EXHIBIT A - PART 1
RULE 26 EXPERT REPORT OF PROF. DR. MED. UWE KLINGE

I. SUMMARY OF OPINIONS

Based on my background training and experience as a general and abdominal surgeon who used Prolene mesh for hernia repair in patients and treated Prolene-mesh-related complications in patients, and based on 20 years of studying Prolene and other surgical meshes as a biomaterials scientist, ten years of which were as a consultant to Ethicon in their preclinical studies of Prolene and other surgical meshes, performing histopathological analysis on hundreds of explanted hernia, sling and prolapse meshes, being an invited lecturer at conferences around the world on the topic of surgical meshes, authoring or co-authoring over 100 peer-reviewed publications regarding surgical meshes, including numerous ones regarding Prolene mesh, reviewing thousands of pages of scientific literature, thousands of pages of internal Ethicon documents and thousands of pages of deposition testimony, the following is a summary of my opinions in this case, all of which I hold to a reasonable degree of medical and scientific certainty:

**The Prolene mesh in TVT undergoes a Chronic FBR.**

After implantation of the TVT mesh, there is a chronic (permanent) foreign body reaction in a woman’s pelvic tissue whereby the woman’s body will react to the polypropylene indefinitely, creating a chronic inflammatory response that leads to scarring around the mesh fibers. Claims by Ethicon in its TVT Instructions for Use (IFU) that “a transient foreign body response may occur” and in its TVT marketing brochures that there is “[n]o foreign body reaction after PROLENE mesh implantation” are inconsistent, false and misleading, and Ethicon knew or
should have been known them to be untrue at the time the company employees wrote these documents and certainly prior to the launch of TVT in 1998.

**The Prolene mesh in TVT is a heavy weight mesh (“overengineered”).**

The greater the surface area of a medical implant, the greater the foreign body reaction and the inflammatory response will be. Ethicon had critical mesh design information regarding the negative consequences in the human tissue of heavy weight, small pore meshes beginning as early as 1998. The heavy weight Prolene mesh (105-110 g/m2) in Ethicon’s TVT products is over 10 times stronger than it needs to be for its intended purpose of treating stress urinary incontinence and thus, it is “overengineered” and leaves much more polymer material in a woman’s delicate and sensitive pelvic tissues than is necessary. Any pelvic mesh designed with this much excess surface area and weight unreasonably increases the risk of injury to the patient and is a less safe design than lighter weight mesh as it causes an unnecessarily increased FBR and inflammatory response.

**The Prolene mesh in TVT is a small pore mesh.**

The smaller the pores (open space between the fibers) of a mesh implant, the greater the risk of scar tissue forming in the pores (“bridging fibrosis” or “fibrotic bridging”) will be. As early as 1998, and certainly by the early 2000’s, Ethicon had critical design information that the risk of bridging fibrosis is increased by surgical mesh with pore sizes less than 1mm in all directions, which in turn increases the risk of a rigid scar plate forming throughout the mesh, leading to integration of the entire mesh in scar tissue. Any pelvic mesh designed with pores this small unreasonably increases the risk of injury to the patient and is a less safe design than mesh with pore sizes greater than 1mm in all directions. The pore size of the Prolene mesh in Ethicon’s TVT products is, according to Ethicon, less than 1mm.

Ethicon’s failure to implement new, critical mesh design changes (lighter weight, larger pore) in its TVT products before its launch in 1998 was unreasonable, compromised patient safety and has led to patient complications like chronic inflammatory reaction, excessive scarring through and around the mesh, nerve entrapment, chronic pain, dyspareunia, erosions, recurrence and the necessity of reoperation in an attempt to correct these problems. The Prolene mesh in Ethicon’s TVT products is unsuitable for use as a permanent implant for treatment of a woman’s stress urinary incontinence. Ethicon did not act as a reasonable manufacturer in choosing to use the “Old Construction 6 mil” Prolene mesh in its TVT products.

**The Prolene mesh in TVT undergoes pore deformation under minimal load.**

A knitted surgical mesh device like the TVT that is permanently implanted in human tissue must be designed in such a manner that the pores of the mesh do not collapse and deform upon the expected forces of implantation as well as the expected in vivo forces. Under minimal strain, the TVT mesh pores deform and collapse thereby increasing the risk of injury to patients in which it is implanted and is a less safe design than products that better withstand these in vivo conditions and do not display these poor outcomes. Permanent deformation and pore collapse of
the TVT mesh leads to fibrotic bridging, scar plate formation, excessive scarring through and around the mesh and a host of tissue complications that can lead to chronic pain, recurrence, erosions, dyspareunia and need for reoperation, to name a few, making it unsafe for its intended purpose of being permanently implanted in a woman’s pelvic tissue. As such, Ethicon failed to act as a reasonable manufacturer of surgical mesh intended to treat stress urinary incontinence in women by marketing and selling a product that lacks sufficient stability while undergoing these forces.

**The Prolene mesh in TVT contract/shrinks.**

The Prolene mesh in Ethicon’s TVT products contracts or shrinks 30-50% after implantation. This shrinkage was known to Ethicon prior to the launch of TVT in 1998. TVT mesh shrinkage leads to nerve entrapment and thus, chronic pelvic pain, erosions, urinary/defecatory/sexual dysfunction, and the need for reoperation to remove some or all of the contracted mesh and excessive scar tissue, thereby making TVT unsuitable for its intended use as a permanent pelvic implant to treat stress urinary incontinence in women. As such, Ethicon failed to act as a reasonable manufacturer of surgical mesh intended to treat stress urinary incontinence in women by failing to design a sling device that would resist such a high level of shrinkage.

**The Prolene mesh in TVT degrades/oxidizes.**

The Prolene mesh in Ethicon’s TVT products is not biologically inert and does in fact undergo degradation of the mesh fiber after implantation in a woman’s pelvic tissues leading to an increased host inflammatory response. When the surface area of the mesh increases, so does the inflammatory response. Also, after the surface of the polypropylene fibers degrades and peels off into the surrounding tissue, the body’s inflammatory mediators and chemical products associated with the inflammatory process (like peroxides, superoxide and hypochlorous acid) will continue to attack and degrade the underlying polypropylene. This is especially true given that the only two protective anti-oxidants have leached away from the fibers leaving all of the exposed surfaces of the mesh vulnerable to further oxidation/degradation. Claims by Ethicon in its TVT IFU that Prolene mesh is not “subject to degradation…by the action of tissue enzymes is false and misleading” because the Prolene mesh does degrade in the presence of the chemical process inherent in the body’s inflammatory reaction to the mesh in the pelvic tissue of women and thus, the TVT products are not suitable for their intended purpose as a permanent prosthetic implant for the treatment of stress urinary incontinence.

**The Prolene mesh in TVT frays, loses particles, curls and ropes.**

The TVT mesh is a knitted textile design without a border and therefore, it has frayed edges that tend to shed particles of polypropylene before, during and after the surgery. As tension is placed on the mesh, it curls, ropes and sheds these particles, all of which make both TVT Mechanical-cut mesh (MCM) and TVT Laser-cut mesh (LCM) unsafe for their intended purpose of being permanently implanted in a woman’s pelvic tissues. The frayed edges and the lost, migrating particles of both TVT MCM and TVT LCM as well as the increased stiffness and rigidity of TVT LCM can all lead to increased inflammatory response, chronic foreign body reaction, erosions, chronic pelvic pain, failure of the implant, dyspareunia, organ damage,
urinary dysfunction and the need for surgical intervention. Ethicon failed to act as a reasonable mesh manufacturer by failing to properly design its TVT slings to avoid fraying, particle loss, curling and roping.

**The Prolene mesh in TVT causes secondary, mesh-related infections.**

The Prolene mesh in Ethicon’s TVT products is susceptible to an increased risk of secondary, mesh-related infections as a result of the bacteria that has both adhered to the mesh during the operative procedure and as it is passed through and implanted into a clean/contaminated environment. Ethicon’s statements in its TVT IFU that its Prolene mesh used in the TVT products “may potentiate an existing infection” and that the plastic, removable sheath around the sling “is designed to minimize infection” are both inadequate and misleading regarding these secondary, mesh-related infections. Thus, the Prolene mesh in TVT is not suitable for its intended purpose of being implanted permanently in a woman’s pelvic tissues, and Ethicon did not act as a reasonable manufacturer by failing to properly study and analyze this critical reality of its Prolene mesh.

**The Prolene mesh in TVT does not match the biomechanics of the pelvis.**

Once implanted, the TVT mesh will be subjected to various three-dimensional and dynamic forces, stains and stresses. Ethicon had no basis for claiming that its Prolene mesh used in TVT had “bi-directional elasticity” given the anisotropic behavior of its Prolene meshes, nor did Ethicon have a basis for claiming that its Prolene mesh, or any of its mesh for pelvic tissue repair, “allows adaptation to various stresses encountered in the body” when Ethicon admittedly has never properly defined what those stresses are in the pelvis much less how the elasticity of TVT properly adapts to those unknown stresses.

From the time of the launch of TVT in 1998 until the present, Ethicon has continually lacked sufficient knowledge regarding pelvic floor in vivo forces and has never adequately calculated or estimated such forces through appropriate testing and therefore, it has never designed a pelvic mesh that is adapted to the physiological environment in which it is implanted. This mesh design failure by Ethicon in its prosthetic implants for stress urinary incontinence has led to numerous patient complications and causes the TVT sling to be unsuitable for its intended purpose of being permanently implanted in a woman’s pelvic tissue. Ethicon failed to act reasonably in designing their slings without designing the biomechanical/physiological requirements of its intended purpose and its intended environment.

Once implanted, the TVT mesh will be subjected to various three-dimensional and dynamic forces, stains and stresses. Ethicon had no basis for claiming that its Prolene mesh used in TVT had “bi-directional elasticity” given the anisotropic behavior of its Prolene meshes, nor did Ethicon have a basis for claiming that its Prolene mesh, or any of its mesh for pelvic tissue repair, “allows adaptation to various stresses encountered in the body” when Ethicon admittedly has never properly defined what those stresses are in the pelvis much less how the elasticity of TVT properly adapts to those unknown stresses.
There are safer alternative pelvic mesh design characteristics than those of TVT.

There are alternative design characteristics of pelvic floor meshes that would be safer in a woman’s pelvic tissues as a treatment for incontinence than some of the design characteristics of the Prolene mesh in TVT.

One such safer alternative design would be a mesh product with larger pores (> 1mm in diameter after accounting for reasonable implantation and in vivo forces) and lighter weight (closer to their Ultrapro mesh which is 25 g/m²). Ethicon has developed a number of meshes for hernia repair and for prolapse repair which are at least closer to fulfilling these requirements. However, even with larger pores and less weight, the knitted structure design would require greater stability, both short and long term, to resist curling, roping, fraying and particle loss. Structural stability under strain and a mesh with finished edges (sealed outer border) would be safer than the Prolene mesh.

Another safer design would be a polymer that better resists degradation and elicits a more favorable inflammatory response. PVDF, as a synthetic, non-absorbable suture or mesh material has improved textile and biological properties over polypropylene. It is thermally stable and more abrasion resistant than other fluorooplastics and induces a minimal cellular response, shows exceptional chemical stability and has excellent resistance to aging. Based on these characteristics, my studies comparing PVDF to polypropylene, Ethicon’s internal documents and other scientific literature, as well as my background, training and experience over 30 years, PVDF, in the appropriate design, is a safer alternative mesh material for human tissues than Ethicon’s TVT Prolene mesh.

Based upon these facts, I am able to conclude, to a reasonable degree of medical and scientific certainty, that the Prolene mesh used in Ethicon’s TVT products is designed in such a way that it does in fact cause a greater inflammatory response and greater foreign body reaction that can, and in some patients does, lead to harmful complications. I am also able to conclude that these materials were inadequately tested and studied and that as a result of all of these factors, set forth more fully in this report, the TVT device is not adequately designed to be safely implanted in a woman’s pelvis for the rest of her life.

II. BACKGROUND AND QUALIFICATIONS

With regard to my medical training, I attended medical school in Aachen, Germany from 1977 to 1983. I began my medical profession at the surgical department of the University Hospital of the RWTH, Aachen, Germany (Department heads/Mentors: Prof. Reifferscheid - 1985, Schumpelick 1985-2010, Neumann 2010-). From 1995 to 2006, my practice was focused primarily on abdominal surgery, and specifically, hernia repair. As a hernia surgeon, I used textile implants (flat meshes) for the repair of abdominal wall hernia or defects in more than 300 patients mainly groin hernia, umbilical hernia, incisional hernia and para stomal hernia. Although I never performed surgery for repair of SUI or POP, I implanted and studied the Prolene mesh used in TVT, extensively over many years.

In 1993, in addition to my surgical practice, I began focusing on surgical research in the area of biomaterial science including tissue engineering and material characteristics, and I designed
preclinical models for surgical mesh and histopathology. I am the author/co-author of approximately 200 peer-reviewed publications listed in PubMed, over 100 of which involve hernia and/or surgical mesh. I have authored and/or contributed to more than 50 book chapters and have been an invited lecturer to more than 160 speaking engagements/conferences. I have received numerous research grants from various institutions and corporations including several grants from the German Ministry for Education and Research, the Ministry for Economics, the German research foundation DFG, the NRW Ministry for Education and Research, the Interdisciplinary Center for Clinical Research of the University of Aachen (RWTH), as well as from industry (Ethicon, Covidien). (Attached hereto as Appendix “A” is a current copy of my Curriculum Vitae with a list of my publications).

III. BRIEF HISTORY OF TEXTILE MESHES FOR TISSUE REPAIR 1958-1993 – THE ABDOMINAL WALL

The current use of textile meshes is based on Usher who, in 1958, started to publish the successful reinforcement of the abdominal wall in six dogs. Initially, meshes were regarded as an alternative procedure, particularly in big hernias. In 1986, Lichtenstein presented his procedure of mesh implantation as the new standard for groin hernia repair. With this technique, the mesh reinforces the tissue in a so-called “tension free” manner. In the early years, Usher used a knitted structure of polypropylene, later widely known as Marlex®. However, Marlex® had increased stiffness after implantation along with considerable complications. Alternatives to Marlex were the polyester mesh Mersilene® from Ethicon or the ePTFE mesh from Gore.

In the late 1980’s and early 1990’s, when polypropylene surgical mesh was increasingly used in hernia surgeries, there was a general lack of knowledge about the materials and about the clinical outcomes associated with these materials. Side effects often manifested with a considerable delay of up to several years. Correspondingly, reports dealing with pain as a major postoperative complication (less than 10% of all hernia publications in PubMed) were published with a delay of years [Fig.1]. We began to look at the scar formation pathologically and developed the theory that incisional hernias could be due to a defective wound healing process with an impaired collagen formation, favoring the necessity to support tissues in these patients by prosthetics.
IV. DEVELOPMENT OF THE FIRST LARGE PORE MESH CONSTRUCTION THAT WAS ADAPTED TO PHYSIOLOGICAL REQUIREMENTS

In the early 1990’s, we speculated that an adaptation of the strength of surgical meshes to the physiological requirements of the tissues in which they would be implanted may allow a considerable material reduction which could improve biocompatibility. We felt that the textile characterization of meshes at that time did not sufficiently reflect the physicochemical properties of the textile, so we had to start almost from the beginning to first identify the relevant parameters.

RWTH University initiated a research program such that in conjunction with various grants, we could add some basic investigations to this project. Through cooperative efforts with Ethicon and the support by these research grants, the project went on for about 10 years. In this period, we gained significant knowledge about the textiles; we defined standard biomechanical characterization for better comparison; we established models for testing the tissue response in animals; we looked for parameters that reflected the inflammatory and fibrotic activity of the foreign body reaction; and we developed a technique to quantify the biomechanical impact on, and the biomechanical properties of, tissues.

As our research progressed, we calculated that hernia meshes needed a tensile strength of 16 N/cm and an elasticity of about 20-30% at this strain. Ethicon provided our research team with thin (about 40 μm) polypropylene threads. Because we were provided only with these 40-μm fibers, we had to combine 5 strands of them at interval distances of 2-3 mm to withstand a strain of 16 N/cm. As this polypropylene net was very floppy, we added an absorbable fiber of Vicryl® (Ethicon) to temporarily make it stiffer. After absorption of the Vicryl®, there would remain just an open structure, with about 30% of the material of the Prolene. This new structure with pores larger than 2 mm, later marketed as Vypro® by Ethicon (1998) and patented in 2000 in the US
(6,192,962), was then studied extensively in several experimental studies. The results were presented at several conferences and most of it has been published in PubMed-listed journals. Vypro® was the first truly lightweight, large pore surgical mesh and became the first of the second-generation surgical meshes. This development would become what is known as the “Lightweight Large Pore Concept” which has been adopted by surgical mesh manufacturers worldwide in developing newer generation meshes and was set forth in a publication by my colleagues and me in 2005.¹ Ethicon’s own employees have testified that they agree with our work, including that light weight meshes with pore sizes of greater than 1 millimeter in all directions will reduce the foreign body response compared to heavyweight meshes with small pores. Dr. Axel Arnaud, Ethicon’s Medical Affairs Group Director, testified that our lightweight large pore concept is “agreed upon by most of the people involved in the science of meshes...this is the basic science about meshes [and] I certainly will not challenge this.”²

V. BIOCOMPATIBILITY

A. Foreign Body Reaction

All experimental and clinical studies indicate that mesh products on the market today cause an initial and chronic inflammatory tissue response in the recipient after implantation. The quality of the inflammatory reaction to foreign bodies of different natures is surprisingly constant, characterized by a rapid accumulation of huge numbers of phagocytic cells, in particular, blood monocytes and tissue-derived macrophages. This type of inflammatory process is known as a foreign body reaction (FBR). It is characterized by an initial inflammatory burst caused by a release of a huge combination of potent inflammatory mediators which then attract other cell types including T-cells, polymorphonuclear granulocytes (PMNs), plasma cells and fibroblasts. Within a few days, this cellular activity forms an early granuloma layer recognized by the very typical foreign body giant cells and an outer layer of fibrosis with deposition of collagen. This late stage granuloma is not a static type of chronic inflammation but rather, it represents a chronic wound with an increased cell turnover even years after implantation. The various inflammatory cells e.g. macrophages, at the interface and in contact with the polymer, undergo apoptotic cell death and are replaced. [Fig. 2]

² Arnaud deposition 9/25/13 772:25 to 777:16; 779:4-11
We published our results in 1998 and 1999 of the histological analyses from explanted mesh from rats, dogs and humans. The tissue response in humans was almost identical to the morphological observations in the animal models. In our 1999 study, we reviewed approximately 350 human explant samples of various mesh modifications gathered from centers all over Europe. Even 15 years after explantation, the longest observation in our study, a persistent chronic FBR could still be detected, indicating that mesh is likely never completely inert with respect to local inflammatory processes. The persistence of this FBR is important, especially in younger patients in whom the mesh will remain for several decades. The delay before explantation of mesh for infection of up to 56 months, for chronic pain of up to 48 months and for recurrence of up to 180 months established that in many clinical studies with shorter surveys of less than 1-2 years, the morbidity rates are underestimated.4,5 It is well known in the medical community that the vagina is to be considered a “clean-contaminated” field. The implantation of mesh may result in a biofilm which will make it difficult for the host cells to kill the mesh infection; in fact, the development of these biofilms will protect the harmful bacteria that the host

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3 Semin Immunopathol (2011) 33:235-243 – Formation of a foreign body granuloma at the mesh to host tissue interface
cell set out to kill (See Bacterial Adherence/Biofilms/Mesh-related Infections Section below).\(^6\)

Furthermore, my colleague and Ethicon’s top pathology consultant for 20 years, Bernd Klosterhalfen, informed Ethicon at an expert meeting at Ethicon’s Norderstedt facilities in 2006 that based on our studies, the tissues in the body can react to the mesh for up to 20 years.\(^7\)

At another Ethicon expert meeting at Norderstedt the following year, in a PowerPoint presentation to the experts in attendance, Ethicon stated that there can be “excessive FBR > massive scar plate > more shrinkage” depending on the type of mesh.\(^8\) Ethicon stated in that presentation that “small porous meshes (<1mm) lead to ‘fibrotic bridging’ > increased shrinkage.”

Ethicon employees have testified that Ethicon knew before the launch of its pelvic meshes, for both incontinence and prolapse repair, that in some women, there would be a severe FBR and chronic life-altering inflammatory reaction causing debilitating and chronic pain, erosions, recurrence, need for revision surgery and dyspareunia in some women.\(^9\)\(^,\)\(^10\)\(^,\)\(^11\)\(^,\)\(^12\)

It is my opinion to a reasonable degree of medical and scientific certainty that after implantation of the TVT mesh, there is a chronic (permanent) foreign body reaction in a woman’s pelvic tissue whereby the woman’s body will react to the polypropylene indefinitely, creating a chronic inflammatory response that leads to scarring around the mesh fibers. Claims by Ethicon in its TVT Instructions for Use (IFU) that “a transient foreign body response may occur” and in its TVT marketing brochures that there is “[n]o foreign body reaction after PROLENE mesh implantation” are inconsistent, false and misleading, and Ethicon knew or should have been known to them to be untrue at the time the company employees wrote these documents and certainly prior to the launch of TVT in 1998.\(^13\)\(^,\)\(^14\) In addition to abundant scientific literature to the contrary, deposition testimony of numerous Ethicon employees in this litigation also indicates their knowledge of the falsity of this statement.\(^15\)\(^,\)\(^16\)\(^,\)\(^17\)

B. Weight

As is evidenced in countless pages of deposition testimony of Ethicon employees and internal Ethicon documents, Ethicon was aware that meshes with lighter weight and larger pores versus the heavy weight, small pore, “Old Construction” TVT Prolene mesh, lessened the risk of these harmful tissue reactions and thus, lessened the risk of injury to patients.

\(^7\) ETH.MESH.00870466 2006 Expert Meeting Norderstedt
\(^8\) ETH.MESH.01782867 “Factors Related to Mesh Shrinkage” Powerpoint presentation by Kestin Spychaj
\(^10\) Owens deposition 9/12/2012 98:11to 99:07;
\(^11\) Batke deposition 08/01/13 257:23 to 259:13
\(^12\) Arnaud deposition 9/25/13 769:23 to 770:4
\(^13\) ETH.MESH.00339437-442 “5 Years of Proven Performance” Feb 2002
\(^14\) ETH.MESH.02340504 TVT IFU
\(^15\) Barbolt deposition 10/9/13 137:01 to 137:17;
\(^16\) Holste deposition 07/29/13, 51:3 to 53:6
\(^17\) Hellhammer deposition 9/11/2013, 60:24-61:1; 210:15-211:16
Ethicon’s Medical Affairs Director, Piet Hinoul, recounts the history of Ethicon’s attempts to develop lighter weight, larger pore meshes and the multiple reasons for doing so in a 2012 Clinical Expert Report for their light weight, large pore mesh, Ultrapro/Prolift + M.\(^{18}\)

Knitted, polypropylene mesh as a reinforcement for Hernia Repair has been used for 40+ years and is an accepted method for reducing recurrence of abdominal wall defects seen in both incisional and inguinal hernias. However, implantation of polypropylene mesh is associated with an increase in problems associated with the foreign material implant. Complications associated with these materials have led to changes in implant materials and construction with a goal to 1) reduce implant mass and 2) increase the mesh pore size. The impact of such reductions in material mass on the durability of the repair must be considered. Assessing the breaking strength of healthy tissue, in vivo measurements of maximum pressure during the stresses of coughing, jumping and Valsalva maneuver, and mathematical modeling of abdominal wall forces, have led to the conclusion that synthetic mesh implants, even the lower mass mesh implants, are significantly stronger than required (Deprest et 2006, Cobb et al. 2005).\(^{19}\)

The Cobb 2005 article states that heavy weight meshes with pores of 800 microns or smaller lead to bridging across the pores (“fibrotic bridging”). He lists several meshes of varying weights in the article of which Prolene is one of the heavyweight meshes. [See Figures 1 and 2]\(^{20}\)

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\(^{19}\) ETH.MESH.08315779 “Clinical Expert Report” dtd 9-25-2012 at 782.

Figures 1 and 2

It is my opinion, to a reasonable degree of medical and scientific certainty, that the greater the surface area of a medical implant, the greater the foreign body reaction and the inflammatory response will be. Ethicon had critical mesh design information regarding the negative consequences in the human tissue of heavy weight, small pore meshes beginning as early as 1998. The heavy weight Prolene mesh (105-110 g/m²) in Ethicon’s TVT products is over 10 times stronger than it needs to be for its intended purpose of treating stress urinary incontinence and thus, it is “overengineered” and leaves much more polymer material in a woman’s delicate and sensitive pelvic tissues than is necessary. Any pelvic mesh designed with this much excess surface area and weight unreasonably increases the risk of injury to the patient and is a less safe design than lighter weight mesh as it causes an unnecessarily increased FBR and inflammatory response.
C. Pore Size

Polypropylene filaments cause an intense inflammatory response in the abdominal wall as well as in the tissues of the pelvic floor. There is an increased fibrotic reaction hindering the physiological remodeling at the tissue/implant interface. This intense scar formation contributes to the wound contraction.21

In our studies from the late 1990’s, in which we evaluated the inflammatory response and fibrotic reaction in the tissues at the interface with the mesh implant, we saw that that large pore mesh (Vypro) was integrated into a loose network of perifilamentous fibrosis with fat tissue present in between the fibers. In contrast, the small pore mesh was incorporated entirely in perifilamentary granulomas and scar tissue, which bridged the whole pore diameter <1 mm. This phenomenon, known as “fibrotic bridging”, exists when granulomas, side by side, form a common outer fibrotic capsule joining each mesh fiber and forming a rigid “scar plate” covering the whole mesh. This scar plate leaves no space for further tissue ingrowth and leads to a number of complications including loss of elasticity and pain associated with the rigidity, shrinkage or contraction of the mesh, mesh erosion, nerve entrapment, bacterial encasement, chronic pain and dyspareunia.

The concept of fibrotic bridging was and is well known to Ethicon and is evident in numerous internal Ethicon documents. 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 [Figure 3]
With the development of Vypro, we were able to increase the pore size by up to 500-600% (Vypro 3-5 mm vs. Prolene <1mm) and decreased the weight from 105-110 g/m² (Prolene) to 25g/m² (Vypro). Given that the risk of bridging fibrosis is increased by mesh with pore size < 1mm in all directions, any mesh designed with pores this small increases the risk of injury to the patient and is a less safe design than mesh with pore sizes > 1mm in all directions. Simply put:
the greater the pore size or open space in between fibers, the less the risk of fibrotic bridging and formation of a rigid and potentially dangerous scar plate encapsulating the mesh. Again, Ethicon had this critical mesh design information regarding the consequences in the human tissue of heavy weight, small pore meshes beginning as early as 1998, and this is evident in numerous depositions of Ethicon scientists.  

![Figure 4](image)

**Figure 4**

A rather infamous DVD produced by Ethicon and featuring an Ethicon consultant and fellow hernia surgeon, Dr. Todd Heniford, was shown at conferences and seminars in the late 2000’s. Ethicon was involved in the production of that DVD as evidenced by the cover of the DVD and their name at the end of it. That DVD touts the benefits of lightweight, large pore meshes and, importantly, describes the dangers of heavy weight, small pore meshes. Dr. Heniford uses slides in the DVD that are from his published literature with his colleague, Dr. William Cobb that has been referenced in numerous Ethicon documents, PowerPoint presentations, professional education materials, expert meetings and Clinical Expert Reports.

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35 Batke deposition 08/01/012 113:3 to 114:3, 172:6 to 174:15, 118:10 to 120:25  
36 Hellhammer deposition 09/12/13 403:18 to 404:9; 407:13-23  
37 Holste depositions 07/29/13 51:3 to 53:6; Holste Deposition 12/14/12 89:20 to90:21  
38 Semin Immunopathol (2011) 33:235–243 - a Scar net formation following large pore (~3 mm) and b scar plate formation following small-pore (~0.3 mm) mesh implantation  
39 Arnaud deposition 9/25/13 756:9 to 757:8  
40 B. Todd Heniford 2007 "The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair" Video  
41 B. Todd Heniford 2007 "The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair" Video  
At one point in the DVD, published with an Ethicon/JNJ logo from 2007, Dr. Heniford states that with the advent of lightweight, large pore meshes “there really is not a reason to use heavy weight polypropylene in the human body…to say well this is the mesh I’ve always used is not an excuse to continue to use it.” Ethicon internal documents by Joerg Holste and Boris Batke indicate Ethicon’s knowledge of this DVD and were concerned that Prolene is very similar to the Marlex listed in the DVD.\textsuperscript{46, 47}

In the work of Dr. Cobb, the weight of TVT Prolene is listed as the heaviest weighted mesh. Ethicon cites to this work repeatedly. The Prolene mesh in TVT was first marketed in 1974 and as such, is Ethicon’s oldest, heaviest weight, smallest pore mesh yet to this day; Ethicon continues to sell it in all of their currently-marketed TVT products. In their depositions, Ethicon employees have acknowledged that they knew that the heavy weight, small pore mesh in TVT Prolene mesh can lead to an increased risk of a greater FBR, more intense and chronic inflammatory response, shrinkage or contraction of the mesh, nerve entrapment in the pelvic tissues, erosions and chronic pelvic pain.\textsuperscript{48-50}

Ethicon has used its “Old Construction” 6 mil Prolene hernia mesh (first marketed in 1974) in all of its TVT meshes since the original TVT was launched in 1998.\textsuperscript{51} Axel Arnaud, the Medical Director of Ethicon France acknowledged that the Prolene mesh used in TVT products has never changed.\textsuperscript{52} It is my opinion, to a reasonable degree of medical and scientific certainty, that the “Old Construction” 6 mil Prolene hernia mesh in Ethicon’s TVT products is heavy weight, small pore (<1mm in diameter) mesh which causes a greater FBR and more intense inflammatory response in human tissues than lighter weight, larger pore meshes, making it more susceptible to fibrotic bridging, scar plate formation and encapsulation of the mesh in scar tissue leading to a cascade of harmful reactions in human tissue, including pelvic tissues.

A number of Ethicon employees have testified that they became aware of the lightweight large pore concept by 1998 through Ethicon’s collaboration with both Dr. Bernd Klosterhalfen and me during the development of Vypro.\textsuperscript{53} Numerous Ethicon internal documents demonstrate the Ethicon was acutely aware of the heavyweight, small pore problem.\textsuperscript{54-56, 57-58, 59-60, 61, 62, 63-64}
Ethicon employees have also admitted that the Prolene mesh used in TVT products was lightweight and small pore mesh. 65, 66

A decision was apparently made in 1998 to change the TVT Prolene mesh construction. In 1998, Ethicon indicated that its “long-term desire [was] to support the PHS and TVT devices with the new construction material.” 69 [Emphasis added] Ethicon seemingly planned from the time of the launch of TVT to replace the “Old Construction 6 mil” mesh with a new mesh construction; however, they delayed making these improvements for the purpose of getting the TVT device on the market in Europe by October 30, 1997:

Product’s improvements

In order to meet our objective and launch TVT on October 30th, 1997, we decided to simplify our activity both at manufacturing and development level. As we have moved ahead in our European activity, we have in fact realised that product improvement is not a major issue in Europe. Anyhow, we recognise that some amendments are desirable and therefore are going to work on a second generation product to be released 1Q99.

Following changes will be made:
• new construction Prolene* mesh to be used (after clinical test by Prof. Ulmsten and Prof. Nilsson
  - 40 patients with 6 moths follow-up)
• 5 mm needles instead of 6 mm (width)
• shiny surface of needles (instead of opaque) to provide "slim" effect
• new shrinking tube (transparent) for needle-tape swaging
• blister pack

Manufacturing and operations will be followed up during 1998, so as to ensure release of second generation product 1Q99. 70 [Emphasis added]

Unfortunately for patients, Ethicon chose not to replace its “Old Construction 6 mil” Prolene mesh in its TVT products but rather, chose to use the same mesh they had been marketing since 1974, without regard to critical design developments and considerations that they had studied, developed and were ready to launch.

59 ETH.MESH.04015102 3/01/12 Batke, Boris to Mayes, Casey SUBJECT: AW: AGES Pelvic Floor Conference-Gala Dinner Invitiation
60 ETH.MESH.04037600 Mesh Innovations PowerPoint
61 ETH.MESH.09651393 Invention Disclosure;
62 ETH.MESH.05585066 “Ultrapro” PowerPoint presentation by Boris Batke;
63 ETH.MESH.05916450 “Chronic Pain Prevention/future – Bioengineer’s point of view”
64 ETH.MESH.04037600 “Innovations in Mesh Development” PowerPoint presentation by Boris Batke;
65 ETH.MESH.02337968 “R&D Perspective – The Journey from Prolift to Prolift +M” PowerPoint presentation by Cliff Volpe;
66 ETH.MESH.01203957 The Future of surgical meshes: the industry’s perspective PowerPoint by Piet Hinoul
67 Hellhammer deposition 09/12/13 550:1-14
68 ETH.MESH.05479535
69 ETH.MESH.09264884
70 ETH.MESH.10183005
It is my opinion, to a reasonable degree of medical and scientific certainty that the smaller the pores (open space between the fibers) of a mesh implant, the greater the risk of scar tissue forming in the pores (“bridging fibrosis” or “fibrotic bridging”) will be. As early as 1998, and certainly by the early 2000’s, Ethicon had critical design information that the risk of bridging fibrosis is increased by surgical mesh with pore size less than 1mm in all directions, which in turn increases the risk of a rigid scar plate forming throughout the mesh, leading to integration of the entire mesh in scar tissue. Any pelvic mesh designed with pores this small unreasonably increases the risk of injury to the patient and is a less safe design than mesh with pore sizes greater than 1mm in all directions. The pore size of the Prolene mesh in Ethicon’s TVT products is, according to Ethicon, less than 1mm.

It is also my opinion, to a reasonable degree of medical and scientific certainty, that Ethicon’s failure to implement new, critical mesh design changes (lighter weight, larger pore) in its TVT products before its launch in 1998 was unreasonable, compromised patient safety and has led to patient complications like chronic inflammatory reaction, excessive scarring through and around the mesh, nerve entrapment, chronic pain, dyspareunia, erosions, recurrence and the necessity of reoperation in an attempt to correct these problems. The Prolene mesh in Ethicon’s TVT products is unsuitable for use as a permanent implant for treatment of a woman’s stress urinary incontinence. Ethicon did not act as a reasonable manufacturer in choosing to use the “Old Construction 6 mil” Prolene mesh in its TVT products.

D. Pore Deformation

In approximately 2005, I applied for and received a grant to study the porosity of textile meshes in an attempt to objectify porosity in a reproducible manner. Working with an engineer at the FH Aachen University of Applied Sciences, Prof Thomas Muehl, we published the results of this granted project in 2008 in the Journal of Biomedical Materials Research Part B: Applied Biomaterials. 71

Our research was based on my research since the late 1990’s that pore sizes that prevent fibrotic bridging and will permit ingrowth of physiological tissues should exceed 1 mm between two polypropylene filaments. As stated in our publication, “To exclude large pore areas that may be provided by long and thin pores with narrow parts of pores, the pore geometry has to be evaluated as well. Therefore, only those pores and those parts of the pores are extracted, which have dimensions greater than 1mm or 1000 μm in all directions. The remaining porosity is defined as ‘effective porosity’”.

We published another study of the pore size/porosity of surgical meshes in 2013 based on our 2008 work which studied and analyzed Ethicon’s Prolift and Prolift +M pelvic organ prolapse meshes. 72

72 J. Otto, et al., Elongation of textile pelvic floor implants under load is related to complete loss of effective porosity, thereby favoring incorporation of scar plates; J Biomed Mater Res A 2013 Apr 29
In connection with this litigation, Prof. Muehl has performed similar testing on Ethicon’s surgical mesh products using the same porosity test methods as we used in our studies in 2008 and 2013.73 (NOTE: An Ethicon R&D Scientist, Vincenza Zaddem, Team Leader of Prolift +M and Technical Lead of Prolift, was shown the Muehl study from 2007 and she testified that it sounded like a valid test and that she believed that it would be a good test for Ethicon to look into in order to determine the effective porosity and effective porosity under strain of their pelvic meshes.74) This was again confirmed in testimony by Ethicon employee, Joerg Holste and circulated numerous times within Ethicon as a “more sophisticated set up” than Ethicon’s method of porosity testing. 75, 76, 77 Ethicon was also aware of the concept of “effective porosity” and the necessity of maintaining pore sizes of >1mm after stretch. 78, 79, 80, 81, 82, 83

![Conventional PP mesh diagram](image)

Figure 584

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73 Prof. Thomas Muhl Report
74 Zaddem deposition 03/28/12, 387:14 to 387:20
75 Holste deposition 10/9/2013, 417:9 to 418:22
76 ETH.MESH.02184130 2008 email circulating New Objective to Characterize the Porosity of Textile Implants
77 ETH.MESH.04945136 2010 email circulating New Objective to Characterize the Porosity of Textile Implants
78 ETH.MESH.03021946 T-Pro Stage Gate Meeting on August 25, 2008
79 ETH.MESH.02587926 When the Implant Worries the Body
80 ETH.MESH.01752532: Mesh Design Argumentation Issues
81 ETH.MESH.01785259 January 17, 2010 Email re: +M relaxation
82 ETH.MESH.02587925 “When the implant worries the body” PowerPoint presentation
83 ETH.MESH.02185582 “Biomechanical Considerations for Pelvic Floor Mesh”
84 ETH.MESH.03021946 T-Pro Stage Gate Meeting 8/25/08
Ethicon estimates that its TVT slings will encounter elongation or stretch once placed in a woman’s body to 20%.85 In other Ethicon internal documents, Ethicon estimates the in vivo forces placed on its TVT slings will be approximately 1N.86 In other Ethicon documents, Ethicon scientists quote the intra-abdominal pressures as follows: 87

· Standing: 23cm H2O
· Lifting 5kg: 22 cm H2O
· Valsalva: 79 cm H2O
· Coughing: 96 cm H2O
· Bearing down: 102 cm H2O

Moalli et al. cited our published work in 1999 that “forces applied to mid-urethral slings in vivo is estimated to be in the range of approximately 5 to 15 N or 1.1 to 3.4 lbs.” 88

When developing the protocol for testing the TVT meshes, I determined the uniaxial forces that would be placed on the mesh as following assumptions:

· In contrast to flat meshes without tensile stress, narrow slings may be considered to work as ligaments having to withstand uniaxial strain.89 This is undisputable for the process of implantation and the early postoperative time. To mimic the mechanical strain in this phase, we applied strain to the mesh in an uniaxial setting;

· The strain applied should cover the forces and the elongation that can be assumed to be relevant;

· Forces were related to the width of the sling, and thus N/cm was used for comparison with estimated membrane tensions;

· Membrane tension of 16 N/cm was calculated as requirement for the abdominal wall. As the diameter of the pelvis is less than a half of the abdominal wall, the membrane tension should be less than half; 90

· Experimental studies by DePrest et al resulted in a membrane tension of 2 to 5 N/cm as strain to be expected in the pelvic floor, 1 N/cm in non-prolapsed tissues;

· The tensile strain in the pelvic floor is expected to lead to an elongation of the textile. An elongation of up to 20% is considered to form the comfort zone, and elongation of 40% defines the safety zone; 91

85 ETH.MESH.00541379 Memo to File from Martin Weisberg re: Mesh Fraying to TVT Devices
86 ETH.MESH.00584491 2006 email re AFNOR standards; ETH.MESH.01219414: Elongation Characteristic of Laser Cut PROLENE Mesh for TVT; Smith deposition 08/21/2013, 587:22 to 588:23
87 ETH.MESH.05237872 “Mesh Properties – How important are they?” by Peter Meier
89 ETH.MESH.04048515 at 8518: KOL Interview of Carl G. Nilsson
90 ETH.MESH.02010834 "Biomechanical consideration for Pelvic floor mesh design" by Juergen Trzewik and Christoph Vailhe; ETH.MESH.04048515 Nilsson KOL interview; Trzewik deposition 09/18/2013 226:20-22; ETH.MESH.02227224 Thunder PowerPoint 05/09/2008
The tensile force during implantation procedure of a pelvic mesh is considered to be up to 30 N, and correspondingly, the in vitro simulation should have less tensile strength;

The intra-abdominal pressure to the pelvis is estimated by Janda to be 8.3 kPa, whereas an intra-abdominal pressure of 20 kPA is estimated to stress the abdominal wall to 16 N/cm - a lower intra-abdominal pressure leads to a lower tensile load. Considering the lower diameter of the pelvis, a mechanical load of less than 10 N/cm would be reasonable;

Pullout force is considered by Ethicon to be 1.6 N/cm (20% elongation; 164 g = “physiological” load);

As a consequence, although the burst strength of Prolene is 91 N/cm (REF Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. Klosterhalfen B, Klinge U, Schumpelick V. Biomaterials. 1998 Dec;19(24):2235-46.)

We applied forces of 1 to 10 N to the slings, which should cover an elongation of less than 40%; altogether, a range that is used in internal studies of Ethicon as well.

Ethicon’s biomechanical engineer, Juergen Trzewik’s “Invention Disclosure” helped to further define our porosity testing parameters and protocols. In his Invention Disclosure, Dr. Trzewik wrote:

The physiological, mechanical boundary conditions can be separated into two main conditions. The comfort zone is defined by the load situation within the implant under normal physiological conditions.

Here, 'the main load of 2.5 kPa is delivered by the weight of internal organs 2.5 kPa


The material of the implant basic structure is designed to be characterized by a comfort zone of high elasticity at a low physiological load
and a safety zone characterized by low elasticity at high loads. Both zones are separated by the construction of the yield point by tangential approximation of the stress strain curve for the zone of initial elongation and the slope of region of high stress. The yield point for vaginal tissue is considered to be between 10%-200% of area strain.


The stretch of vaginal tissue may exceed 300% under certain conditions.


The yield point is individually defined for the different structures of the implant (e.g., the arms of the implant are characterized with a lower yield point than the implant body). The material behaviour simulates the behaviour of tendon structures is described by a significantly reduced elasticity compared to the implant body. [H. Yamada, Strength of Biological Materials. Baltimore: The Williams & Wilkins Company, 1970] The yield point for the arms should not exceed 10%.

The implant material is anisotropic and stretches differently in longitudinal and transversal direction. The yield point in the transversal direction exceeds the longitudinal direction between 100%-500%.


Biomechanical features like increased flexibility are undesired during the surgical procedure of implant placement, to avoid any uncontrolled or undefined stretching of the implant during implantation. Pre-straining of the implant would change the mechanical properties of the implant. A temporary stress-shielding of the long-term implant is necessary during implantation and wound contraction.

The yield point of the implant is lower than <10% before absorption of the supporting stress shielding structure.

As a consequence of all this information, we performed measurements to 11 mm TVT and TVT-O slings at a strain of

- 102 g (0.9 N/cm)
- 164 g (1.5 N/cm)
- 250 g (2.2 N/cm)
- 500 g (4.5 N/cm)
- 1000 g (8.9 N/cm)

The significance of the Muehl method of testing these mesh products is that it provides useful data in terms of how a mesh will perform in the human body, particularly in regard to the risk of fibrotic bridging. The first most important observation from this testing was that the textile porosity, the textile porosity under strain, the effective porosity and the effective porosity under strain in TVT produced results that did not meet the most basic requirements that Ethicon was aware of since the late 1990’s, early 2000’s. As minimal strain was applied to the test sample, the geometric shape of the pores deformed and ultimately collapsed. This deformation led to even smaller pores that make the Prolene mesh highly susceptible to fibrotic bridging, encapsulation by a rigid scar plate and the array of potential complications that occur as a result of this inflammatory process.

Another significant observation during the porosity testing by Prof. Muehl, was the “curling”, sometimes referred to as “roping”, that occurred in the TVT under minimal strain. We published an article in 2007, 97 in which we showed the tissue reaction and fibrotic ingrowth of PP due to curling/roping of the mesh due to scar shrinkage after H&E staining. [Fig. 6] As strips of mesh begin to curl, the fibers become situated too close together enhancing the inflammatory response and leading to fibrotic bridging. Our recent publication regarding Muehl testing of Ethicon’s meshes showed similar characteristics.98

98 Otto, J., Kaldenhoff, E., Kirchner-Hermanns, R., Muhl, T., Klinge, U. Elongation of textile pelvic floor implants under load is related to complete loss of effective porosity, thereby favoring incorporation in scar plates. Wiley Online
Figure 6

Yet another significant observation during the porosity testing by Prof. Muehl both in the current testing as well as the testing published in 2013 was the “fraying” at the edges of mesh which could be seen upon removal from the package but became markedly worse in the TVT mesh sample at minimal strain, especially in the mechanical cut slings. These frayed edges create an increased inflammatory process, and increases the tendency for curling. As fraying occurs, mesh particles can be released into the tissue, increasing the local load with foreign body surfaces, and creating an even greater inflammatory response in the tissues. (See Sections below on Fraying/Particle Loss/Mechanical Cut Mesh (MCM)/ Laser Cut Mesh (LCM)/Curling and Roping

After being subjected to even minimal strain or tension, the TVT slings, like the arms in the Prolift and Prolift +M in our 2013 publication, not only curled, frayed and demonstrated deformation of the pores, they also failed to return to their original or near-original geometric shape and design. This phenomenon of permanent elongation “is mostly due to a rearranging of the sling’s architecture and should not be confused with the traditional mechanics definition of plastic deformation of an elastic material.” It is my opinion, to a reasonable degree of medical and scientific certainty, that this permanent elongation of TVT slings leads to permanent pore deformation or collapse and increases the risk of an enhanced inflammatory reaction in the human tissues and thus excessive scarring and the cascade of events related to an enhanced and

100 Moalli P., Papas, N., Menefee S., Albo, M., Meyn, L., Abramowitch, D., Tensile properties of five commonly used midurethral slings relative to TVT. Int Urogynecol J (2008) 19:665-633
chronic inflammatory response. It was determined in 2009 by Ethicon that Prolene mesh in its TVT products would distort irreversibly at 164 grams of force.\textsuperscript{101, 102} This irreversible damage would lead to the series of events that is known with permanent distortion or deformation. The TVT original suprapubic sling also undergoes such permanent elongation.

In fact, Ethicon Biomechancial Engineer, Juergen Trzewik, proposed various ideas to prevent pore collapse in Ethicon’s pelvic floor meshes. [Figure 5 and 6]

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{example.png}
\caption{Stress shielding needed to avoid pore-collapse, deformation and pre-stretch.}
\end{figure}

\textsuperscript{101} ETH.MESH.00345806 2009 email re Preclin
\textsuperscript{102} ETH.MESH.00072085 Final Report PSE Accession Number 05-0396 Project Number 67379
\textsuperscript{103} ETH.MESH.02227224 MGPP Thunder Decision Meeting PowerPoint presentation
In a 2006 email discussing new French AFNOR standard for testing, a Senior Scientist at Ethicon, Gene Kammerer states, while referencing the Lin article “the article shows the maximum forces applied to the sling under the urethra is about 1N or 100 grams. So, for in vivo function (while the mesh is in the body) a force to elongate should correspond to about 1N”, which is in sharp opposition to the tensile forces provided by the Prolene hernia mesh.

In its “Gynecare TVT Tension-free Support for Incontinence Sales Force Update” dated July 3, 2001, Ethicon states that the properties of its TVT mesh fiber construction was such that the Prolene mesh in TVT “is like a rubber band while other meshes are like silly putty.” Based on Muehl’s testing of TVT meshes and my work with Prolene mesh both as a surgeon and a researcher, it is my opinion to a reasonable degree of medical and scientific certainty, that this is a clear misrepresentation by Ethicon. A rubber band has elasticity such that when it is stretched, it springs back into its original or near-original shape. Prolene mesh, due to both the polypropylene material and the knitted design, does not return to its original shape upon being subjected to mechanical stresses, which has to be considered as realistic at least during the implantation, but rather, it undergoes permanent elongation and permanent pore geometry deformation as proven by both the Muehl testing and the testing by Moalli et al. as referenced herein.

In testing by Moalli et al. of the Ethicon TVT slings, they found in uniaxial testing, similar to that of Prof Muehl, that “the permanent elongation after C1 (ten cycles between 0.5 and 5 N or roughly 0.1 and 1.1 lbs.) of the Gynecare mesh was different from that of all the other samples tested. Gynecare samples permanently elongated by 17.5 +/- 4.2%, indicating that although very little force applied, there is irreversible deformation of the TVT.” The study authors went on to state:

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104 ETH.MESH.02010849
105 ETH.MESH.00584491 2006 email re AFNOR standards
The most important finding of the paper is that Gynecare TVT mesh has a unique tensile behavior which is characterized by an initial region of very low stiffness in which the mesh easily elongates in response to small changes in force...As a result of this behavior, after cyclical loading at low loads...Gynecare mesh permanently elongated by more than 10% of its initial length, confirming the easy permanent deformability of this mesh that is observed clinically during placement.” (emphasis added)
In his recent deposition, the Medical Director of Ethicon France, Axel Arnaud, states: “My understanding of this is there are two – normally two types of pores, and when you pull on them, their size might change.” He also agrees that when tension is placed on the mesh that the pore sizes change. Both Dr. Arnaud and another Ethicon Medical Director, Piet Hinoul have testified in this litigation that they respect my work and the work of my colleagues, including Dr. Klosterhalfen and that we are highly qualified in this very specific field of biomaterials research on surgical meshes. In fact, Dr. Hinoul testified that he would defer to me as to whether the pores in Ethicon’s meshes collapse and deform under load and further stated that if Ethicon’s pelvic floor meshes (in that case, Prolift) do collapse and deform making them, in essence, microporous meshes, “Ethicon would not have wanted to sell that mesh.”

My opinion, to a reasonable degree of medical and scientific certainty is that a knitted surgical mesh device like the TVT that is permanently implanted in human tissue must be designed in such a manner that the pores of the mesh do not collapse and deform upon the expected forces of implantation as well as the expected in vivo forces. Under minimal strain, the TVT mesh pores deform and collapse thereby increasing the risk of injury to patients in which it is implanted and is a less safe design than products that better withstand these in vivo conditions and do not display these poor outcomes. Permanent deformation and pore collapse of the TVT mesh leads to fibrotic bridging, scar plate formation, excessive scarring through and around the mesh and a host of tissue complications that can lead to chronic pain, recurrence, erosions, dyspareunia and need for reoperation, to name a few, making it unsafe for its intended purpose of being permanently implanted in a woman’s pelvic tissue. As such, Ethicon failed to act as a reasonable manufacturer of surgical mesh intended to treat stress urinary incontinence in women by marketing and selling a product that lacks sufficient stability while undergoing these forces.

E. Mesh Contraction

Mesh contraction, also known as mesh shrinkage, retraction, bunching or wrinkling, is a common phenomenon after mesh implantation that is closely related to scarring and fibrotic bridging. Mesh contraction can be defined by a reduction of the surface area of the original implanted mesh. The surface reduction is due not to shrinkage of the mesh fibers themselves but rather to a retraction of the fibrotic scar tissues around the mesh. Retraction of the scar is a physiologic reaction of maturing scar that is characterized by a constant water loss and, consequently, a subsequent surface area decrease to an average of 60% of the former wound region. It is known to take place in the first few weeks after implantation but can last as long as 12 months or more after surgery. The medical literature and Ethicon’s own internal documents

107 Arnaud deposition 09/17/2013 108:17 to 109:11
108 Hinoul trial 01/1616 1112:17 to 1114:4
109 Hinoul deposition 09/19/12 1054:9 to 1055:5; 1063:5 to 1065:11
110 Arnaud deposition 11/16/12 370:9 to 371:13; 373:20 to 375:2
report that there is considerable mesh contraction of surgical meshes made of polypropylene.\textsuperscript{111, 112, 113, 114, 115, 116, 117} [Figures 7, 8, 9a and 9b]
Figure 8\textsuperscript{119}

![Image of hernia mesh](image.jpg)


Figure 9a\textsuperscript{120}


While developing its prolapse meshes, the TVM group in 2006 advised Ethicon of the common occurrence of retraction or shrinkage which then creates a “cord-like” mesh. This issue not only leads to poor coverage leading to recurrence, but will also increase locally the amount of foreign body reaction due to pore collapse. This phenomenon then leads to additional complications depending from the location of the mesh including: pain, dyspareunia, nerve entrapment, increased inflammation, urinary and fecal incontinence, urinary retention, blood vessel injury and others.

In referencing his internal Ethicon paper “Shrinking Meshes?”, Ethicon scientist Joerg Holste stated in an email on March 13, 2006 “this was our scientific statement on mesh shrinkage: Basically, small pores, heavy weight meshes induce more fibrotic bridging tissue reaction causing more mesh shrinkage during maturing of the collagenous tissue. See my presentation about biocompatibility.” That email was in response to a string of internal Ethicon emails in which Ethicon employees were discussing their concerns over a study by Ramshaw in which polypropylene meshes actually shrank more than polyester.

In February of 2007, Dr. Kerstin Spychaj, Ethicon R&D prepared a presentation entitled, “State of the knowledge in ‘mesh shrinkage’ – What do we know?” which she presented at an Ethicon Expert Meeting on February 23, 2007 at Ethicon’s Norderstedt facility. Dr. Spychaj did a literature review and concluded that the “ideal mesh” in order to avoid shrinkage would be a

121 Carolyn Lewis Explant Photos – Dr. Phillipe Zimmern 09/10/13
122 ETH.MESH.01774758 December 2006 email regarding TVM Group mesh design input
123 ETH.MESH.05446127 Email from Holste to Engel et al. re: Mesh and tissue contraction in animals
124 ETH.MESH.05446127 Email from Holste to Engel et al. re: Mesh and tissue contraction in animals
lightweight material (partially absorbable) with a pore size > 1mm and mild but not excessive FBR and wound contraction with swift and adequate tissue growth. Not only had Ethicon determined that shrinkage was obviously critical to the quality of its mesh products, they knew it could cause “vaginal anatomic distortion which may eventually have a negative impact on sexual function.” Furthermore, they knew that “its treatment is difficult.” Several other Ethicon employees and/or consultants provided testimony or presentations regarding the issue of mesh shrinkage. The Prolene mesh in TVT is both heavyweight and has pore sizes <1mm in all directions, making it highly susceptible to harmful, painful contraction.

Johnson & Johnson hired an outside consulting firm named PA Consulting in 2010 to do a comprehensive and confidential analysis of its surgical meshes in order to look at the increased risk of erosions in its meshes. The final report was issued in June 2011. As part of their investigation and study, PA Consulting interviewed both outside and in-house Ethicon experts. One such expert was Dr. Bernd Klosterhalfen, a KOL for Ethicon and consultant for 20 years. In his interview on January 18, 2011, Dr. Klosterhalfen informed PA Consulting and an Ethicon representative of many variables inherent in Ethicon’s meshes that lead to patient complications and failures of the devices. Regarding the shrinkage of Ethicon’s meshes, Dr. Klosterhalfen restated what was known or should have been known for greater than a decade:

At the high level, there are two classes of “shrinkage” observed with mesh implant (Note: the term ‘shrinkage’ is a misnomer. Tissue reaction over time encapsulates the mesh with connective tissue and effectively ‘crushes’ the mesh into a ball (like crushing a sheet of paper); the mesh does not truly shrink):

- The first is in the immediate short term following implant; the implant is observed to lift and may ‘roll up’ from its position. This occurs as a result of poor positioning, placement and/or suturing of the implant by the clinician

- The second class of shrinkage is the formation of scar tissue; observed in the longer term (months) following implantation. This scar tissue can reduce and compact, causing the mesh to crumple up.

That last quote is important because as was known widely in mesh science and manufacturing industry, older heavy weight, small pore meshes like the Prolene in Ethicon’s TVT slings, experience greater amounts of mesh shrinkage or contraction – up to 50% of the area of the mesh. By this time in 2011, Dr. Klosterhalfen had received approximately 1,000

125 ETH.MESH.01218361-01218367: Dr. Kerstin Spychaj, State of the knowledge in “mesh shrinkage” – What do we know? 04/05/2007
126 ETH.MESH.02992139 Lightning Clinical Strategy dtd 11/22/06
127 Robinson deposition 03/13/12, 260:5-22
128 Ciarrocca deposition 3/29/12, 340:9 to 340:12
129 Kirkemo deposition 04/18/12, 105:14 to 108:16
130 ETH.MESH.03924887 Meshes in Pelvic Floor Repair
131 ETH.MESH.00870466 06/2/2006 Expert Meeting
132 ETH.MESH.07192412 PA Consulting meeting notes with Dr. Klosterhalfen
mesh explant samples over 10 years, and he and I had published a widely-circulated and discussed publication regarding our analysis of these 1,000 explants. He and I had also published a significant amount of peer-reviewed literature regarding explants, animal models and newer designs for more “ideal” meshes and had explained this phenomenon to Ethicon for many years as their consultants. Thus, in this interview, Dr. Klosterhalfen was not informing Ethicon of anything that they did not already know – all of their polypropylene meshes shrink from 30-50%, and the heavier the weight and smaller the pores, the more this shrinkage phenomenon will occur.

It is my opinion, to a reasonable degree of medical and scientific certainty, based upon my background training and experience as a general and abdominal surgeon who used Prolene mesh for hernia repair in dozens of patients and treated Prolene-mesh-related complications in dozens of patients, and based on 20 years of studying Prolene meshes, ten years of which were as a consultant to Ethicon in their preclinical studies of Prolene and other surgical meshes, authoring or co-authoring numerous peer-reviewed publications regarding Prolene mesh, reviewing hundreds of internal Ethicon documents and hundreds of pages of deposition testimony that the mesh used in all of Ethicon’s TVT sling products is a heavy weight (105-100 g/m2), small pore (<1mm pore diameter) mesh that leads to an increased risk of intense and chronic FBR, severe and chronic inflammatory response, excessive scar formation, fibrotic bridging, increased risk of mesh encapsulation, scar plate formation, mesh shrinkage, nerve entrapment, chronic pelvic pain, erosions, dyspareunia, recurrence, need for painful and, at times, dangerous revision surgery and multiple, life-long, debilitating injuries in some women.

It is also my opinion, to a reasonable degree of medical and scientific certainty that the Prolene mesh in Ethicon’s TVT products contracts or shrinks 30-50% after implantation. This shrinkage was known to Ethicon prior to the launch of TVT in 1998. TVT mesh shrinkage leads to nerve entrapment and thus, chronic pelvic pain, erosions, urinary/defecatory/sexual dysfunction, recurrence and the need for reoperation to remove some or all of the contracted mesh and excessive scar tissue, thereby making TVT unsuitable for its intended use as a permanent pelvic implant to treat stress urinary incontinence in women. As such, Ethicon failed to act as a reasonable manufacturer of surgical mesh intended to treat stress urinary incontinence in women by failing to design a sling device that would resist such a high level of shrinkage.

F. Degradation

Studies as early as the 1960’s demonstrated concern over the degradation/oxidation effects of polypropylene when used in the human body.\textsuperscript{134-136} It was presumably due to such concerns that Ethicon adds anti-oxidative additives to its compound batches when formulating and extruding the polypropylene resin – a process that has barely been revisited, retested or changed since the late 1960’s.\textsuperscript{137}

\begin{itemize}
\item 136 H.J. Oswald, E. Turi, The Deterioration of Polypropylene By Oxidative Degradation, \textit{Polymer Engineering and Science}, 5 (1965) 152-158
\item 137 ETH.MESH.0228619 Prolene Resin Manufacturing Specifications
\end{itemize}
More recently, there has been growing concern regarding the degradation of polypropylene in prosthetic mesh implants. It is believed that oxidation of the mesh occurs as a result of the chemical structure of polypropylene and the physiological conditions to which it is subjected. This leads to embrittlement of the material, and after implantation in contrast to materials with permanent smooth surface to an increased surface of the prosthesis, due to impaired cellular mobility at the interface to an increased shearing stress, and likely to a stimulation of the inflammatory foreign body reaction, and via subsequent increase of fibrosis eventually enhances the risk for chronic pain.

Costello, et al. reported in 2007 on the degradation of polypropylene surgical mesh. The authors reported that certain by-products of the inflammatory process cause the polypropylene to be more susceptible to the oxidative effects of the metabolites produced by phagocytic cells during the inflammatory response. They saw cracks and other surface degradations such as peeling of the polypropylene fibers under Scanning Electron Microscopy (SEM).\(^{138}\) [Figure 10] The Costello publication was widely circulated in mesh manufacturing and scientific circles and at conferences, seminars and other lecturing forums that I attended.

Ethicon was aware of the Costello publication as evidenced by a string of emails in 2007 after the article was published.\(^{139}\) An Ethicon Medical Affairs employee, Tom Divilio, M.D., referenced the article to fellow employees in both Ethicon U.S. and Ethicon Germany, indicating that one of the authors, a well-known hernia surgeon Dr. Bruce Ramshaw was “challenging our perception of polypropylene as an ‘inert’ material after implantation.” Dr. Divilio of Ethicon stated that “I think it’s important that we understand what they are seeing as this group has a well-funded lab that will be looking at explanted mesh in great volume over the next couple of


\(^{139}\) ETH.MESH.05588123 7/9/07 Email from Stephen Wolhert to Brigitte Hellhammer re Costello Article
years and our current concepts are going to be challenged. **Would appreciate it if we could think of some study designs that would confirm or refute their assumptions.**” (Emphasis added)

Another Ethicon scientist, Dr. Dieter Engel, with whom I worked closely over the years, also commented in that email string “there have been a number of anecdotal reports that polypropylene mesh shows some changes in the surface with time. The Aachen group, who has so far collected more than 1000 explanted meshes, showed examples many years back.” This is true.

In that email string, Dr. Divilio also erroneously stated that Ethicon “previously had implanted PROLENE suture into dogs and explants after 10 years revealed no changes in the material.” Actually, the Ethicon dog study regarding degradation of various Ethicon sutures was supposed to be 10 years in duration, but was stopped after seven years and did demonstrate degradation of the Prolene material.140 (See further discussion on Seven-year dog study below.)

Other studies have also demonstrated that polypropylene is not biologically inert. In 2011, Clave, et al. performed a comparative analysis of 100 pelvic mesh explants. The average period of removal was 790.6 days. Over 20% showed such degradation damage to the fibers. [Fig. 11] The article states that the lead author of the study had an educational position for Ethicon Europe.141 Other authors have also written about the degradative effects of polypropylene in the human body. 142, 143, 144, 145

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140 ETH.MESH.09557798 7 Year Dog Study
142 Cozad MJ, Grant DA, Bachman SL, Grant DN, Ramshaw BJ, Grant SA. Materials characterization of explanted polypropylene, polyethylene terephthalate, and expanded polytetrafluoroethylene composites: spectral and thermal analysis
144 Ostergard, D. Degradation, infection and heat effects of polypropylene mesh for pelvic implantation: what was known and when it was known. Int Urogynecol J. 2011; 22:771-774
Like the published results of the Costello degradation study, the Clave study has become an important and often-cited article regarding the degradation of polypropylene meshes, and also like the Costello study, Ethicon became aware of the Clave publication and had internal discussions regarding its implications for its surgical meshes; this time, it was the MHRA, the UK equivalence of the FDA, who questioned Ethicon in an email dated 01/26/2012 regarding this latest degradation study. The MHRA request not only asked Ethicon to comment on the degradation of its meshes but also, whether their meshes contract or “shrink”.

I observed in many of my studies that macrophages and foreign body giant cells were key-players in ‘frustrated phagocytosis’. These cells are known to release mediators such as reactive oxygen intermediates, degradative enzymes and acid, which favor the elimination of cells. However, foreign body giant cells will initiate the degradation of a biomaterial. This high concentration of degradative agents will cause visible damage to the biomaterial that is easily visible in electron microscopy.

Ethicon held meetings to discuss the MHRA email and how to fashion a response. Daniel F. Burkley, MS, “Principal Scientist” in Ethicon’s analytical characterization department for 34

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146 ETH.MESH.07226377 03/01/2012 email including 01/26/2012 email from MHRA re Clave Article