

From: [REDACTED]
To: [Devices Clinical Advice](#)
Subject: FW: JJM2019-003 Circular Staplers ARTG 124512 [SEC=OFFICIAL, ACCESS=Commercial]
Date: Wednesday, 27 March 2019 10:40:11 AM
Attachments: [JJM2019-033 Ethicon OUS letter.docx](#)

Hi [REDACTED]
J&J are asking what is the TGAs appetite to do a 'delayed recall' as per the email trail below?
FYI
[REDACTED]

Recalls Section

Manufacturing Quality Branch

This response is general information given to you without prejudice; it is not binding on the TGA and you should get your own independent legal advice to ensure that all of the legislative requirements are met.

From: [REDACTED]
Sent: Monday, 25 March 2019 4:08 PM
To: [REDACTED]
Cc: [REDACTED]
Subject: RE: JJM2019-003 Circular Staplers ARTG 124512 [SEC=No Protective Marking]
Good afternoon [REDACTED]

As per our discussion, please find attached the OUS customer letter provided by Ethicon as you can see we have not "Australianised" it or put on AUST letterhead

Cheers [REDACTED]

From: [REDACTED]
Sent: Friday, 22 March 2019 4:15 PM
To: [REDACTED]
Cc: [REDACTED]
Subject: JJM2019-003 Circular Staplers ARTG 124512
Good afternoon [REDACTED]

Thank you for calling us back this afternoon , please see attached risk document and below, the proposed field action strategy for your consideration , regarding Ethicon Circular Staplers in ANZ .
In Australia Ethicon has approx. 85% of the circular staple market - this device is used predominately in the colorectal surgery market .

This strategy has been proposed similarly to the FDA – however; to date we do not have their outcome.

Background

The Ethicon Endo-Surgery Intraluminal Staplers (ILS) are anastomotic staplers available in four sizes to permit proper matching of instrument to diameter of the lumen. The instrument permits tissue attachment to the anvil shaft in a location remote from the main body of the instrument to improve access and visibility. The instruments allow the surgeon to control tissue compression by varying the height of the closed staple. The instruments have been designed to facilitate insertion, operation, and removal. The Ethicon Endo-Surgery Intraluminal Staplers (ILS) have application throughout the alimentary tract for end-to-end, end-to-side, and side-to-side anastomoses. The ETHICON Circular Stapler is designed to promote healing, more tissue control and less tension on the anastomosis, with distinct audible and tactile feedback during firing.

Ethicon has confirmed customer complaints on 4 returned circular staplers. Investigation of the manufacturing process detected a shift in a process performance starting in March 2018 to 8th March, 2019. Each device is fired into test skin during manufacturing to confirm that the force to fire (i.e. force required to break the washer and form staples) is within specification. During this test, the percent firing stroke, meaning the distance travelled before reaching maximum force and breaking the washer, is also measured, but is not specified, and a shift of approximately 10-15% from historical norms was identified. This shift is associated with an observed increased rate of complaints for malformed staples.

Ethicon (JJM) provides approximately 85% of circular staplers in the Australian market.

Product Information

Product Number	Product Name	ARTG
CDH21A	Curved Intraluminal Staplers, 21 mm diameter	124512
CDH25A	Curved Intraluminal Staplers, 25 mm diameter	124512
CDH29A	Curved Intraluminal Staplers, 29 mm diameter	124512

CDH33A	Curved Intraluminal Staplers, 33 mm diameter	124512
ECS21A	Endoscopic Curved Intraluminal Stapler, 21 mm diameter	124512
ECS25A	Endoscopic Curved Intraluminal Stapler, 25 mm diameter	124512
ECS29A	Endoscopic Curved Intraluminal Stapler, 29 mm diameter	124512
ECS33A	Endoscopic Curved Intraluminal Stapler, 33 mm diameter	124512
SDH25A	Straight Intraluminal Staplers, 25 mm diameter	124512
SDH29A	Straight Intraluminal Staplers, 29 mm diameter	124512

Legal Manufacturer

Ethicon, LLC
475 C Street
Los Frailes Industrial Park
Suite 401
Guaynabo, PR 00969 USA

Product Distribution

TOTAL product manufactured worldwide is 495,258 eaches, (701 lots)

TOTAL product commercially distributed worldwide is 439,047 eaches

TOTAL product commercially distributed in Australia is 37,463 eaches.

Issue Description and Proposed Strategy

Event Description

Analysis of 4 products returned and tested in simulated use conditions (in tissue, across staple lines) confirmed that the returned devices had insufficient firing stroke to break the washer and completely form staples. Investigation of the manufacturing process detected a shift in a process parameter which is associated with an observed increase in rate of complaints for malformed staples. A shift occurred in March 2018 and continued to 8th March 2019, at which time the line was shut down. This shift in manufacturing is associated with an increased rate of complaints for devices. CPMO 2017-2018 = 287; 2018-2019=293.

Proposed Action

Ethicon's proposed strategy is to communicate the following information to customers:

- Notification that we have confirmed complaints for malformed staples related to insufficient firing stroke to break the washer and completely form staples.
- Prior to this issue the estimated occurrence for malformed staples was 0.03% based on product complaint data. The predicted rate for impacted product is 0.05%.
- If alternative product is available, please return products subject to this notification.
- If alternative products to complete required surgeries are not available and in view of the increased risk of malformed staples and possibly associated anastomotic failure, it is critical to adhere to the following steps in the instructions for use:
 - Caution: The firing stroke must be completed. Do not partially fire the instrument. Incomplete firing can result in malformed staples, incomplete cut line, bleeding, and leakage from the staple line and/or difficulty removing the device.
 - Ensure that the firing trigger is fully squeezed to ensure proper staple formation and cutting of tissue.
 - After removing the instrument, examine the staple lines for hemostasis/ pneumatosis and proper staple closure.
 - Warning: Always inspect the anastomotic staple line for hemostasis and check the completed anastomosis for integrity and leakage. Metal clips, staples, or sutures contained in the area to be stapled may affect the integrity of the anastomosis. Corrective action, if required, may include the use of sutures or electrocautery
 - In addition:
 - If an intra-operative leak is observed, remediation should be dictated by your clinical judgement.
 - A negative peri-operative leak test does not guarantee the absence of a leak during the post-operative course; normal clinical surveillance remains essential.

Our proposed strategy is aimed at minimising the impact of potential product shortage.

I have not contacted Medsafe as yet and we do distribute in the New Zealand Market – I will advise Medsafe on

Monday (due to the current time in NZ)

I look forward to your feedback

Regards

Johnson & Johnson Medical Pty Ltd ABN 85 000 160 403
1-5 Khartoum Road, North Ryde, NSW 2113 Australia
P.O. Box 134, North Ryde, NSW 1670 Australia



This document is Johnson & Johnson (J&J) Proprietary. You may forward this document within J&J on a need to know basis. You may not forward this onto the Internet without the author's permission. This e-mail transmission may contain confidential or legally privileged information that is intended only for the individual or entity named in the e-mail address. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution, or reliance upon the contents of this e-mail is strictly prohibited. If you have received this e-mail transmission in error, please reply to the sender, so that J&J can arrange for proper delivery, and then please delete the message from your in-box. If you wish to receive no further e-mails please contact us via e-mail at jjmail@medau.jnj.com or phone us — Australia 1800 252 194, New Zealand 0800 803 988.

URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Staplers (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

March XX, 2019

Dear Operating Room Supervisors, Materials Management Personnel, and Chief of Surgery,

At Ethicon Endo-Surgery, LLC. ("Ethicon"), our first priority is to our customers and their patients, and that includes the safe and effective use of our products.

We have initiated a medical device **Field Action (notification)** of 701 (WW) lots of Intraluminal Staplers (ILS). Through investigation of complaints and returned products, we have confirmed occurrence of uncut washers and malformed staples with our ILS circular staplers, which can compromise staple line integrity. If a problem with the staple line is not adequately addressed or is not recognized, there is a potential risk of postoperative anastomotic leak, gastrointestinal injury, hemorrhage, or hemorrhagic shock.

Ethicon has received reports of Adverse Events related to this field action (notification).

Based on Ethicon's analysis of complaints received to date and estimated device usage, the predicted occurrence of complaints for malformed staples has increased but is expected to remain below 0.1%. Ethicon is implementing corrective actions to resolve the shift in product performance.

Customer Action:

If you have alternative product available, please return all product subject to this notification (Reference Table 1 for product listing). Ethicon recognizes due to worldwide supply issues with Intraluminal Staplers (ILS), alternative product may not be available. If alternative products to complete required surgeries are not available, it is critical to adhere to the following information.

- The firing stroke must be completed. Do not partially fire the instrument. Incomplete firing can result in malformed staples, incomplete cut line, bleeding, and leakage from the staple line and/or difficulty removing the device.
- Ensure that the tissue thickness is within the indicated range, and that it is evenly distributed within the instrument. Excess tissue on one side may result in unacceptable staple formation and can result in staple line leakage.
- Ensure that the firing trigger is fully squeezed to ensure proper staple formation and cutting of tissue.
- The surgeon should notice both tactile and audible feedback during the firing sequence when cutting through the breakaway washer.
- Ensure that donuts and cutting washer transections are both complete. If donuts or cutting washer transection are not complete, the anastomosis should be carefully checked for leakage and appropriate repairs made.

URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

- Always inspect the anastomotic staple line for hemostasis and check the completed anastomosis for integrity and leakage. Metal clips, staples, or sutures contained in the area to be stapled may affect the integrity of the anastomosis. Corrective action, if required, may include the use of sutures or electrocautery.
 - In addition:
 - If an intra-operative leak is observed, remediation should be dictated by your clinical judgement.
 - A negative peri-operative leak test does not guarantee the absence of a leak during the post-operative course; normal clinical surveillance remains essential.

The scope of this Field Action includes **ALL** Intraluminal Staplers (ILS) from the product codes and expiration dates listed in the table below.

Table 1 – Product Subject to this Field Action

PRODUCT NAME	PRODUCT CODE	All Lots within EXPIRATION Date Range	DESCRIPTION/SIZE
Curved Intraluminal Stapler (ILS)	CDH21A	February 2023 – March 2024	21mm Curved Intraluminal Stapler
Curved Intraluminal Stapler (ILS)	CDH25A	February 2023 – March 2024	25mm Curved Intraluminal Stapler
Curved Intraluminal Stapler (ILS)	CDH29A	February 2023 – March 2024	29mm Curved Intraluminal Stapler
Curved Intraluminal Stapler (ILS)	CDH33A	February 2023 – March 2024	33mm Curved Intraluminal Stapler
Endoscopic Curved Intraluminal Stapler (ILS)	ECS21A	February 2023 – March 2024	21mm Endoscopic Curved Intraluminal Stapler
Endoscopic Curved Intraluminal Stapler (ILS)	ECS25A	February 2023 – March 2024	25mm Endoscopic Curved Intraluminal Stapler
Endoscopic Curved Intraluminal Stapler (ILS)	ECS29A	February 2023 – March 2024	29mm Endoscopic Curved Intraluminal Stapler
Endoscopic Curved Intraluminal Stapler (ILS)	ECS33A	February 2023 – March 2024	33mm Endoscopic Curved Intraluminal Stapler
Straight Intraluminal Stapler (ILS)	SDH21A	February 2023 – March 2024	21mm Straight Intraluminal Stapler
Straight Intraluminal Stapler (ILS)	SDH25A	February 2023 – March 2024	25mm Straight Intraluminal Stapler
Straight Intraluminal Stapler (ILS)	SDH29A	February 2023 – March 2024	29mm Straight Intraluminal Stapler
Straight Intraluminal Stapler (ILS)	SDH33A	February 2023 – March 2024	33mm Straight Intraluminal Stapler

Product subject to this Field Action in your inventory can be identified by using the Product Identification Tool (Attachment 1).

URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

ACTION REQUIRED:

1. Ethicon is requesting that you examine your inventory to determine if you may have impacted product. Refer to **Attachment 1** for the Product Identification Tool to identify the products that are subject to this Field Action (notification) by using package labels.
2. If you have alternative product available, please return all products subject to this notification (Reference Table 1 for products listing). Ethicon recognizes due to worldwide supply issues with Intraluminal Staplers (ILS), alternative product may not be available. If alternative products to complete required surgeries are not available and in view of the increased risk of malformed staples and possibly associated anastomotic failure, it is critical to adhere to the instructions provided above.
3. If any product subject to this action has been forwarded to another facility, contact that facility to make them aware of the notification.
4. Complete the Business Reply Form (BRF) (Attachment 2) confirming receipt of this notice and send to **[Insert Affiliate Information]** within three (3) business days. **Please return the BRF even if you do not have the product lots subject to this notification.**
5. To return product subject to this action, photocopy the completed BRF, place it in the box with the product, and affix the pre-paid authorized shipping label included with the field action notification letter. Ethicon will pay for the shipping charges only if the authorized label is used. Extra shipping labels may be obtained by calling Stericycle at 1-888-345-5368 Your account number and mailing address have been pre-populated on the BRF.
6. If you are returning impacted product in your inventory, please contact us for replacement/credit and return the product to **[Insert Affiliate Information]**. If you require any assistance with returning product, please contact **[Insert Affiliate Information]** and reference **Event#**.

If you have additional questions regarding this field action or to report any customer complaints, please contact Ethicon Customer Support Center at 1-877-ETHICON (1-877-384-4266). The Customer Support Center is open Monday through Friday, 7:30 AM to 6:30 PM ET.

As with any medical device, adverse reactions or quality problems experienced with the use of this product should be reported to the FDA's MedWatch Adverse Event Reporting program online, by regular mail or by fax:

- Online: www.fda.gov/medwatch/report.htm
- Regular Mail:
Use postage-paid FDA form 3500 available at: www.fda.gov/MedWatch/getforms.htm
Mail to: MedWatch 5600 Fishers Lane, Rockville, MD 20852-9787
- Fax: 1-800-FDA-0178

URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

ATTACHMENTS:

Attachment 1: Product Identification Tool

Attachment 2: Business Reply Form (BRF)

URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

ATTACHMENT 1: Product Identification Tool for Intraluminal Staplers (ILS)

This tool will help customers identify product codes and expiration dates of Intraluminal Staplers (ILS) subject to this notification by using the packaging labels. Please refer to table above for a list of all product codes with expiration dates subject to this notification.

SINGLE UNIT CARTON (CONTAINING (1) SEALED TYVEK TRAY)

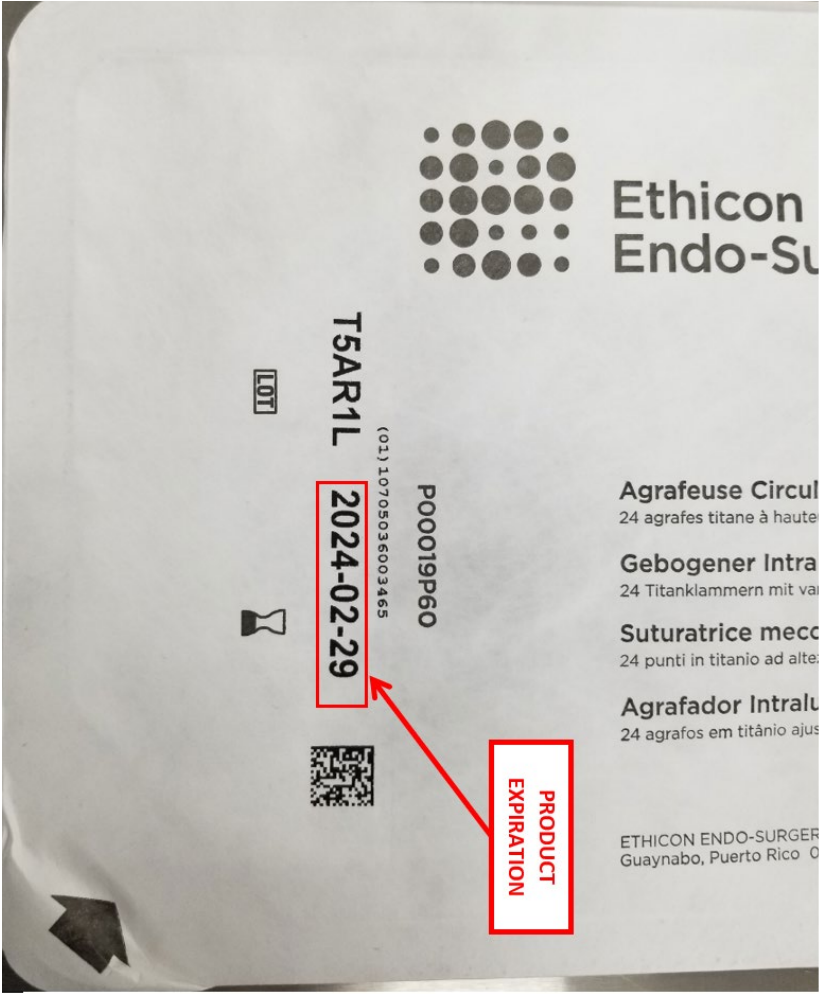
FRONT OF SINGLE UNIT CARTON



URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A



URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

ATTACHMENT 2: Business Reply Form (BRF)

Your timely response to this customer notification is requested. Please complete and fax this form to [INSERT AFFILIATE NAME] at [INSERT FAX NUMBER] at or e-mail the form to [INSERT AFFILIATE EMAIL ADDRESS] within 3 business days, even if you do not have product subject to this field action to return.

Please complete the following information: - add check box

- ☐ We hereby acknowledge receipt of this medical device field action letter from Ethicon regarding Intraluminal Staplers (ILS). We have distributed this information to all staff within our facility that use the impacted products and will maintain a copy of this notice with the identified product(s).

Product Receipts – please check one:

- ☐ We have NO impacted Intraluminal Staplers (ILS) subject to this field action (notification), however we will maintain a copy of this notice within our facility.
- ☐ We have impacted Intraluminal Staplers (ILS) subject to this field action (notification), however we do not have an acceptable alternative product and we chose to continue to use the product. We will maintain a copy of this notice within our facility.
- ☐ We are returning impacted Intraluminal Staplers (ILS) and below are the quantities noted.

PRODUCT NAME	PRODUCT CODE	EXPIRATION Date	Quantity Returning (Eaches)
Curved Intraluminal Stapler (ILS)	CDH21A		
Curved Intraluminal Stapler (ILS)	CDH25A		
Curved Intraluminal Stapler (ILS)	CDH29A		
Curved Intraluminal Stapler (ILS)	CDH33A		
Endoscopic Curved Intraluminal Stapler (ILS)	ECS21A		
Endoscopic Curved Intraluminal Stapler (ILS)	ECS25A		
Endoscopic Curved Intraluminal Stapler (ILS)	ECS29A		
Endoscopic Curved Intraluminal Stapler (ILS)	ECS33A		
Straight Intraluminal Stapler (ILS)	SDH21A		
Straight Intraluminal Stapler (ILS)	SDH25A		
Straight Intraluminal Stapler (ILS)	SDH29A		
Straight Intraluminal Stapler (ILS)	SDH33A		

URGENT: MEDICAL DEVICE FIELD ACTION (NOTIFICATION)

Intraluminal Stapler (ILS)

Product Codes: ECS21A, ECS25A, ECS29A, ECS33A, SDH21A, SDH25A, SDH29A, SDH33A, CDH21A, CDH25A, CDH29A, CDH33A

[Account Name]

[Account Address]

Print Name of Person Completing Business Reply Form:	Telephone Number:
Account Number: (number used to order J&J product)	Date:
Signed*:	
<i>* Your signature provides confirmation that you have received and understood this notification</i>	
<i>Your comments are welcome.</i>	

Health Risk Evaluation

Long Form HRE

PIA1449714 / PIE 1454854 – Circular Stapler Malformed Staples

Product name:

ILS Proximate Circular Stapler

Product Code/ Modification Code:

ECS21A; ECS25A; ECS29A; ECS33A; SDH21A; SDH25A; SDH29A; SDH33A; CDH21A; CDH25A; CDH29A; CDH33A

Clinical Use Context:

The Ethicon Endo-Surgery Intraluminal Staplers (ILS) are anastomotic staplers available in four sizes to permit proper matching of instrument to diameter of the lumen. The instrument permits tissue attachment to the anvil shaft in a location remote from the main body of the instrument to improve access and visibility. The instruments allow the surgeon to control tissue compression by varying the height of the closed staple. The instruments have been designed to facilitate insertion, operation, and removal. The anvils for the Intraluminal Staplers (ILS) having the same lumen size are interchangeable. For example, an anvil from a SDH25A can be used on a CDH25A or ECS25A.

The Ethicon Endo-Surgery Intraluminal Staplers (ILS) have application throughout the alimentary tract for end-to-end, end-to-side, and side-to-side anastomoses.

The ETHICON Circular Stapler is designed to promote healing, more tissue control and less tension on the anastomosis, with distinct audible and tactile feedback during firing.

Segment of the population most at risk:

There are no specific clinical conditions that may render a person more susceptible to experience harm on exposure to the product with this issue.

All patients are potentially at equal risk of experiencing prolonged surgery from a device with this issue as this can reasonably be expected to necessitate the use of an alternative similar device or an alternative technique such as suturing or re-stapling to complete the procedure.

All patients are also potentially at equal risk of experiencing gastrointestinal injury that may require surgical intervention such as a diversional ostomy resulting in permanent impairment or change in nutritional regimen.

Bleeding and anastomotic leak are other harms where all segments of the population are potentially at equal risk and will require medical and surgical intervention.

Related Clinical Factors:

Current manufacturing controls include 100% fire out in-line check where each device is fired out 100% at high B setting on a test skin using the force to fire machine. Staple lines are visually assessed. Also, 1 every 20 gets fired out a second time at Low B. A sample of devices taken for FGQA inspection are reviewed for force-to-fire performance, visually inspected for visual criteria, and functionally assessed for a variety of functional criteria.

Routine inspection by all surgeons of the staple line for its integrity, hemostasis/pneumostasis, and possible leakage prior to completion of surgery aids in identifying potential issues resulting from malformed staples. In addition, leak tests are routinely done by the vast majority of surgeon when using this device. Also, the device IFU states "after removing the instrument examine the staple lines for hemostasis/pneumostasis and proper staple closure." Other than use of the device in

accordance with IFU, there are no clinical factors that may mitigate the risk of using the device with this issue.

Potential harm(s):

Severity Level Definitions:

Severity Term	Level	Description
Limited	S1	Limited (transient, minor impairment or complaints) ; symptoms related to temporary discomfort. Condition will resolve itself without treatment or long term consequences. Intervention is not indicated; if provided, it is intended to reduce symptoms.
Reversible	S2	Reversible without medical intervention; symptoms may temporarily limit activities of daily living. Condition will resolve itself without treatment or long term consequences. Intervention is indicated to alleviate symptoms, improve recovery time and/or allow normal activities of daily living.
Intervention necessary	S3	Necessitates or can be reasonably expected to result in medical or surgical intervention, including hospitalization. Symptoms prevent normal activity. Condition will result in permanent impairment or life-threatening event without treatment. Intervention is indicated to prevent additional injury, life-threatening condition or permanent impairment. Interventions include but are not limited to elective invasive procedures, hospitalization, IV antibiotics.
Permanent	S4	The outcome of the event results, or can be reasonably expected to result, in permanent impairment of body function or permanent damage to a body structure. An injury that prevents the patient from normally conducting the activities he/she was capable of performing before the injury occurred.
Life-threatening	S5	Life-threatening (death has or could occur) .Reasonable expectation of the conditions resulting in death in the absence of specific medical intervention. Threat to life is imminent and requires immediate professional medical intervention.

Probability of Harm Level definitions:

Term	Level	Definition
Extremely Rare	pH1	The product problem has not resulted in the identified harm, or could only result in harm from extremely rare circumstances.

Unusual	pH2	The product problem has been known to result in the identified harm, but only occasionally and/or under unusual circumstances.
Some times	pH3	The product problem has resulted, or can be reasonably expected to result, in the identified harm under normal circumstances.
Almost always	pH4	The product problem, when it exists, will always or almost always result in the identified harm.

- **Direct Consequences:**

Bleeding: Postoperative hemorrhage/major bleed may result from this product issue necessitating reoperation to control the bleeding. In the unlikely event that the surgeon could not control the bleeding, hemorrhagic shock could result, and death may occur.

Anastomotic Leak: If a problem with the staple line is not adequately addressed or is not recognized, there is a potential problem of postoperative anastomotic leak. The symptoms of this condition could occur within a week after the surgery and would consist of abdominal pain, fever, and malaise. Treatment with antibiotics and reoperation to correct the condition would be necessary. However, the resultant infection could progress to peritonitis and sepsis which conceivably could result in death.

Gastrointestinal injury: In gastrointestinal surgeries, if the situation would prove difficult or impossible to perform a second anastomosis after malformed staples appear and staple line integrity was compromised, the surgeon may need to create a permanent colostomy should there not be enough length of the area of the colon to perform a re-anastomosis.

Procedural complication/ Surgical Intervention (Additional): With the issue of staple malformation or staple height integrity being compromised, some intervention would need to be performed. Upon finding this during the routine evaluation of the staple line after the device has been fired and removed, this situation could be addressed immediately with suture, cautery, or redoing the staple line. In addition, there may be problems with a secondary anastomosis or suturing of the open staple line and the surgeon may elect to perform a temporary colostomy to promote better healing.

- **Indirect Consequences:**

Prolonged surgery is an indirect health consequence as a result of the product issue as this can reasonably be expected to necessitate the use of an alternative similar device or a different technique such as suturing or re-stapling to complete the procedure.

Summary of potential Harms:

<u>Potential Harm</u>	<u>Greatest Risk Severity</u>	<u>Greatest Risk Probability</u>	<u>General Population Severity</u>	<u>General Population Probability</u>
Prolonged surgery	Not Applicable	Not Applicable	S2	PH2
Gastrointestinal injury	Not Applicable	Not Applicable	S4	PH2
Procedural complication/ Surgical intervention (additional)	Not Applicable	Not Applicable	S3	PH2
Hemorrhage/ Major Bleed	Not Applicable	Not Applicable	S3	PH1
Hemorrhagic shock	Not Applicable	Not Applicable	S5	PH1
Impaired healing/ anastomotic leak	Not Applicable	Not Applicable	S5	PH1

Assessment against existing documentation:

Known potential harm; severity or probability of harm higher than previously documented

Date Issue first discovered: 03/06/2019

Form ID#: PIA1449714 / PIE 1454854

Public Health Impact:

- **Impact beyond users:**
The health consequence has no impact beyond the users.
- **Impact from product removal:**
Product removal would have significant impact on public health due to likely product unavailability, as these devices comprise 49.2% of the market for circular staplers in the US and around 43-45% in the world. (Decision Resources Group Market Share Data 2018)

Health Hazard Evaluation Conclusion:

Four returned product complaint devices for ILS Circular stapler confirmed to have a poor staple line (malformed staples) during device analysis on 3/6/2019. Initial analysis included reloading and firing by hand into test skins at the high B setting (this is normal practice as part of the product investigation analysis and mimics manufacturing firings). They were reloaded a second time and fired into indicated thickness tissue over crossed staple lines by hand and dialed down per the IFU (dialed down into the green range until finger tight, waited 15 seconds, tighten again and then fired). Devices are typically not fired into tissue during routine analysis, and this was an additional test performed by the Lifecycle Engineering team in order to create an environment similar to the described clinical firing with the device. When fired into test skins, one of the four complaint devices did not cut a washer and had malformed staples (the other 3 had conforming fire outs). When fired into tissue, all four did not cut the washer and had a poor staple line (malformed staples). At the time of testing, there were 3 additional devices tested using the methods described above with conforming staple lines in test skins and indicated thickness tissue over crossing staple lines. Two were control CDH29A devices (new out of box sterile devices) and one was a returned complaint device.

Initial complaint review included Patient Experience Code (PECs):

Cutting Issue, Firing Issue, Hemostasis Controllable, Hemostasis Intervention, Incomplete Donut, Incomplete Staple Line, Leak Controllable, Leak Intervention, Malformed Staple, Non-specific Noise, and Would-not-Staple. These complaints were reviewed for related harms, however it was determined that Malformed staples were most related to this specific issue and were included in this assessment.

The focus was placed on both Unconfirmed and Confirmed complaints for malformed staples. All complaints with an Analysis Code (AC) of Malformed Staples (13) were reviewed. Only complaints where malformed staples were seen during test firing of the complaint device during Investigation (5) were included. Devices with re-fires resulting in conforming firing, conforming staple line, conforming staple form, conforming cut media, and conforming cut washers were excluded from the count of confirmed complaints (4). Two of the confirmed complaints resulted in serious injury where misfiring of the two CDH devices resulted in resection of the mid/lower rectum instead of the originally intended upper rectum only. The patients are reported as recovering well but will suffer with long term consequences as they are left with less rectum than intended. The other two complaints involved malfunctions with no patient consequences.

Investigation of the manufacturing process detected a shift in a process performance starting in March 2018 and continuing through March 8, 2019 (bounded time frame).

Complaints rates were compared for the bounded time frame (March 2018 – March 2019) to the previous year. Complaints filtered by created date for malformed staples during the 2017-2018 timeframe was 150 (CPMO 279), and from March 2018 through March 2019 (bounded period) was 212 (CPMO 429). Complaints filtered by manufacture date for malformed staples during the 2017-2018 timeframe was 154 (CPMO 287), and from March 2018 through March 2019 (bounded period) was 145 (CPMO 293). We anticipate that the count (and rate) during the bounded period will continue to increase because receipt of complaints is lagging when plotted against manufacturing date.

In the bounded time period, three patient deaths were identified in whom the circular stapler at hand had been used during the procedure. In one of these, the death could conceivably be related to the identified malformed stapling issue in this escalation. In that particular patient, malformed staples (using a CDH29A stapler) were observed on the anterior portion of the anastomosis during a recto-sigmoidectomy. The observed “opening of staples in the anterior portion” was oversewn. Three days later the patient returned to the OR and the surgeon observed dehiscence of the stapling line of the posterior part; the etiology of which is unknown. The anastomosis was restored, but the elderly female patient (80+ years old) succumbed to subsequent complications (pneumonia and congestive heart failure) in the intensive care unit two weeks after the index procedure. As no device was returned the relationship to the patient’s demise cannot be confirmed.

A second patient, of whose death Ethicon was informed, occurred in Iran during an unspecified procedure. A postoperative CT scan indicated “malformed staples across one quarter of the staple line”. In the lab, malformed staples are observed across 360 degrees in malfunctioning devices with this issue, making it unlikely to be related. No device was returned.

The third patient underwent an esophagectomy during which the surgeon described that “...while firing the orange bar in the window began to move upward and that after firing, the tissue wasn’t sealed at all and the staple didn’t form enough B shapes.” The device will be analyzed upon being received, but the event description doesn’t appear to be related to the issue in this escalation. No details are currently known.

Upon reviewing the other 24 unconfirmed, serious adverse events, it was determined that the relationship to the issue being escalated was conceivable but could not be confirmed without analysis of the devices which were not returned.

Exposure to a device with this product issue can lead to prolonged surgery as it can be reasonably expected to necessitate the use of an alternative similar device or an alternative technique such as suturing or re-stapling to complete the procedure. Therefore, a severity of harm of S2 is assigned. Since the product problem has resulted in prolonged surgery, the probability of harm is pH2.

With the issue of staple malformation, some intervention would need to be performed. Upon finding this during the routine evaluation of the staple line after the device has been fired and removed, this situation could be addressed immediately with suture, cautery, or redoing the staple line. Since there would be a need to routinely address these and the procedure that was previously planned might need to be significantly changed, the potential harm of Procedural Complication/Surgical Intervention (additional) is assigned with an S3 as the severity. In addition, there may be problems with a secondary anastomosis or

suturing of the open staple line and the surgeon may elect to perform a temporary colostomy to promote better healing. All of these would apply to the potential harm above. With that said, there have been two confirmed complaints where misfiring of the CDH devices necessitated further surgery, thus pH2 is the probability.

Another potential harm is if the situation would prove difficult or impossible to perform a second anastomosis after malformed staples appear, and staple line integrity was compromised. In gastrointestinal surgeries, the surgeon may need to create a permanent colostomy should there not be enough length of the area of the colon to perform a re-anastomosis. Since this would be regarded as a permanent impairment of a body function, the potential harm of Gastrointestinal Injury is assigned a severity of S4. The probability is pH2 since in two of the confirmed complaints, the resection was supposed to be the upper rectum and was moved to mid/lower due to the misfiring of the two CDH devices. The patients are reported as recovering well but will suffer with long term consequences as they are left with less rectum than intended.

If a problem with the staple line is not adequately addressed or is not recognized, there is a potential problem of postoperative anastomotic leak. The symptoms of this condition could occur within a week after the surgery and would consist of abdominal pain, fever, and malaise. Treatment with antibiotics and reoperation to correct the condition is usually necessary. However, the resultant infection could progress to peritonitis and sepsis which conceivably could result in death. This would be uncommon, but the potential harm of Impaired Healing/ Anastomotic leak is applicable here and thus the severity would be S5. The probability is pH1 as there have been no confirmed complaints, the surgeon routinely tests for pneumostasis, and checks the staple line for any malformed staples.

The potential harm of Hemorrhage/Major Bleed is chosen with a severity of S3 since the product issue may result in a postoperative bleed necessitating reoperation to control the bleeding. In the unlikely event that the surgeon could not control the bleeding, hemorrhagic shock could result, and death may occur, therefore the potential harm of Hemorrhagic Shock is assigned a severity of S5. The probability of both events is pH1 as there have been no confirmed complaints of this nature in relation to this specific product issue and the surgeon routinely inspects for bleeding both during the procedure and afterwards, if need be, via endoscopic examination for excessive rectal bleeding.

The risk document currently lists the potential harms for malformed staples as "Tissue Trauma: Inadvertent mechanical or thermal damage to unintended tissue requiring major surgical intervention. Loss of critical tissue apposition or tissue injury that requires significant intervention" with a severity of serious (S4). Since the highest severity of the potential harms in the risk document associated with the malformed staples is listed only as serious (S4), an update to the risk document is recommended based on the potential harms identified from this escalation.

Routine inspection by all surgeons of the staple line for its integrity, hemostasis/ pneumostasis, and possible leakage prior to completion of surgery would detect potential issues resulting from malformed staples. In addition, leak tests are routinely done by the vast majority of surgeons when using this device. There are no nonconformances associated with malformed staples in the last three years. There have been no CAPAs opened for malformed staples caused by insufficient firing stroke and/or stiffness. However, current root cause hypothesis is that we may have devices that do not have enough firing stroke and/or stiffness to be able to cut the washer and form staples (e.g. the travel distance of the knife is not long enough). As of the writing of this HRE having performed a screening DOE it was found that several variables had an impact on percent firing stroke which is now considered root cause and will be addressed. Analysis of the confirmed complaint devices show the possibility that devices may have been able to cut test skins during production inspections (thus conforming to manufacturing specifications) but when variables such as crossing staple lines and tissue resistance were added, it was not enough to cut the washer and form staples in situations that mimic clinical reality. The Severity and probability of these Harms are the same. However, with the findings described in the above complaint analyses coupled with the fact that there has been a shift in the manufacturing data that affects function impacts the benefit/risk ratio of the product. However, product removal without consideration of available alternative supply, may have significant impact, as described below.

In the US, Ethicon has 49% market share of the circular stapler market, with Ethicon having a penetration in the colo-rectal surgery market of 56% versus Medtronic 44%. The market share outside of the US share is estimated to be 42-43% (This may vary by market). Current availability of competitive product may be adversely affected by the recent Illinois EPA shutdown of Sterigenics. Removal of Ethicon circular staplers will thus impact at least 50% of all US patients and up to 43% of OUS patients.

A shortage of circular staplers would force surgeons to retreat to handsewn anastomoses, exposing patients to a potential learning curve effect as the use of staples is currently standard of care and handsewn anastomoses is only rarely used. Also, to perform a handsewn anastomosis, the vast majority of patients will have to be subjected to an open procedure, increasing the peri-operative morbidity (bleeding, infection, pulmonary embolism, impaired wound-healing, herniation, prolonged length of stay, ...) [Arezzo A, et al. Laparoscopic right colectomy reduces short-term mortality and morbidity. Results of a systematic review and meta-analysis. Int J Colorectal Dis. 2015 Nov;30(11):1457-72 [Lorenzon L, et al. Evidence based medicine and surgical approaches for colon cancer: evidences, benefits and limitations of the laparoscopic vs open resection. World J Gastroenterol. 2014 Apr 7;20(13):3680-92.]

A recent meta-analysis of stapled versus hand-sewn esophagogastric anastomosis analyzing fourteen randomized controlled trials (2,260 patients) showed improved outcomes following the use of circular staplers. Compared to hand-sewn anastomosis, stapled anastomosis can reduce the rate of anastomotic leaks, shorten the operating time, and reduce the rate of anastomotic stricture, while also reducing the rate of the blood-borne infections and recurrent laryngeal nerve palsy. [Xuefei Zhang, et al. Meta-analysis of stapled versus hand-sewn esophagogastric anastomosis. Int J Clin Exp Med 2018;11(11):11606-11618]

Those surgeons that decide to stay with a minimally invasive approach, without using a circular stapler, will likely elect to apply a temporary ostomy; transforming what is to be a single procedure into a staged procedure for the ostomy reversal. The risk to incur permanent gastrointestinal injury following exposure to a device with insufficient firing stroke is only to be expected in unusual circumstances. Mitigating steps are already articulated in the Instructions for Use which surgeons are aware of and that Ethicon will reinforce during its communication to the field.

Because of these existing mitigations in place already, in only extremely rare circumstances will the malformed staple line go unnoticed during surgery. Therefore, only in extremely rare cases, will delayed management secondary to an anastomotic failure result in permanent or life-threatening complications. Leaks resulting from a malformed staple line present early in the post-operative period, hence, most patients will still be in a hospital setting when becoming symptomatic.

The following mitigating steps are listed in the IFU.

- Always inspect the anastomotic staple line for hemostasis and check the completed anastomosis for integrity and leakage. Metal clips, staples, or sutures contained in the area to be stapled may affect the integrity of the anastomosis. Corrective action, if required, may include the use of sutures or electrocautery.
- After removing the instrument, examine the staple lines for hemostasis/ pneumostasis and proper staple closure.
- The firing stroke must be completed. Do not partially fire the instrument. Incomplete firing can result in malformed staples, incomplete cut line, bleeding, and leakage from the staple line and/or difficulty removing the device. Ensure that the firing trigger is fully squeezed to ensure proper staple formation and cutting of tissue.

Even though the identified manufacturing process shift has impacted the benefit risk profile of the device, it is our belief that allowing the circular stapler to remain on the market is required to allow continuity of care of patients without exposing them to the well-known increased risks that are expected to be associated with the alternatives, i.e. handsewn anastomoses and, or ostomies.

Health Risk Level

Harm	Severity Level	Probability of Harm	Consideration for QRB
Prolonged surgery	Reversible	Unusual	Optional
Gastrointestinal injury	Permanent	Unusual	Required
Procedural complication/ Surgical intervention (additional)	Intervention Necessary	Unusual	Required
Hemorrhage/ Major Bleed	Intervention Necessary	Extremely Rare	Required
Hemorrhagic Shock	Life -threatening	Extremely Rare	Required
Impaired healing/ anastomotic leak	Life -threatening	Extremely Rare	Required

Other Risk Evaluation

N/A

Approvals

Quality: N/A

Signature: N/A

Date: N/A

Regulatory: N/A

Signature: N/A

Date: N/A

Medical Safety:

[Redacted Signature]

Signature:

Date: See electronic signature

Business Quality Head (If required by HHE): N/A

Signature: N/A

Date: N/A