harmonized standard EN ISO 10993-6 describes preclinical methods for assessing the inflammatory response of an implantable medical device, such as urogynaecological surgical meshes. It should therefore be clarified that the lack of preclinical models pertains to preclinical animal functional models only for POP and SUI. Finally, several test methods used for characterizing mesh implants are available in the textile industry and are commonly used by mesh manufacturers. The Opinion should therefore consider these standards, while outlining the lack of harmonization by the CENELEC committees of these test methods.

- Outside of the scope of the mandate

### 119. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

p18 line 9f. All medical devices must have a design dossier which is part of the technical file. For class III devices, the technical files are reviewed by a notified body.

- Reference to MDD is made. No changes to the Opinion are required.
### 120. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

Section 4.1.2, Regulatory framework, p. 18. The Opinion specifies that “because synthetic surgical meshes are non-active, implantable and intended for long term use, according to rule 8 of the Medical Devices Directives (MDD) when lacking supporting pharmaceutical coating, they belong to risk class IIb (otherwise class III).” This is incorrect in that synthetic absorbable materials may be added to the mesh design to provide specific features (e.g. fixation, handling,...), which would classify the device as a class III product. In addition, the incorporation and/or use in the manufacture of animal-derived components would also classify the device as a class III product under rule 17 of the current medical devices directive. The Opinion should therefore include these specific cases, or clarify that the class IIb pertains to a large number of mesh implants currently available on the market, and the rule related to drug coatings should be given as an example only.

Outside of the scope of the mandate
No changes to the Opinion are required.

### 121. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

Section 4.1.2, Regulatory framework, p. 18. The Opinion states that “sufficient clinical data should be available for surgical meshes to allow adequate risk assessment (...).” This statement should be reworded to add the notion of benefits, when assessed versus the adverse effects, in accordance with the fundamental principles of the medical devices directive.

The statement is clear and refers to risk assessment rather than risk/benefit analysis.
No changes to the Opinion are required.

### 122. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy

Section 4.1.2, Regulatory framework, p. 18. The Opinion states that “in the case of meshes no mandatory testing of the device and not even a third-party test of its design dossier is requested”. This statement should be reworded to reflect the principles of the medical devices directive that require manufacturers to demonstrate safety and performance of their devices.

It is hereby reminded that:

- Not all surgical mesh implants are in class IIb and prior design dossier examination by a notified body is required for class III implants
- The quality management system of manufacturers - that includes design, manufacturing and quality controls aspects – is subject to certification audits by a notified body qualified for the category of implants
- Technical files for class IIb devices are subjected to periodic reviews by a notified body qualified for the category of implants

The text is clear.
The comment confirms the written text. Third party device testing is not mandatory e.g. at full QM systems. QM auditing must not be confused with third party device testing.
No changes to the Opinion are required.
- The recommendations of the European Commission of September 2013 include unannounced audits with product testing, for all medical devices where notified bodies are involved in the conformity assessment (i.e., all surgical mesh implants). Designation and supervision of Notified Bodies is the responsibility of Member States.

<p>| 123. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | p19 line 4ff. At point 4.2.1 „Treatment without using meshes“, the interdisciplinary D-A-CH guidelines are not considered, so on p20 line 18 there is also no finding of the worsening of the results of the colposuspension after 5 years. Furthermore, we consider that the explicit statement on p25 line 10f is no longer necessary in the summary, which proves the rate of recurrences using own tissue of 20 – 30 %. | See comments above |
| 124. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | 4.2.1 Treatment without meshes, Page 20 23 Open retropubic colposuspension is associated with high rates of objective and subjective cure rates, especially in the long-term (Lapitan et al., 2012). After 5 years, 25 approximately 70% of women were still symptom-free or no longer complained of 26 incontinence. While the focus of the SCENIHR Opinion is the safety of surgical mesh, in order to assess risk versus benefit, the safety of alternative methods should be presented. The statement describing open colposuspension presents a summary of effectiveness, but it does not summarize the consequences or complications associated with open surgery. For instance, Ogah et al.² conducted a large meta-analysis and found that Burch colposuspension was associated with more perioperative complications, longer operative times, longer hospital stays, more de novo urgency and less voiding dysfunction. We would recommend including a summary of expected adverse events for open retropubic colposuspension in this Opinion.² Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2009 Oct;7;(4):CD006375. doi: 10.1002/14651858.CD006375.pub2. | The Opinion is focused on meshes. No changes to the Opinion are required. |</p>
<table>
<thead>
<tr>
<th>Page</th>
<th>Author</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>125.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p21 line 10. Although we believe there to be an insufficient amount of data, a positive rating is given at the references on p64, line 28ff.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>126.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p22 line 34. According to new guideline and confirmed by leading anatomists e.g. Prof. Wedel, Kiel, the colporaphia anterior is not an adequate descensus-therapy.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>127.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Section 4.2.1, Surgical treatment without mesh, pg. 22, lines 39-42. The use of this reference is fraught with problems and the authors of the proposal appear to use this to say that NTR is not as bad as people believe it is when you use the right measures. The paper is a retrospective analysis. The authors of the paper report that 1)The sample size was small, which led to inadequate power to detect anything other than very large differences among the 3 treatment groups; 2) the primary goal of this reanalysis was to provide estimates of clinically relevant treatment success for anterior colporrhaphy and not to compare different methods of anterior colporrhaphy or to evaluate the role of polyglactin mesh; 3) this study was also limited by the lack of validated pelvic floor symptom or quality-of-life questionnaires.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>128.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p23 line 21. Whereas on p46 fig.2 and fig.3 the sexual function is valued as a success criterion, here the method of colpoclaisis is given without a discussion of the consequences for the women.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>129.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p23 line 34. According to the guideline, hysterectomy is not among the descensus surgeries. This might be even counterproductive.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>130.</td>
<td>Eucomed, Thecla Sterk</td>
<td>p25 line 4ff. At point 4.2.1 „Treatment without using meshes“, we believe that the interdisciplinary D-A-CH guidelines should be considered.</td>
<td>See comments above</td>
</tr>
<tr>
<td>131.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Section 4.2.2, Treatment using meshes, p. 25. It is stated that Authorities have been critical about the performance of synthetic meshes in their reports. This statement is not correct in that it does not reflect all conclusions of Authorities and does reflect the</td>
<td>It is not stated “all Authorities”. No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>
conclusions that were dependent on the surgical approach (i.e. transvaginal or abdominal). The U.S. Food and Drug Agency (FDA) notably concluded that there was a consensus for confirming that the safety and performance of surgical mesh indicated for abdominal sacrocolpopexy is well-established. (Obstetrics and Gynecology Devices Panel Meeting, Surgical Mesh Panel Meeting, September 8-9, 2011, Meeting summary).

This statement should therefore be reworded to clarify that concerns from health Authorities were related to transvaginal mesh repair, while abdominal sacrocolpopexy with mesh was confirmed as a well-established procedure.

| Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.2, Treatment using meshes, pp. 25-29 | Biological grafts are not the focus of the Opinion. Only facts are mentioned and no recommendations are made. | No changes to the Opinion are required. |
|----------------------|----------------------------------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| 132.                  |                                        | The introduction related to biological grafts is essentially incorrect and should be either considerably reworded or deleted. This section looks overall biased in the judgment of biological materials, especially in that the SCENIHR excluded these products from the assessment but provides harsh criticism without any methodological substantiation. |
|                       |                                        | - It is unclear why the Opinion presents the processing of biological materials as a disadvantage, since it is specifically intended to enhance the foreign body reaction to such xenografts |
|                       |                                        | - Processes are said to critically degrade their biomechanical properties. This statement is too vague and it is unclear why this would be an issue if the biomechanical requirements are met by the finished device |
|                       |                                        | - Crosslinking is said to provide persistent inflammatory response with fibrosis, and that crosslinked collagenous matrices induce little cell infiltration, hence there is limited collagen remodeling and graft degradation. This observation is supported by limited preclinical studies and it excludes the large amount of references that counter-balance this observation, as well as the abundant clinical literature available on crosslinked mesh materials. The risk of viral or prior transmission is true for any animal-derived components. The viral risk is however rendered negligible by application of the EN ISO 22442 standards. Numerous published peer-reviewed studies, including randomized clinical trials comparing biological mesh materials versus |
105

<table>
<thead>
<tr>
<th>133.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4.2.2</strong> Treatment using meshes, Page 26</td>
<td>In examining the literature on meshes, the SCENIHR searched Medline for articles from 1990 to 2013 containing clinical and animal studies of pelvic floor repair materials and found 10 studies on autologous materials, 11 on allograft materials, 23 on xenografts and 30 on polypropylene meshes. These articles form the basis of the review included in the Opinion and are summarised in Appendices I-IV. The literature search method used by SCENIHR to inform their clinical Opinion is not well defined or reproducible based on the information provided. We respectfully request that SCENIHR provide additional details regarding the literature search strategy utilized.</td>
<td>The particular literature search refers only to the section of materials, not the clinical evidence. No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>134.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>p26 line 1ff and line 8ff</td>
<td>The factors that influence the biological response to synthetic meshes are indeed the material and the production technology in a high rate, but the other two factors (patient and surgeon) are no longer honored later in the summary. It should be clarified that this degradation mode is specific to absorbable materials and not to permanent synthetic materials.</td>
<td>No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>135.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2.2. Xenografts, p28 lines 17-19</td>
<td>The comment about DNA in SIS used for treatments of SUI or POP is inaccurate and should be removed. The evidence is based on an article about an orthopaedic product (Zheng 2005), which notably is made by an orthopaedic company and is sourced separately and processed differently than the product manufactured and sold by that manufacturer that was sold into the urogynaecological market.</td>
<td>No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>136.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section 4.2.2, Treatment using meshes, pp. 29-34</td>
<td>This section is intended to address preclinical synthetic mesh behaviour. However, it only covers polypropylene mesh implants and does not address polyester meshes, although listed in the Opinion.</td>
<td>No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>
| Page | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | 4.2.2 Treatment using meshes, Page 30 | 2However, there is evidence that stiffness increases over time. (Melman et al., 2011; Mangera et al., 2012). The SCENIHR draft states, “there is evidence that stiffness increases over time.” The provided references do not match the conclusions associated with this statement. Melman et al. (2011) indicates that there is no change in stiffness over time, specifically stating, "No significant difference in stiffness was detected between the mesh types or between time points (p>0.05 for all comparisons)". Mangera et al. (2012) is a systematic literature review that attempts to compare the uniaxial properties across a variety of mesh types. A key reference within this article found a decrease in stiffness of the mesh over a nine month implantation duration (Pierce AJOG 20093). Industry would therefore recommend a revision of this section.  

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>138.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p30 line 2ff The statement that polypropylene will be firmer inside the body is not entirely correct from our point of view. There is surely a correlation between the construction of the mesh (small pore size) and the building of plates of scar tissues, but this is not up to the chemical material at first.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>139.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p30 line 15ff. For example the ULTRAPRO was named, which already loses its stability after a few months. But this is essential on the partially absorbable product, because what provides for a high stability at the beginning (PP + MONOCRYL), that is after the absorption even only PP. Furthermore different studies are demonstrated on SPARC and TVT (both have the same material and same textile structure!) and in table on p31, fg. 1 two TVT are yet referred (TVT-mac and TVT-pp).</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>140.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>Section 4.2.2, Surgery using mesh; pg. 30 line 6-7; pg. 33 lines 13-14; pg. 33 lines 23-24 “...could lead to thinning of the surrounding tissue...”; “…and may lead to thinning of the surrounding vaginal tissue predisposing to erosion.” “…and contribute to tissue thinning and mesh exposure”: We believe these statements to be theoretical and could lead the reader to believe that thinning happens and is the cause of erosion. It is unclear whether this statement is based on observations in clinical practice or simply on animal and bench testing. The Feola et al., 2013 study uses nonhuman primates and only two types of mesh (Gynemesh and UltraPro {Prolift Plus M}). Can these results be extrapolated to other meshes? We would propose to modify the language to state that this is a theory and has not been proven and may not be the cause of erosion, but other factors such as physician experience and implant technique may also impact thinning.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>141.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p32 line 9ff and line 28ff Here multifilament polyester meshes are compared with monofilament polypropylene meshes, but the differences in the presentation of results is not considered. The summary is not in direct proportion to previous passages of the text and is by no means applicable to all mesh structures. You could therefore conclude that generalizations based on all PP meshes (on page 33, line 3 ff) are inappropriate. Modern, big pore sized and lightweight meshes no longer form such stiff scar plates.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>142.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>4.2.2 Treatment using meshes, Page 33 8 The major issue with 9 polypropylene meshes are the associated serious complications, in particular, vaginal or 10 urinary tract exposure (up to 10-14%) and because of greater stiffness, the surrounding 11 tissue weakens, which is termed stress shielding (Feola et al., 2013). The sentence links exposure directly to the concept of stress shielding, and fails to recognize that modern mesh materials differ from early generation, heavier weight mesh materials. We believe this statement to be inconsistent with other sections of the SCENIHR report where the committee recognizes that a variety of factors may influence surgical outcome; such as Section 1, page 7, line 26-28, page 10, lines 33-43. We suggest including all factors that may influence surgical outcome; such as route of implantation, patient characteristics, concomitant procedures, and the surgeon’s experience.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>143. Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>4.2.2 Treatment using meshes, Page 33 18 With materials which the body 19 cannot remodel or integrate such as polypropylene meshes, the response is an 20 aggressive M2 macrophage response (Remes and Williams, 1992; Wolf et al., 2014). Although all meshes promote a pro-inflammatory M1 response, not all meshes promote a similar magnitude of M1 response. Nolfi (JPRMS 2014) showed that lighter weight, higher porosity Type 1 meshes showed higher levels of anti-inflammatory cytokines and that these meshes attenuated M1 macrophage response. Early macrophage response (polarization towards M2 from M1 response) may lead to improved tissue remodelling (Brown Acta Bio 2012) and potential clinical outcomes. 4Brown B, et al. Macrophage Phenotype as a Predictor of Constructive Remodeling following the Implantation of Biologically Derived Surgical Mesh Materials. Acta Biomater. 2012 March; 8(3): 978-987.</td>
<td>No changes to the Opinion are required.</td>
<td></td>
</tr>
<tr>
<td>144. Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p34 line 16ff We would recommend considering the latest results of the interdisciplinary D-A-CH guideline when combining the results.</td>
<td>See comment above</td>
<td></td>
</tr>
<tr>
<td>145. Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p35 line 17ff At point 4.2.3 „Results of treatment using meshes” the interdisciplinary D-A-CH guidelines are not considered, which induces a contradiction to this on p45, line 4ff.</td>
<td>See comment above</td>
<td></td>
</tr>
<tr>
<td>146. Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>Section 4.2.3, Results of treatment using meshes, pg. 45, lines 23-26 There is not enough focus and emphasis on the fact that meta-analysis and the Milani paper demonstrated no difference in post-op dyspareunia or de novo dyspareunia even though only mesh causes erosion. One would believe that mesh erosion should mean more pain but these studies don’t show that. Also what was not mentioned from the Milani paper is that most mesh erosions are simple to deal with and the rare ones that are more significant are difficult. The following statements from the Milani paper are important for mesh and were not cited in the proposal: “The most commonly reported complication of mesh is “exposure” in which the (mesh) is exposed (4-19%); this is usually treatable. Pain due to shrinkage of vaginal tissue around the mesh is rare but can be severe and difficult to treat. “Randomized trials could</td>
<td>No changes to the Opinion are required.</td>
<td></td>
</tr>
</tbody>
</table>
not however, find a difference between demonstrating a surgery (using) own tissue (NTR) or surgery with mesh on the origin of this pain.” “(pain determined by vaginal examination, by sex, by physical activity – there was no differences between the surgical approaches that could determine which procedure pain could be sourced by a particular method – exam, sex, activity)” “The main risk factor for having pain one year after surgery with a mesh was the presence of pain before this operation.”

Important conclusions from the study:

1) anatomically effective than ‘own’ tissue; 2) functional probably better than ‘own’ tissue; 3) no difference in sexual function; 4) no difference in post-operative dyspareunia; 5) no difference in de novo-dyspareunia; 6) increased risk of de novo prolapse untreated compartment; 7) smoking increases the risk of mesh exposure; 8) operator experience lowers the risk of complication; 9) mesh removal is not easy and risky

| 147. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | p47 table 1. According to new guideline and confirmed by leading anatomists e.g. Prof. Wedel, Kiel, the colporaphia anterior is not an adequate descensus-therapy. | No changes to the Opinion are required. |
| 148. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 47, Table 1 Anterior: subjective (bulge symptoms) and objective recurrence significantly higher for NTR; QOL no difference; no difference in reoperation; no difference in de novo dyspareunia; no difference in sexual functioning (PISQ-12); less de novo prolapse with NTR but numbers very low (2/15 and 13/26); less de novo SUI with NTR; NTR protects against mesh erosion (64/563 or 11.4%). These data indicate that NTR may not be a better choice in the anterior compartment. | No changes to the Opinion are required. |
| 149. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 47, Table 2 Posterior: no difference in recurrent POP symptoms (low denominator); no difference in recurrent anatomical prolapse; less de novo anterior prolapse with NTR but numbers very low (4/24 and 16/30); less anatomical recurrence of posterior prolapse with mesh (numbers low – 9/25 and 1/30); Mesh exposure 5/32 or 15.6% (1 study). These data indicate little difference in the use of NTR or mesh in this compartment. | No changes to the Opinion are required. |
| 150. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 47, Table 3. Multiple: subjective (bulge symptoms) recurrence higher with NTR; objective recurrence of prolapse higher with NTR; posterior recurrence higher with NTR (numbers low 3/26 and 13/32); no difference in de novo dyspareunia; no difference in sexual function scores; no difference in de novo SUI; mesh increases risk of exposure (39/256, 15.2%); lower de novo prolapse of the anterior compartment with NTR but numbers low (7/33 and 16/30). These data indicate little difference in the use of NTR or mesh when treating multiple compartments. | No changes to the Opinion are required. |
| 151. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | p51 line 2ff Indeed in the terminal summary it is in line 3 yet reported from the superiority of using meshes compared with „native tissue repair“ (like also in the DGGG-guideline), however in the abstract this is not mentioned. The increased rate of recurrences in the compartment nearby would be rather caused by the usually two-timed performed surgery in Germany to prevent an overtreatment and to do justice to the DRG-system. But even this accepted rate of recurrences falls off the described rate with own material for 20-30%. Although in line 31 the erosion even as potentially asymptomatic or as described on page 46 Fig. 2 and 3 or Page 52 4ff. / 14ff. are described with no difference in dyspareunia or pain, is nevertheless designed the main problem with vaginal meshes from a rate of 4% (Line 29). There is the possibility excluded that modern meshes achieve better results in the hands of experienced surgeons. Here again we are missing the reference to the D-A-CH guideline or current studies on these meshes (see PARETO - SERATOM, TiLoop 6, Elevate): PARETO: [http://drks-neu.uniklinik-freiburg.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00004566](http://drks-neu.uniklinik-freiburg.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00004566) DRKS-ID der Studie: DRKS00004566 Studienbeschreibung - Titel der Studie: Prospektiv randomisierte multizentrische Studie zur Beeinflussung der Erosionsrate durch partiell resorbierbare transobturatorische Netze bei der Therapie von Beckenbodendefekten im vorderen Kompartiment TiLoop 6: [https://clinicaltrials.gov/ct2/show/NCT01084889](https://clinicaltrials.gov/ct2/show/NCT01084889) ClinicalTrials.gov Identifier: NCT01084889 Anterior Pelvic Prolapse Reconstruction With TiLOOP® Total 6 Elevate: [https://clinicaltrials.gov/ct2/show/NCT00388947?term=elevate+ams&rank=2](https://clinicaltrials.gov/ct2/show/NCT00388947?term=elevate+ams&rank=2) | See comment above |
ClinicalTrials.gov Identifier: NCT00388947 Observational Data Collection of Surgical Outcomes in the Treatment of Vaginal Prolapse With AMS Products (POWER1012))

| 152. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 51, lines 30-31 | “Mesh exposure……is the most frequently reported complication with rate ranging from 4-19%.” “These exposures can cause pain during sexual intercourse……” – the authors have not mentioned that NTR also causes this and that the literature found that there is no difference between the two regarding dyspareunia, whether post-operative or de novo. This finding points to the fact that most exposures do not lead to symptoms. We believe that this should be clearly stated. | No changes to the Opinion are required. |

| 153. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 52, lines 20-22 | There is no difference in pain and no difference in dyspareunia, either post-op or de novo. This is important data that is not well presented in relation to mesh exposure. Mesh exposure is a complication but most are readily treated (see Milani et al. 2013). You should combine not only the safety of a procedure but also the efficacy of the procedure when you are considering the risk benefit analysis. | No changes to the Opinion are required. |

| 154. Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | 2.4 Learning curve and clinical experience, Page 55 | Concerning the prevalence of vaginal mesh exposure, Guillibert et al., (2009) observed 2 that women treated by vaginal estrogens and those operated by the most experienced 3 surgeon had less exposure. However, following multivariate analysis, the only 4 independent risk factors of exposure were the kind of prosthesis, age under 60 and 5 concomitant hysterectomy (Guillibert et al., 2009).

The surgeon’s technical expertise impacts patient outcomes. For example, Withagen et al. evaluated differences between native tissue repair and a tension-free mesh in a randomized clinical trial. This study included 13 centers with 22 surgeons and found that exposure rates varied from 0-100%. As the mesh material was the same across sites, one can conclude that this variation was a function of the surgical skill among the implanting surgeons. Surgical skill is potentially a confounding factor and is typically not controlled for in any study. It is important to note that while manufacturers are required by law to provide product | No changes to the Opinion are required. |
specific related training to physicians to ensure the safe and effective use of their product, the success rate of a surgery can vary depending on the skill of the surgeon. Industry supports the establishment of evidence based guidelines and training programs, created and governed by healthcare professionals, established in cooperation with the relevant European scientific societies.

| 155. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | p57 line 9ff Here potential risk factors for mesh implantation are mentioned: user experience and patient factors. Interestingly, this is precisely determined (line 16 f) that a previous surgery in the pelvic floor increases the risk for future mesh deposits. Yet the opposite is precisely required in the Abstract: meshes only if all other surgeries were unsuccessful. This contradicted the D-A-CH-guideline which certainly looks the mesh implantation the method of first choice (after exhausting the non-invasive options) in certain circumstances. | see answers above. |

| 156. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 56, lines 12-14; pg. 57 line 6; The summary data in Tables 1-3, pages 47-51 does not appear to fully support caution for primary cases. The data may support a statement that NTR should be considered with caution as well. | No changes to the Opinion are required. |

| 157. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 4.2.3, Results of treatment using meshes, pg. 57 lines 13-22 We recommend providing a list of co-morbidities for NTR to demonstrate that these are not unique to mesh and are expected for general pelvic organ surgery. We also recommend providing references for each of the potential risk factors. | No changes to the Opinion are required. |

<p>| 158. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Section 4.2.6 Patient counselling, pg. 57 lines 28-30 Patients should be counselled that TV NTR has data but the data does not show significantly better results than TV mesh. The summary data in Tables 1-3 pages 47-51 does not present a clear advantage for NTR. | No changes to the Opinion are required. |
| 159. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | 4.2.7 Risk assessment and recommendations by national associations, Page 58 Industry notes that the MHRA report titled, &quot;A summary of the evidence on the benefits and risks of vaginal mesh implants&quot; is missing from Section 4.2.7. We believe that a summary of the document should be included, as the MHRA report provides the most current assessment of the benefits and risks of vaginal mesh from a regulatory body. | The SCENIHR agrees with the comment. The text was changed accordingly and the reference list updated. |
| 160. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Section 4.2.6 Patient counselling, pg. 58 lines 5-11 It should be made clearer that although NTR is an alternate treatment, it is not always better than mesh and that the data does not clearly point to NTR as significantly better | No changes to the Opinion are required. |
| 161. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Section 4.2.7 Risk Assessment and Recommendations by NA, pg. 58 lines 38-39 Interesting that mesh in abdominal route was approved. The mesh is no different than what is placed TV, so it is the route rather than the device itself or the technique by which the mesh is placed. | No changes to the Opinion are required. |
| 162. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Section 4.2.7, Risk assessment and recommendations by National Associations, p.59 The U.S. Food and Drug Agency (FDA) notably concluded that there was a consensus for confirming that the safety and performance of surgical mesh indicated for abdominal sacrocolpopexy is well-established. (Obstetrics and Gynecology Devices Panel Meeting, Surgical Mesh Panel Meeting, September 8-9, 2011, Meeting summary). This statement should therefore be reworded to clarify that concerns from health authorities were related to transvaginal mesh repair, while abdominal sacrocolpopexy with mesh was confirmed as a well-established procedure. | This is not in the remit of the SCENIHR and it is outside of the mandate. |
| 163. | Eucomed, Thecla Sterk | Manager Regulations &amp; Industrial Policy | Section 4.2.7 Risk Assessment and Recommendations by NA, pg. 60 lines 1-10 Other than &quot;mesh erosion and shrinkage&quot; all of these complications occur with NTR. This needs to be stated as the implication is that these are mesh issues and not NTR. | The SCENIHR agrees with the comment. |</p>
<table>
<thead>
<tr>
<th>164.</th>
<th>Eucomed, Thecla Sterk</th>
<th>Manager Regulations &amp; Industrial Policy</th>
<th>Section 5.1.1, Risks associated with the use of mesh in urogenital surgery, p.61 The Opinion only refers to synthetic mesh implants. This excludes mesh implants incorporating and/or being processed from animal origin components (e.g. biological mesh implants). It is unclear why these implants were not considered in the review, while the European Commission Mandate was broader.</th>
<th>No changes to the Opinion are required.</th>
</tr>
</thead>
<tbody>
<tr>
<td>165.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>Section 5.1.1, Risks associated with the use of mesh in urogenital surgery, pp.61-62 It is suggested that only Type 1 (macroporous, monofilament) polypropylene are the most appropriate synthetic meshes for implantation via the transvaginal route, while other mesh materials have insufficient evidence. This statement should therefore be reconsidered while including literature references that were missed by the SCENIHR. In addition, the classification used (Amid, 1997) may be too limited in that porosity is not well defined in the scientific literature and dependent on the test methods that are non-standardized to date (Klinge, 2013). Amid P. Classification of biomaterials and their related complications in abdominal wall surgery. Hernia. 1997;1(1):15–21. Klinge U, Park JK, Klosterhalfen B'The ideal mesh?' .Pathobiology. 2013;80(4):169-75.</td>
<td>See the answers above</td>
</tr>
<tr>
<td>166.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>Section 5.1.1, Risks associated with the use of mesh in urogenital surgery, pp.61-62. It is stated that available evidence suggests that non-synthetic (biological) mesh materials do not have sufficient evidence. It is unclear whether this statement refers to the treatment of SUI, POP or both. This conclusion is inappropriate in that the SCENIHR Opinion did not assess this category of implants. In addition, numerous published peer-reviewed studies, including randomized clinical trials comparing biological mesh materials versus synthetic mesh implants with conclusive outcomes, were found and not considered in the SCENIHR Opinion (Auknkalaivanan, 2003; Altman, 2006; Doumerc, 2006; Maher, 2013; Meschia, 2007; Hvid, 2010; Natale, 2009; Guerrero, 2010; Menefee, 2011; Dahlgren, 2011). This statement should either be removed, or the Opinion should be reconsidered to include non-synthetic mesh in its scope. It is besides unclear why this statement does not distinguish between the surgical approach, clinical indications and type of materials. Arunkalaivanan AS, Barrington JW. Randomized trial of porcine dermal sling (Pelvicol implant) vs. tension-free vaginal tape (TVT)</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>167.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>5.0 Opinion, Page 63</td>
<td>What are the risks of surgical interventions using mesh compared to classic surgical interventions? 7 When treating SUI, sling procedures are associated with more storage and voiding 8 symptoms than other repositioning procedures. The use of synthetic non-absorbable 9 mesh is associated with a risk of mesh exposure. 10 When treating POP by vaginal route, the use of synthetic non-absorbable mesh is 11 associated with a risk of mesh exposure and de novo prolapse of the untreated vaginal 12 compartment as well as the development of de novo stress urinary incontinence. The response to this question, does not define “classic” interventions, which are presumably open surgical procedures. As such, the response does not address the risks associated with the classic surgical procedures which are potentially more serious that those associated with less invasive surgical approaches. We respectively request that SCENIHR define classic surgical procedures and include a summary of the adverse events associated with classic interventions, including whether the need for repeat surgery is considered a complication of traditional surgical interventions.</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>169.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p63 line 5ff</td>
<td>If an abdominal positioned mesh is not laid down under the vagina, there can be no vaginal erosions. But it is also not said that you can fix only central defects with the most abdominal mesh technologies and the cystocele / rectocele is not treated.</td>
</tr>
<tr>
<td>170.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>p63 line 16ff</td>
<td>Factors which influence the success of the surgery are material (here the choice is up to Polypropylene), construction (here Amid I was given) and “surface” or size or proportion of foreign material (modern BB-meshes are quite different from hernia meshes). We believe the last four parameters to be influenced by the surgeon and the patient.</td>
</tr>
<tr>
<td>171.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>Section 5.0 Opinion, pg. 63 lines 10-15 A companion statement about the risks of NTR needs to be added since it is titled “…..compared to classic surgical interventions”. NTR Risks are higher failure rates – higher subjective and objective recurrence rates, anatomical recurrence of posterior vaginal prolapse, etc. Alternatively, we would recommend making a statement about what risks mesh reduces compared to NTR.</td>
<td>No changes to the Opinion are required.</td>
</tr>
<tr>
<td>172.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>5.0 Opinion, Page 64 31Develop training programs for surgeons in association with European medical associations The impact of surgeon technique has been largely underappreciated within the medical literature. Industry supports the recommendation of a surgeon certification system, created and governed by medical professionals, based on existing international guidelines and established in cooperation with the relevant European Surgical Associations. Faber and Fromer, How I do it: techniques to avoid complications in transvaginal mesh surgery. Canadian Journal of Urology; 22(3), June 2015</td>
<td>This comment refers to risk management. Risk management is not in the remit of the SCENIHR. No changes to the Opinion are required.</td>
</tr>
<tr>
<td>173.</td>
<td>Eucomed, Thecla Sterk</td>
<td>Manager Regulations &amp; Industrial Policy</td>
<td>5.0 Opinion, Page 64 24 Establish scientific studies to assess the long-term (at least 5 years) safety and performance of the synthetic non-absorbable meshes. The ongoing 522 studies for certain products within the United States support the call for long-term safety and performance data. These long-term, multi-centre, comparative studies are statistically powered to demonstrate that transvaginal mesh products for POP repair and for SUI are non-inferior to recognized standards of care. The studies are conducted under FDA oversight and follow the highest rigor of clinical study conduct. We believe that the data will be sufficient to address the need for additional clinical evidence for mesh products to treat POP and SUI. The studies evaluating transvaginal POP repair are conducted within a registry database platform managed by AUGS. Industry suggests establishing a working group in collaboration with AUGS and European medical societies, regulatory bodies,</td>
<td>No changes to the Opinion are required.</td>
</tr>
</tbody>
</table>
Industry supports the establishment of evidence based guidelines and training programs, created and governed by healthcare professionals, established in cooperation with the relevant European scientific societies. We recognize that several societies and governmental agencies already have established guidelines such as AUGS, IUGA, AAGL, and NAFC.

It is important to note that while manufacturers are required by law to provide product specific related training to physicians to ensure the safe and effective use of their product, the success rate of a surgery can vary depending on the skill of the surgeon.

No changes to the Opinion are required.
| 175. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 5.2, Recommendations, p. 64 The use of European implant registries and clinical studies is welcome. The demand for studies with 5+ years follow-up should however be re-considered in light of the feasibility of such researches in the “real world”. Studies with 2 years follow-up appear feasible, more scientifically-grounded in that it will limit the amount patients lost to follow-up and enable proper data analysis, while providing a clinically-relevant assessment of the safety and performance. | No changes to the Opinion are required. |
| 176. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 5.2, Recommendations, p. 64 Encouraging technological development to enhance patient’s outcomes and restore health is welcome. However, it is unclear why technologies such as electrospinning is cited in this Opinion, in that it is not based on available clinical evidence. | See answers above |
| 177. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Section 9. List of References We believe that the draft Opinion fails to mention many recent quality peer-reviewed articles, which suggests that the literature search may not be complete and therefore does not bring forward comprehensive data on performance of the full range of products available currently. It is also unclear whether the methodology used for the clinical data review complies with current recommended methods for clinical evaluations. | See answers above |
| 178. | Eucomed, Thecla Sterk | Manager Regulations & Industrial Policy | Pg 77 This list may be misinterpreted as an exhaustive list of all devices and manufacturers currently on the market. Industry therefore proposes to delete this table. Also some brand names that are used are inappropriate or incomplete. | See answers above |