Colorectal Product Innovations and Evidence Presentation
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Colorectal Market Landscape

About 500,000 colectomies are performed annually in the United States and that number is expected to grow with aging baby boomers and a surging Medicare population.¹

About 32% of colorectal surgeries are performed each year for cancer. The other 68% are performed for noncancerous diseases.²

In addition, colorectal surgery is the #2 readmission procedure in the United States.³

Readmission after colorectal surgery is associated with a cost of approximately $9,000 per readmission.⁴

The patients most at risk for readmission include those with surgical site infections (SSIs), anastomotic leaks, bleeding, and incisional hernia.⁴

### READMISSION AFTER COLECTOMY

**ACS NSQIP® 2012 RESULTS³**

<table>
<thead>
<tr>
<th></th>
<th>Number of Patients (3,830)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>990</td>
<td>25.8%</td>
</tr>
<tr>
<td>Obstruction</td>
<td>693</td>
<td>18.1%</td>
</tr>
<tr>
<td>Bleeding</td>
<td>255</td>
<td>6.7%</td>
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</tbody>
</table>

ACS NSQIP=American College of Surgeons National Surgical Quality Improvement Program®

Reducing the risks associated with leaks, bleeding, and infections could lead to better clinical and economic outcomes
The Ethicon Colorectal Solution

Our goal is to optimize outcomes, even in the most complicated colectomy procedures and colorectal cases.

Ethicon supports your efforts to reduce complications such as anastomotic leaks, bleeding, and infections through dedicated programs in research, innovative products, and education.

**RESEARCH**

focused on the characteristics of colorectal tissue to reduce complications.

**INNOVATIVE PRODUCTS**

specifically designed for unmatched precision in colorectal cases.

**EDUCATION**

for you and your OR team on the latest techniques—in lab, in person, or via remote learning.

Every day, you face challenges associated with the growing epidemic of comorbidities and complex disease conditions. Every day, Ethicon is working with surgeons like you to advance new solutions through research, innovative products, and education.

At Ethicon, we share your interest in improving the standard of care for colorectal patients. Partner with Ethicon Every Day.

5. Benchtop testing on porcine colon, comparing Ethicon CDH29P to Medtronic EEA2835, p<0.001. (C2280).

6. Benchtop testing on porcine rectum. Normalized mean tissue movement along the cut line from before clamping on tissue to after firing the CONTOUR® Curved Cutter Stapler (CS40G) vs Endo GIA® ULTRA Handle (EGIAUSTND) and Endo GIA® Radial Reload with Tri-Staple™ Technology (EGIARADMT) on 2.1 mm to 2.9 mm thick tissue. 3.8 mm (9.4%) vs 17.4 mm (32.5%), p<0.001. (C2099).

7. Preclinical test of distal tip bleeding (ENSEAL® vs Impact-LF4318) in thick porcine mesentery base. (p<0.001). (C2169). (062631-161101).

8. Preclinical testing on porcine carotids (ENSEAL® vs Impact-LF4318) that measured mean max lateral thermal damage via histology (p=0.005). (C2155). (062746-161103).

9. Benchtop testing in porcine stomach tissue. Mean tissue movement from after clamping on tissue to after firing ECHELON FLEX™ Powered Plus Stapler (PSEE60A) and ECHELON Reload with GST vs Endo GIA® ULTRA Handle (EGIAUSTND) and Endo GIA® Reload with Tri-Staple™ Technology at 3.3 and 4.0 mm tissue thicknesses (3.3 mm: GST60T 0.642 mm vs EGIA60AMT 4.806 mm p<0.001; 4.0 mm: GST60T 0.654 mm vs EGIA60AXT 5.116 mm p<0.0001).

10. ECHELON FLEX™ GST System Blue and Green Reloads compared to Endo GIA with TriStaple™ Technology Purple Reloads evaluated via gross observations of firings in 1.5 mm to 3.0 mm thick animate porcine ileum. Firings rated as fully captured by GST 12.1% vs Tri-Staple at 17%. Results can vary based on tissue characteristics, device design, technique and other factors.

11. Design Validation Study with surgeons (n=33) operating in simulated procedures in an animate porcine laboratory model (O51950-160425).

12. In a design validation study with surgeons (n=33) operating in simulated procedures in an animate porcine laboratory model (26G33) (053344-160516).
OUR GOAL IS TO OPTIMIZE OUTCOMES IN COLORECTAL SURGERY

Surgical innovations to help reduce complications at every critical moment of colectomy procedures and colorectal surgery

<table>
<thead>
<tr>
<th>SURGICAL GOAL</th>
<th>ETHICON PORTFOLIO</th>
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<tbody>
<tr>
<td>Achieve optimal mobilization and vessel sealing</td>
<td>ENSEAL® X1 Large Jaw</td>
</tr>
<tr>
<td>Gain visibility and ease of access in the lower pelvis for distal transection</td>
<td>CONTOUR® Curved Cutter Stapler</td>
</tr>
<tr>
<td>with adequate margins and perfusion</td>
<td>ECHELON FLEX™ GST System</td>
</tr>
<tr>
<td>Create an anastomosis that helps reduce the chance of leaks</td>
<td>Ethicon ECHELON CIRCULAR™ Powered Stapler</td>
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<tr>
<td></td>
<td>Ethicon Endoscopic Curved Intraluminal Circular Stapler</td>
</tr>
<tr>
<td>Address risk factors associated with surgical site infections (SSIs)</td>
<td>PDS® Plus Antibacterial (polydioxanone) Suture</td>
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<tr>
<td></td>
<td>MONOCRYL® Plus Antibacterial (poliglecaprone 25) Suture</td>
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<td></td>
<td>STRATAFIX™ Knotless Tissue Control Devices</td>
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<td>DERMABOND ADVANCED® Topical Skin Adhesive</td>
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<tr>
<td>Achieve hemostasis with adjunctive methods</td>
<td>SURGICEL® Absorbable Hemostats</td>
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<tr>
<td></td>
<td>EVARREST® Fibrin Sealant Patch</td>
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<td></td>
<td>SURGIFLO® Hemostatic Matrix</td>
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<td></td>
<td>EVICEL® Fibrin Sealant (Human)</td>
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</table>
**Introducing better sealing with ENSEAL® X1 Large Jaw**

**Surgical Goal:** Mobilization and Vessel Sealing

**Surgical Challenge:** Achieving optimal mobilization and vessel sealing is critical for colorectal surgeons

ENSEAL® X1 Large Jaw is an advanced bipolar device designed for use in open surgical procedures. It offers better sealing compared to LigaSure Impact™, with less bleeding,* less thermal spread,† and better ergonomics.13

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### BETTER HEMOSTASIS

- Larger distal electrode surface area.14
- ENSEAL® X1 Large Jaw* had 88% less bleeding in thick tissue compared to LigaSure Impact.™7*

### BETTER TISSUE MANAGEMENT

- Enabled by Adaptive Tissue Technology, ENSEAL® X1 Large Jaw had 41% less thermal spread compared to LigaSure Impact.™8†

### BETTER DESIGN

- ENSEAL® X1 Large Jaw offers an overall better design compared to LigaSure Impact.™13
- Convenient control placement is designed for less hand movement.15
- 360° shaft rotation is designed to improve access to targeted tissue.16

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*Thermal imaging of jaws under IR camera
Results may vary. The above image represents the respective devices being used on porcine mesentery after a single activation that lasted approximately eight seconds.

*Preclinical test of distal tip bleeding (ENSEAL® vs Impact-LF4318) in thick porcine mesentery base (*p<0.001).
†Preclinical testing on porcine carotids (ENSEAL® vs Impact-LF4318) that measured mean max lateral thermal damage via histology (*p<0.005).*
Surgical Goal: Distal Transection in Open Colectomy

Surgical Challenge: Navigating the tight confines of the pelvic region to access hard-to-reach tissues low within the rectum and to precisely place staples on the colon just where you want them.

CONTOUR® Curved Cutter Stapler has a unique curved head designed to cut and staple deep in the pelvis while providing a more precise transection.6*

<table>
<thead>
<tr>
<th>MORE PRECISE TRANSECTION</th>
<th>DEEPER PELVIC ACCESS</th>
<th>UNIQUE DESIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CONTOUR® Curved Cutter Stapler achieves a more precise transection compared to Covidien Endo GIA™ Radial Reload with Tri-Staple™ Technology.6*</td>
<td>• 21% smaller head width than Covidien’s Endo GIA™ Radial Reload with Tri-Staple™ Technology.7*</td>
<td>• Parallel closure and tissue retention pin designed to transect the rectum in a single perpendicular firing.</td>
</tr>
<tr>
<td>• 78% less tissue slippage during firing compared to Covidien Endo GIA™ Radial Reload with Tri-Staple™ Technology.17*</td>
<td>• CONTOUR® allows placement of a 40 mm cut line in the width of a 30 mm space.</td>
<td>• 13% larger jaw aperture than Covidien’s Endo GIA™ Radial Reload with Tri-Staple™ technology.‡</td>
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<tr>
<td>• CONTOUR® Curved Cutter Stapler, with its simultaneous firing, may eliminate one reload per procedure.18*</td>
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</table>

*Benchtop testing on porcine rectum. Normalized mean tissue movement along the cut line from before clamping on tissue to after firing the CONTOUR® Curved Cutter Stapler (CS40G) vs Endo GIA™ ULTRA Handle (EGIAUSTND) and Endo GIA™ Radial Reload with Tri-Staple™ Technology (EGIARADMT) on 2.1 mm to 2.9 mm thick tissue, 3.8 mm (9.4%) vs 17.4 mm (32.5%), p<0.001.

†Ethicon US, LLC. (CONTOUR® head width, 2.5in. / 64 mm), Covidien, Endo GIA™ Radial Reload with Tri-Staple™ Technology Technical Guide (Radial Reload head width, 3.2in./81 mm).

‡Ethicon US, LLC. (CONTOUR® 18.5 mm full jaw opening), Covidien, Endo GIA™ Radial Reload with Tri-Staple™ Technology Technical Guide (Radial Reload 16.3 mm jaw opening).
**SURGICAL STAPLERS**

Mastering movement. To transect as you intend. With the ECHELON FLEX™ GST System.*

**Surgical Goal:** Distal Transection

**Surgical Challenge:** Challenging tissue—diseased, thick, thin, fragile, and varying—can lead to tissue movement or slippage during firing, which can result in exposed tissue layers, poorly formed and spaced staples, and extra firings.

The ECHELON FLEX™ GST System* controls tissue movement to enable you to transect as you intend even on the most challenging tissue.

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**LESS SLIPPAGE**

- ECHELON FLEX™ GST System has 4x less tissue slippage during firing† compared to Endo GIA.™

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**LESS FIRINGS**

- The ECHELON FLEX™ GST System enables transecting colorectal tissue in fewer firings due to less slippage on colon.*

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**MORE MUCOSAL CAPTURE**

- The ECHELON FLEX™ GST System is 7x more likely to fully capture the mucosa in the staple line.‡
- In benchtop testing, the initial leak site is associated with areas of incomplete mucosal capture 78% of the time.§

See Appendix for more information.

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Our enhanced, market-tested, performance stapling solutions deliver exceptional tissue handling during firing across the broadest range of tissue thicknesses and types faced in colorectal procedures.

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*System components include ECHELON FLEX™ Powered Plus Stapler and ENDOPATH ECHELON™ Reloads with Gripping Surface Technology.

†Benchtop testing in porcine stomach tissue. Mean tissue movement from after clamping on tissue to after firing ECHELON FLEX™ Powered Plus Stapler (PSEE60A) and ECHELON Reload with GST vs Endo GIA™ ULTRA Handle (EGIAUSTND) and Endo GIA™ Reload with Tri-Staple™ Technology at 3.3 and 4.0 mm tissue thicknesses (3.3 mm: GST60T 0.642 mm vs EGIA60AMT 4.806 mm p<0.001; 4.0 mm: GST60T 0.654 mm vs EGIA60AXT 5.116 mm p<0.001).

‡ECHELON FLEX™ GST System Blue and Green Reloads compared to Endo GIA with Tri-Staple™ Technology Purple Reloads evaluated via gross observations of firings in 1.5 mm to 3.0 mm thick animate porcine ileum. Firings rated as fully captured by GST 12.1% vs Tri-Staple at 1.7%. Results can vary based on tissue characteristics, device design, technique and other factors.

§Location of leak was associated with site of incomplete mucosal capture in 46 of 59 firings that had incomplete mucosal capture. Benchtop testing of Tri-Staple Purple, GST Green and GST Blue in porcine ileum.
**SURGICAL STAPLERS**

**ECHELON CIRCULAR™ Powered Stapler. Optimize perfusion.**\(^{19,*}\) Reduce staple line leaks.\(^{20,†}\)

**Surgical Goal:** Circular Anastomosis

**Surgical Challenge:** Tissue tension, poor blood supply and variable tissue thickness can compromise the anastomosis and lead to significant complications. Among complications, anastomotic leaks are a dominant surgical concern due to their high mortality risk.

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### EVENLY DISTRIBUTED COMPRESSION

- Designed with offset closure of the staple legs, 3D Stapling Technology evenly distributes compression and reduces potential leak paths.\(^{21,‡}\)

### PRECISE COMPRESSION

- **Gripping Surface Technology** gives precise compression only where it is needed, resulting in a 33% reduction in compressive forces on tissue.\(^{5,§}\)

### REDUCED MOVEMENT AND FORCE TO FIRE

- Produces increased stability with 37% less distal tip movement during firing\(^{12,||}\) and reduces force to fire by 97%\(^{13,¶}\).

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![Conceptual comparisons demonstrating potential effects of tissue compression during firing. Results can vary based on tissue characteristics, device design, techniques and other factors.](image1)

![Illustration depicts actual paths of tip movement during testing—each cube represents a space measuring 5 mm.](image2)

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\(^{*}\) Preclinical perfusion model comparing Ethicon CDH29P to Medtronic EEA2835, in which perfusion was not statistically significantly different between devices (p>0.005).

\(^{†}\) Benchtop testing in porcine tissue at ≤30 mmHg (26 mmHg average pressure experienced during intra-operative leak test), comparing Ethicon CDH29P to Medtronic EEA2835, \(p<0.001\).

\(^{‡}\) Staple line analysis in benchtop testing, comparing Ethicon CDH29P to Medtronic EEA2535.

\(^{§}\) Benchtop testing on porcine colon, comparing Ethicon CDH29P to Medtronic EEA2835, \(p<0.001\).

\(||\) Users firing in a porcine model, comparing Ethicon CDH29P to Medtronic EEA2835, \(p=0.003\).

\(^{¶}\) Benchtop testing, comparing Ethicon CDH29P to Medtronic EEA2835, \(p=0.001\).

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The **ECHELON CIRCULAR™ Powered Stapler** enables surgeons to reduce leaks without compromising perfusion—resulting in 61% fewer leaks\(^{20,†}\) at the staple line compared to the Medtronic DST Series™ EEA™ Stapler.
Surgical Goal: Secure Anastomosis

Surgical Challenge: Many colorectal surgeries are at "high risk" for leaks due to poor blood supply, compromised tissues, or difficult anatomy. Leaks significantly increase morbidity and mortality, as well as length of surgery and cost of care.24,25

The Ethicon Endoscopic Curved Intraluminal Circular Stapler is designed to deliver the right amount of compression for optimal staple formation, leading to a secure anastomosis and effective perfusion to promote healing.

<table>
<thead>
<tr>
<th>LESS TISSUE DRAW</th>
<th>CONTROLLED TISSUE COMPRESSION</th>
<th>LESS TISSUE STRAIN</th>
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</thead>
<tbody>
<tr>
<td>• The Ethicon Intraluminal Stapler, with its continuously smooth anvil shaft, creates 3.9x less excess tissue draw during anvil closure compared to the Covidien DST Series EEA with its stepped anvil shank.*</td>
<td>• The Ethicon Intraluminal Stapler, with its Controlled Tissue Compression and Adjustable Height Staple technology, allows the user to control the formed staple height based on tissue conditions.</td>
<td>• The Ethicon Intraluminal Stapler, with its fixed anvil design, causes less tension on the anastomosis with 1.4 times less strain on the staple line during opening compared to the Covidien DST Series EEA with its tilting anvil.†</td>
</tr>
</tbody>
</table>

Our circular staplers’ designs are grounded in Halsted’s principles of surgery—the importance of hemostasis, the gentle handling of tissue, and the application of appropriate tissue compression for safe and effective surgery.

*Benchmark testing on porcine jejunum. Comparing mean tissue draw during anvil closing of the Ethicon Circular Stapler (CDH25A) and the DST series EEA circular stapler (EEAXL25). 0.437 cm vs 1.708 cm, p<0.005.
†Benchmark testing on porcine jejunum. Comparing mean tissue stretch during anvil opening after firing of the Ethicon Circular Stapler (CDH25A) and the DST series EEA circular stapler (EEA25). 1.558 cm vs 2.228 cm, p<0.005.
WOUND CLOSURE

Triclosan-coated sutures are now supported by the World Health Organization (WHO) for the purpose of reducing the risk of SSIs.*

**Surgical Goal:** Secure Wound Closure

**Surgical Challenge:** Suture as a site for infection. Each tissue layer has a different wound-healing process.

**Ethicon Plus Sutures have been shown in vitro to inhibit colonization of the suture for 7 days or more, including bacteria commonly associated with SSI.**26,27

*The CDC, WHO, ACS and SIS Guidelines on reducing the risk of SSIs are general to Triclosan-coated sutures and are not specific to any one brand.

<table>
<thead>
<tr>
<th>SECURE CLOSURE IN EACH TISSUE LAYER</th>
<th>MORE CONSISTENCY, MORE SECURITY, AND MORE EFFICIENCY</th>
<th>BETTER COSMESIS AND HIGHER PATIENT SATISFACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PDS® Plus Antibacterial (polydioxanone) Suture is specifically designed to provide secure closure in high-tension tissues, such as fascia, for 6 weeks.28</td>
<td>• STRATAFIX™ Knotless Tissue Control Devices provide more strength and security compared to interrupted suturing, without knot-related complications. They deliver more consistent tension control and approximation during closure, and are more efficient than continuous suturing.31</td>
<td>• When used with sutures, DERMABOND ADVANCED® Topical Skin Adhesive was shown ex vivo to add 75% more strength to wound closure than sutures alone. It provides a microbial penetration barrier—99% protection in vitro for 72 hours against organisms commonly responsible for SSIs, including Staphylococcus epidermis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Enterococcus faecium.32,33†</td>
</tr>
<tr>
<td>• MONOCRYL® Plus Antibacterial (poliglecaprone 25) Sutures are designed for deep dermal and subcuticular skin closure because they have a high initial breaking strength to maintain wound approximation.29,30†</td>
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*Petri dish image is for illustrative purposes only, zone of inhibition testing results can vary.

Ethicon is committed to addressing risk factors for wound complications, such as SSI, wound dehiscence, and incisional hernia in colorectal surgeries.

†Clinical significance unknown.
Surgical Goal: Achieve hemostasis

Surgical Challenge: Control bleeding during procedures and maintain visibility.

Hemostasis Optimization Program
A systematic approach to bleeding

Addressing Bleeding through Adjunctive Methods

Continuous oozing
Will not stop with compression/simple packing. The solution for this bleeding is more time consuming than it is difficult.

SURGICEL®
Absorbable Hemostats

Problematic
Even though the bleeding is accessible, it could be trouble. It is more than routine and likely to be resistant to conventional means; it requires immediate attention, causing disruption to the normal progression of surgery.

EVARREST®
Fibrin Sealant Patch

Difficult to access
Bleeding that occurs in tight and irregular spaces—you cannot see the exact source of the bleed. You are concerned that accessing a tight space will cause more harm.

SURGIFLO®
Hemostatic Matrix

Potential re-bleeding risk
Bleeding may be addressed intraoperatively, but could later develop into more serious complications, especially in high-risk patients.

EVICEL®
Fibrin Sealant (Human)

High-pressure vessel bleeding
A leak in a high-pressure vessel (aortic or peripheral vascular suture line) that has been stopped, but could be catastrophic if it leaks post-op.

See Appendix for Essential Product Information and Important Safety Information.
Important Risk Information: Adjunctive hemostats (shown above) are not intended for use on nonbleeding tissue or for prophylactic use. The bleeding situations identified reflect customer insights/market research on optimal adjunctive hemostat utilization. The product solutions should only be used in accordance with their instructions for use. Production recommendations should not supplant medical judgment. Surgeon preference, experience, and patient needs may dictate alternate technique. Review all relevant precautions, especially the indications, contraindications, warnings, and information for use. Please see package inserts for Full Prescribing Information.

The visual does not reflect any sequential order in use.
INDICATIONS
SURGICEL® Absorbable Hemostat (oxidized regenerated cellulose) is used adjunctively in surgical procedures to assist in the control of capillary, venous, and small arterial hemorrhage when ligation or other conventional methods of control are impractical or ineffective. SURGICEL® ORIGINAL, SURGICEL® FIBRILLAR™ and SURGICEL® NU-KNIT® Hemostats can be cut to size for use in endoscopic procedures.

PRECAUTIONS
Use only as much SURGICEL® Absorbable Hemostat as is necessary for hemostasis, holding it firmly in place until bleeding stops. Remove any excess before surgical closure in order to facilitate absorption and minimize the possibility of foreign body reaction.

In urological procedures, minimal amounts of SURGICEL® Absorbable Hemostat should be used and care must be exercised to prevent plugging of the urethra, ureter, or a catheter by dislodged portions of the product.

Since absorption of SURGICEL® Absorbable Hemostat could be prevented in chemically cauterized areas, its use should not be preceded by application of silver nitrate or any other escharotic chemicals.

If SURGICEL® Absorbable Hemostat is used temporarily to line the cavity of large open wounds, it should be placed so as not to overlap the skin edges. It should also be removed from open wounds by forceps or by irrigation with sterile water or saline solution after bleeding has stopped.

Precautions should be taken in otorhinolaryngologic surgery to assure that none of the material is aspirated by the patient. (Examples: controlling hemorrhage after tonsillectomy and controlling epistaxis).

Care should be taken not to apply SURGICEL® Absorbable Hemostat too tightly when it is used as a wrap during vascular surgery (see Adverse Reactions).

ADVERSE EVENTS
“Encapsulation” of fluid and foreign body reactions have been reported.

There have been reports of stenotic effect when SURGICEL® Absorbable Hemostat has been applied as a wrap during vascular surgery.

Paralysis and nerve damage have been reported when SURGICEL® Absorbable Hemostat was used around, in, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm.

Blindness has been reported in connection with surgical repair of a lacerated left frontal lobe when SURGICEL® Absorbable Hemostat was placed in the anterior cranial fossa.

Possible prolongation of drainage in cholecystectomies and difficulty passing urine per urethra after prostatectomy have been reported.

For more information, please consult your doctor or for product quality and technical questions, call 1-800-795-0012.
EVARREST® Fibrin Sealant Patch

IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE
EVARREST® is a fibrin sealant patch indicated for use with manual compression as an adjunct to hemostasis in adult patients undergoing surgery, when control of bleeding by conventional surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical.

LIMITATIONS FOR USE
• Cannot be used in place of sutures or other forms of mechanical ligation in the treatment of major arterial or venous bleeding.
• Not for use in children under one month of age.
• Laparoscopic and other minimally invasive surgeries where manual compression would be difficult to achieve.

IMPORTANT SAFETY INFORMATION
For topical use only. Apply immediate manual compression over the entire surface of the patch and maintain contact pressure for 3 minutes to control the bleeding.
Do not apply intravascularly. This can result in life threatening thromboembolic events.
Do not use to treat bleeding from large defects in arteries or veins where the injured vascular wall requires conventional surgical repair and maintenance of vessel patency or where there would be persistent exposure of EVARREST® to blood flow and/or pressure during absorption of the product. Thrombosis can occur if absorbed systemically.
Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products. EVARREST® can cause hypersensitivity reactions including anaphylaxis.
Avoid application to contaminated areas of the body or in the presence of active infection. Infection can occur.
EVARREST® contains oxidized regenerated cellulose which adheres to bleeding surfaces. Inadvertent adhesions can occur.
Avoid use in, around, or in proximity to, foramina in bone or areas of bony confines where swelling may cause compression.
Use the least number of patches required to cover the entire bleeding area. Portions of excess patch material can become dislodged and migrate to other areas of the body.
Do not use more than eight 2x4 inch (5.1 x 10.2 cm) or more than four 4x4 inch (10.2 x 10.2 cm) patches.
Use in patients who have been previously exposed to EVARREST® has not been studied.
May carry a risk of transmitting infectious agents, eg viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.
The adverse reactions reported during clinical trials occurred in less than 1% of all cases and included deep venous thrombosis, pulmonary embolism, blood fibrinogen increase, anastomotic hemorrhage, post-procedural and intra-abdominal hemorrhage, abdominal distension, anemia, gastrointestinal hemorrhage, thoracic cavity drainage, pleural effusion, abdominal abscess, ascites, localized intra-abdominal fluid collection, cardiac failure, operative hemorrhage, and ischemic bowel.
Pediatrics: Use in children under the age of one month may be unsafe or ineffective due to small size and limited ability to apply the patch as recommended.
Please see package insert for EVARREST® Full Prescribing Information.
To report SUSPECTED ADVERSE REACTIONS, contact ETHICON Customer Support Center at 1-877-384-4266 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
SURGIFLO® Hemostatic Matrix Kit Essential Product Information (Made from Absorbable Gelatin Sponge, USP) with Thrombin

DESCRIPTION
SURGIFLO® with Thrombin (SURGIFLO® Hemostatic Matrix Kit) is intended for hemostatic use by applying to a bleeding surface.

ACTIONS
When used in appropriate amounts SURGIFLO® is absorbed completely within 4 to 6 weeks.

INTENDED USE/INDICATIONS
SURGIFLO®, mixed with thrombin solution, is indicated in surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods is ineffective or impractical.

CONTRAINDICATIONS
• Do not use SURGIFLO® in intravascular compartments because of the risk of embolization.
• Do not use SURGIFLO® in patients with known allergies to porcine gelatin.
• Do not use SURGIFLO® in closure of skin incisions because it may interfere with the healing of skin edges. This interference is due to mechanical interposition of gelatin and is not secondary to intrinsic interference with wound healing.

WARNINGS
• SURGIFLO® should not be used in the presence of infection and should be used with caution in contaminated areas of the body.
• SURGIFLO® should not be used in instances of pumping arterial hemorrhage. SURGIFLO® will not act as a tampon or plug in a bleeding site.
• SURGIFLO® should be removed from the site of application when used in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm because it may swell, resulting in nerve damage.
• Excess SURGIFLO® should be removed once hemostasis has been achieved.
• The safety and effectiveness of SURGIFLO® for use in ophthalmic procedures has not been established.
• The safety and effectiveness of SURGIFLO® has not been established in children and pregnant women.
• The blue flexible applicator tip should not be trimmed to avoid exposing internal guidewire.
• The white straight applicator tip should be trimmed away from the surgical area. Cut a square angle to avoid creating a sharp tip.

PRECAUTIONS
• Safe and effective use of SURGIFOAM® Sponge has been reported in a published neurologic retrospective study involving 1700 cases in Europe. Safe and effective use in neurosurgery has not been proven through randomized, controlled clinical studies in the United States.
• SURGIFLO® is supplied as a sterile product and cannot be resterilized.
• SURGIFLO® should not be used for packing unless excess product that is not needed to maintain hemostasis is removed. SURGIFLO® may swell up to 20% upon contact with additional fluid.
• SURGIFLO® should not be used in conjunction with autologous blood salvage circuits.
• SURGIFLO® should not be used in conjunction with methylmethacrylate adhesives.
• In urological procedures, SURGIFLO® should not be left in the renal pelvis or ureters to eliminate the potential foci for calculus formation.
ADVERSE EVENTS
A total of 142 patients received SURGIFOAM® Sponge during a clinical trial comparing SURGIFOAM® Sponge to another absorbable gelatin sponge. In general, the following adverse events have been reported with the use of absorbable porcine gelatin-based hemostatic agents:

• Gelatin-based hemostatic agents may serve as a nidus for infection and abscess formation and have been reported to potentiate bacterial growth.
• Giant cell granulomas have been observed at implant sites when used in the brain.
• Compression of the brain and spinal cord resulting from the accumulation of sterile fluid have been observed.
• Multiple neurologic events were reported when absorbable gelatin-based hemostatic agents were used in laminectomy operations, including cauda equina syndrome, spinal stenosis, meningitis, arachnoiditis, headaches, paresthesias, pain, bladder and bowel dysfunction, and impotence.
• The use of absorbable gelatin-based hemostatic agents during the repair of dural defects associated with laminectomy and craniotomy operations, has been associated with fever, infection, leg paresthesias, neck and back pain, bladder and bowel incontinence, cauda equina syndrome, neurogenic bladder, impotence, and paresis.
• The use of absorbable gelatin-based hemostatic agents has been associated with paralysis, due to device migration into foramina in the bone around the spinal cord, and blindness, due to device migration in the orbit of the eye, during lobectomy, laminectomy, and repair of a frontal skull fracture and lacerated lobe.
• Foreign body reactions, “encapsulation” of fluid, and hematoma have been observed at implant sites.
• Excessive fibrosis and prolonged fixation of a tendon have been reported when absorbable gelatin-based sponges were used in severed tendon repair.
• Toxic shock syndrome was reported in association with the use of absorbable gelatin-based hemostats in nasal surgery.
• Fever, failure of absorption, and hearing loss have been observed when absorbable hemostatic agents were used during tympanoplasty.
SURGIFLO® Hemostatic Matrix Essential Product Information (Made from Absorbable Gelatin Sponge, USP)

DESCRIPTION
SURGIFLO® Hemostatic Matrix Kit is intended for hemostatic use by applying to a bleeding surface.

ACTIONS
When used in appropriate amounts SURGIFLO® Hemostatic Matrix is absorbed completely within 4 to 6 weeks.

INTENDED USE/INDICATIONS
SURGIFLO® Hemostatic Matrix, mixed with sterile saline or thrombin solution, is indicated in surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods is ineffective or impractical.

CONTRAINDICATIONS
• Do not use SURGIFLO® Hemostatic Matrix in intravascular compartments because of the risk of embolization.
• Do not use SURGIFLO® Hemostatic Matrix in patients with known allergies to porcine gelatin.
• Do not use SURGIFLO® Hemostatic Matrix in closure of skin incisions because it may interfere with the healing of skin edges. This interference is due to mechanical interposition of gelatin and is not secondary to intrinsic interference with wound healing.

WARNINGS
• SURGIFLO® Hemostatic Matrix should not be used in the presence of infection and should be used with caution in contaminated areas of the body.
• SURGIFLO® Hemostatic Matrix should not be used in instances of pumping arterial hemorrhage.
• SURGIFLO® Hemostatic Matrix will not act as a tampon or plug in a bleeding site.
• SURGIFLO® Hemostatic Matrix should be removed from the site of application when used in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm because it may swell resulting in nerve damage.
• Excess SURGIFLO® Hemostatic Matrix should be removed once hemostasis has been achieved.
• The safety and effectiveness of SURGIFLO® Hemostatic Matrix for use in ophthalmic procedures has not been established.
• SURGIFLO® Hemostatic Matrix should not be used for controlling post-partum intrauterine bleeding or menorrhagia.
• The blue flexible applicator tip should not be trimmed to avoid exposing internal guidewire.
• The white straight applicator tip should be trimmed away from the surgical area. Cut a square angle to avoid creating a sharp tip.

PRECAUTIONS
• Safe and effective use of SURGIFOAM® Sponge has been reported in a published neurologic retrospective study involving 1700 cases in Europe. Safe and effective use in neurosurgery has not been proven through randomized, controlled clinical studies in the United States.
• SURGIFLO® Hemostatic Matrix is supplied as a sterile product and cannot be resterilized.
• SURGIFLO® Hemostatic Matrix should not be used for packing unless excess product that is not needed to maintain hemostasis is removed. SURGIFLO® Hemostatic Matrix may swell up to 20% upon contact with additional fluid.
• SURGIFLO® Hemostatic Matrix should not be used in conjunction with autologous blood salvage circuits.
• SURGIFLO® Hemostatic Matrix should not be used in conjunction with methylmethacrylate adhesives.
• In urological procedures, SURGIFLO® Hemostatic Matrix should not be left in the renal pelvis or ureters to eliminate the potential foci for calculus formation.
ADVERSE EVENTS

A total of 142 patients received SURGIFOAM® Sponge during a clinical trial comparing SURGIFOAM® Sponge to another absorbable gelatin sponge. In general, the following adverse events have been reported with the use of absorbable porcine gelatin-based hemostatic agents:

• Gelatin-based hemostatic agents may serve as a nidus for infection and abscess formation and have been reported to potentiate bacterial growth.
• Giant cell granulomas have been observed at implant sites when used in the brain.
• Compression of the brain and spinal cord resulting from the accumulation of sterile fluid have been observed.
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• Toxic shock syndrome was reported in association with the use of absorbable gelatin-based hemostats in nasal surgery.
• Fever, failure of absorption, and hearing loss have been observed when absorbable hemostatic agents were used during tympanoplasty.
EVITHROM® Thrombin, Topical (Human) for Topical Use Only
Lyophilized Powder for Solution

EVITHROM® is a topical thrombin indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.

EVITHROM® may be used in conjunction with an Absorbable Gelatin Sponge, USP.

IMPORTANT SAFETY INFORMATION

• For topical use only.
• Do not inject.
• Apply EVITHROM® on the surface of bleeding tissue only.
• The amount of EVITHROM® required depends upon the area of tissue to be treated and the method of application. In clinical studies, volumes up to 10 ml were used in conjunction with Absorbable Gelatin Sponge.
• Do not use for the treatment of severe or brisk arterial bleeding.
• Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products. Hypersensitivity reactions, including anaphylaxis, may occur.
• There is a potential risk of thrombosis if absorbed systemically.
• May carry a risk of transmitting infectious agents such as viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite manufacturing steps designed to reduce the risk of viral transmission.
• The most common adverse reactions during clinical trial (reported in at least 2% of subjects treated with EVITHROM®) were prolonged activated partial thromboplastin time, increased INR, decreased lymphocyte count, prolonged prothrombin time and increased neutrophil count.
• None of the patients treated with EVITHROM® developed antibodies to human thrombin or to human Factor V/Va. The clinical significance of these findings is unknown.

For complete indications, contraindications, warnings, precautions, and adverse reactions, please reference full package insert.
EVICEL® Fibrin Sealant (Human)

IMPORTANT SAFETY INFORMATION

INDICATION
EVICEL® Fibrin Sealant (Human) is indicated as an adjunct to hemostasis for use in patients undergoing surgery, when control of bleeding by standard surgical techniques (such as suture, ligature, or cautery) is ineffective or impractical.

CONTRAINDICATIONS
• Do not inject directly into the circulatory system. Intravascular application of EVICEL® may result in life-threatening thromboembolic events.
• Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products.
• Do not use for the treatment of severe or brisk arterial bleeding.
• Do not use EVICEL® for spraying in endoscopic or laparoscopic procedures where the minimum recommended distance from the applicator tip to the target site cannot be ensured.

WARNINGS AND PRECAUTIONS
• Life-threatening gas embolism has occurred with the use of spray devices employing pressure regulator to administer fibrin sealants. These events appear to be related to the use of the spray device at pressures higher than recommended and/or at distances closer than recommended to the surface of the tissue. Follow labeled application instructions regarding pressure range and distance when using a spray device and monitor patients for the possibility of gas embolism.
• Monitor changes in blood pressure, pulse oxygen saturation, and end-tidal CO2 when spraying EVICEL® because of the possibility of gas embolism.
• To reduce the risk of potentially life-threatening gas embolism, spray EVICEL® using only pressurized CO2 gas at the recommended pressures and distances.
• Use EVICEL® spray application only if it is possible to accurately judge the spray distance, especially during endoscopic or laparoscopic procedures. Apply as a thin layer.
• Prior to applying EVICEL®, dry surface areas of the wound by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices). Prepare and administer EVICEL® according to the instructions and only with devices recommended for this product.
• May carry a risk of transmitting infectious agents, e.g. viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Most common adverse events reported in clinical trials (≥5%) are bradycardia, nausea, hypokalemia, insomnia, hypotension, pyrexia, graft infection, vascular graft occlusion, peripheral edema, and constipation.

For complete indications, contraindications, warnings, precautions, and adverse reactions, please reference full package insert.
REFERENCES

The ECHELON FLEX™ GST System

Evaluating mucosal capture

**Approach:** Preclinical animal study comparing compression damage, mucosal injury and mucosal "capture" on varying thicknesses of porcine gastrointestinal tissues. After firing an endocutter, a visual inspection of the mucosal surface was evaluated and the level of mucosal capture was rated via a 5-point Likert scale.

**What we learned:**

- Mucosa is **7 times more likely** to be fully captured in the staple line when using the ECHELON FLEX™ GST System vs. Endo GIA™ with Tri-Staple™ Technology.
- GST Blue and Green reloads had overall better mucosal apposition than Endo GIA purple.

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**Better mucosal apposition with the ECHELON FLEX™ GST System**

<table>
<thead>
<tr>
<th>Mucosal capture</th>
<th>Percent occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good apposition (Mucosal damage = 1)</td>
<td></td>
</tr>
<tr>
<td>Tri-Staple Purple reload</td>
<td>30</td>
</tr>
<tr>
<td>GST Blue reload</td>
<td>20</td>
</tr>
<tr>
<td>GST Green reload</td>
<td>15</td>
</tr>
<tr>
<td>Poor apposition (Mucosal damage &gt;4)</td>
<td></td>
</tr>
<tr>
<td>Tri-Staple Purple reload</td>
<td>25</td>
</tr>
<tr>
<td>GST Blue reload</td>
<td>10</td>
</tr>
<tr>
<td>GST Green reload</td>
<td>5</td>
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</tbody>
</table>

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1ECHELON FLEX™ GST System Blue and Green Reloads compared to Endo GIA™ with Tri Staple™ Technology Purple Reloads evaluated via gross observations of firings in 1.5mm to 3.0mm thick anatomic porcine ileum. Mucosal capture was rated via a 5-point Likert scale with the highest rating representing fully captured mucosa.