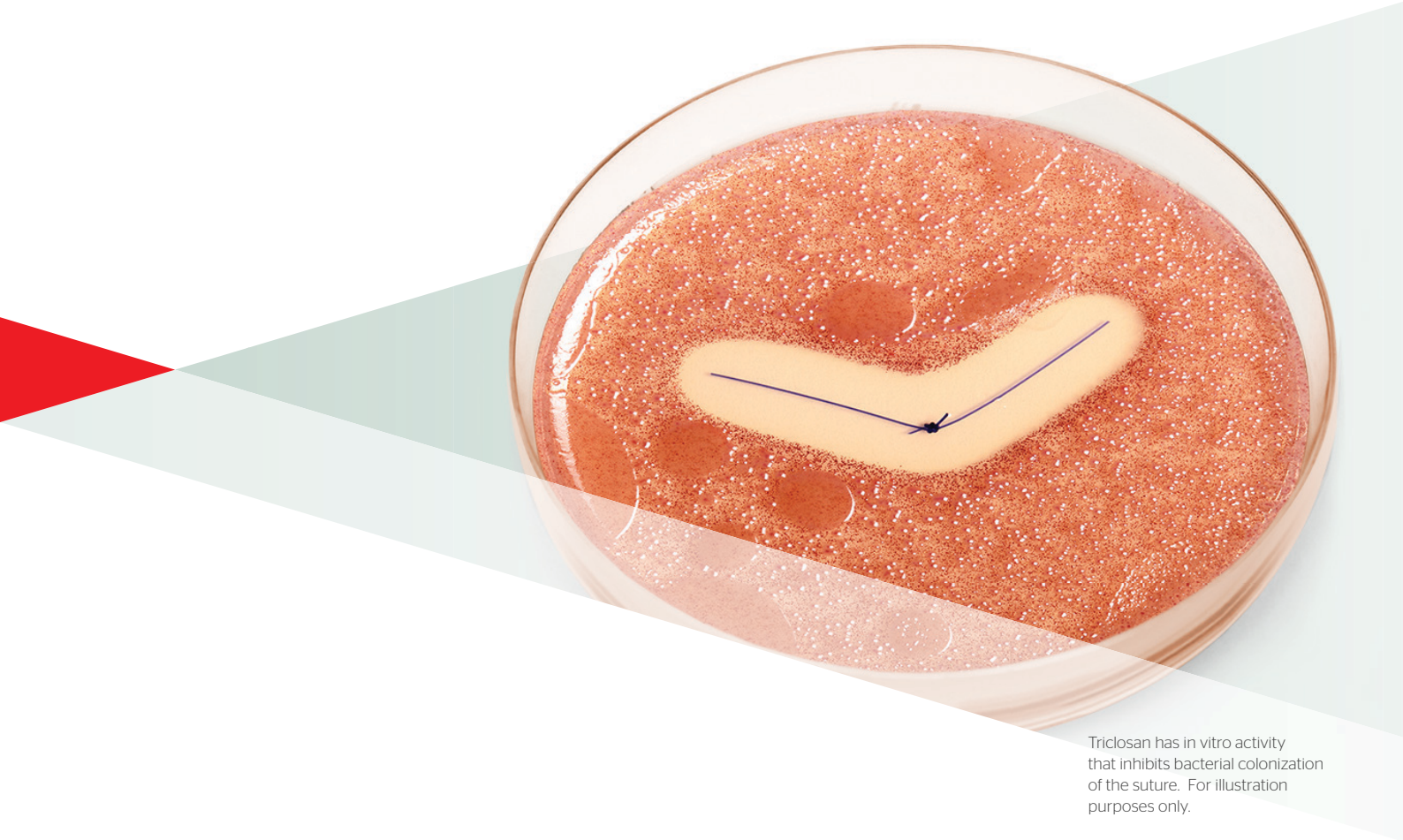
Plus Antibacterial Sutures
Triclosan Resource Guide



Triclosan has in vitro activity that inhibits bacterial colonization of the suture. For illustration purposes only.

ETHICON
PART OF THE Johnson & Johnson FAMILY OF COMPANIES

Shaping the future of surgery

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About triclosan

What is triclosan and why is it in the news?

Triclosan is a broad-spectrum antimicrobial agent, has been used for over 50 years in consumer and professional products, and is recognized as safe, when used as directed.[1] Plus Antibacterial Sutures from Ethicon are manufactured with a medical-grade triclosan, IRGACARE® MP,* which actively inhibits the growth of certain bacteria on the suture.[2-4]

Currently, there is increased scrutiny around the use of triclosan in consumer products due to concerns about an alleged potential impact on patient health (i.e antibacterial resistance, endocrine disruption) and the environment.

TRICLOSAN TIMELINE

General timeline of key triclosan-related actions

1972—US
Triclosan is introduced to the healthcare industry as an ingredient in a surgical scrub.

1976-2010—US
More than 5,245 patents containing the word "triclosan" are issued.

2003—US
First Plus Sutures (Coated VICRYL™ Plus Antibacterial (polyglactin 910) Suture) from Ethicon received US Food and Drug Administration (FDA) approval.

2004—Global
Plus Sutures from Ethicon were introduced to the European market.

2010—US
The use of antibacterial sutures is mentioned in infection prevention guidelines supported by the Association for Professionals in Infection Control and Epidemiology (APIC).

April 2010—US
The FDA issues a formal response to a letter from then-Congressmen Ed Markey (D-MA) and Henry Waxman (D-CA) that recommends the FDA and Environmental Protection Agency (EPA) ban the use of triclosan in consumer products. In its response, the FDA declines to ban triclosan and states its intent to review recent research and release its findings in Spring, 2011. As of the creation of this resource guide, no report has been issued.

June 2010—Europe
The Scientific Committee on Consumer Safety (SCCS) published an opinion that in order to preserve the role of triclosan in infection control and hygiene, they could only recommend its prudent use in applications where a health benefit can be demonstrated.

December 2010—US
Environmental activist groups—Beyond Pesticides, Food & Water Watch, and several other organizations submit a petition to the EPA requesting that triclosan be banned in consumer products.

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2011

March 2011—Europe
SCCS supports the validity of its 2010 report but amends it to say that a regulated amount of triclosan is safe in toothpastes, mouthwashes, hand soaps, body soaps/shower gels, deodorant sticks, face powders and blemish concealers, but not in other "leave on" products such as body lotions.

2011-2013—Global
Some consumer goods companies, including Johnson & Johnson, announce that they will voluntarily remove triclosan from their consumer products. Johnson & Johnson stands behind triclosan in relation to health or safety concerns and fully supports the use of triclosan-coated sutures.

April 2012—Canada
The Canadian government releases its preliminary assessment of triclosan, concluding that triclosan is not harmful to human health, but in significant amounts, it can cause harm to the environment. Some consumer goods companies, including Johnson & Johnson, announce that they will voluntarily remove triclosan from their consumer products.

December 2013—US
The FDA announces a proposed rule requiring manufacturers of antibacterial hand soaps and body washes to demonstrate that their products are safe and effective for long-term daily use; otherwise they would need to be reformulated/relabeled. This proposed rule only affects consumer goods, not hand sanitizers, wipes, or antibacterial products used in healthcare settings. As of the creation of this resource guide, this rule has not been adopted.

April 2014—Europe
The European Commission restricts amounts of triclosan for allowable use in mouthwashes and other cosmetic products.

2015

January 2015—Asia
The Association of Southeast Asian Nations' (ASEAN) Cosmetics Committee announces its intent to regulate triclosan use in mouthwashes and other cosmetic products in line with the European Community decision.

May 2015—US
The EPA rejects the 2010 petition to ban triclosan. The EPA agrees to conduct a biological assessment of the potential for negative effects on listed species under the Endangered Species Act in the ongoing triclosan registration review.

September 2016 -US
The FDA announces Final Rule on antiseptic wash, stating that it does not have sufficient safety evidence to recommend changing consumer use of products that contain triclosan. They went on to explain that they were engaged in a comprehensive scientific and regulatory review of all the available safety and effectiveness data.

2017

December 2017 - US
The FDA announces Final Rule on triclosan usage in healthcare setting, establishing that 24 active ingredients—one of which is triclosan—used in 5 categories of over-the-counter (OTC) healthcare antiseptic products are not generally recognized as safe and effective. However, the rule applies only to healthcare antiseptic washes and rubs, surgical scrubs and rubs, and skin preparation products. Therefore, triclosan used in Ethicon Plus Antibacterial Sutures is not affected by this Final Rule.

Government and nongovernmental organization (NGO) positions on triclosan

The following is a summary of public statements regarding the safety and efficacy of triclosan.

Government agencies

US Food and Drug Administration (FDA)

In its Final Rule, published on December 20, 2017, the FDA established that 24 active ingredients used in 5 categories of over-the-counter (OTC) healthcare antiseptic products are not generally recognized as safe and effective. The 5 categories of healthcare antiseptic products are 1) healthcare personnel hand washes, 2) healthcare personnel hand rubs, 3) surgical hand scrubs, 4) surgical hand rubs, and 5) patient antiseptic skin preparations. The FDA decision was based on a lack of sufficient safety and efficacy data provided by manufacturers of any products containing the 24 active ingredients in response to a request by FDA in 2015.

Although one of the 24 ingredients in this rule is triclosan, the rule applies only to healthcare antiseptic washes and rubs, surgical scrubs and rubs, and skin preparation products. Therefore, triclosan used in Ethicon Plus Antibacterial Sutures is not affected by this Final Rule.

FDA – "5 Things to Know About Triclosan"
https://www.fda.gov/consumers/consumer-updates/5-things-know-about-triclosan

US Environmental Protection Agency (EPA)

In its response to the 2010 petition calling for a ban on triclosan, the US EPA states "...EPA denies the request that the US EPA suspend and cancel all registered products containing triclosan. **The agency's most recent risk assessments of the risks to human health and the environment found that the antimicrobial uses of triclosan met the applicable statutory standards, and the petition and supporting comments did not provide sufficient evidence to significantly change those conclusions...** Nonetheless, the agency is currently engaged in assessing the risks posed by triclosan through the risk assessment process in the registration review program."

US Centers for Disease Control and Prevention (CDC)

The CDC has published on their website a biomonitoring summary on triclosan that concludes, "finding measurable amounts of triclosan in the urine does not imply that the levels of triclosan cause an adverse health effect." Biomonitoring studies on levels of triclosan provide physicians and public health officials with a reference of values so that they can determine whether people have been exposed to higher levels of triclosan than are found in the general population. Biomonitoring data can also help scientists plan and conduct research on exposure and health effects. **In a 2017 update to its Guideline for the Prevention of Surgical Site Infection, the first update to this document since 1999, the CDC advises "Consider the use of triclosan-coated sutures for the prevention of SSI."[5]***

European Scientific Committee on Consumer Safety (SCCS)

In March 2011, SCCS concluded, "The use of triclosan at a maximum concentration of 0.3% in toothpastes, hand soaps, body soaps/shower gels, and deodorant sticks (common-use products as defined by the applicant) is considered safe. Additional use of triclosan in face powders and blemish concealers at this concentration is also considered safe. The use of triclosan in other leave-on products (i.e., body lotions) is not considered safe for the consumer due to the resulting high exposures. **In regard to the usage of triclosan in infection control and hygiene, they could only recommend its prudent use in applications where a health benefit can be demonstrated."**

*CDC guideline on reducing the risk of surgical site infection is general to triclosan-coated sutures and is not specific to any one brand.

Nongovernmental organizations

World Health Organization (WHO)

Triclosan-coated sutures have been included in an evidence-based guideline for SSI prevention by the WHO. Their recommendation states: "The panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery".[6]*

The Association for Professionals in Infection Control and Epidemiology (APIC)

In a March 2014 letter to the FDA regarding the rule on antibacterial hand soaps proposed in December 2013, the APIC expressed support for ongoing evaluation of the safety and efficacy of over-the-counter (OTC) antiseptic personal care products, stating that "APIC is concerned about current industry-sponsored marketing efforts that suggest the unproven effect of consumer antiseptic products on preventing infections. We base this concern on a recent systematic review of the efficacy of antimicrobial (i.e., triclosan) soaps compared to plain soaps. The study found that antimicrobial soaps were no more effective at preventing infectious illness symptoms or reducing bacterial levels on hands than plain soap. In conclusion, APIC does not advocate the use of antiseptic products which are marketed with the implication of preventing infections without clear data to demonstrate clinical benefit."

By contrast, its stance on triclosan use in sutures is unambiguous. APIC's 2018 Infection Preventionist's Guide to the OR points out that triclosan sutures are 1 of only 6 SSI prevention interventions (the other 5 are glycemic control, normothermia, prophylactic antibiotics, alcohol-based skin antisepsis, and supplemental oxygen) recommended by the CDC, WHO, ACS/SIS, and Wisconsin Department of Public Health.

The Alliance for the Prudent Use of Antibiotics (APUA)

In a January 2011 white paper, APUA concluded, **"triclosan has several important medical uses**, and the future aim must be to retain these applications, while eliminating the more frivolous and unnecessary ones. **It would be wise to restrict the use of triclosan to areas where it has been shown to be effective and most needed."**

*Considering the low to moderate quality of the evidence and the low quality of comparisons in the subgroups of the RCTs included in the meta-regression analyses, the GDG agreed that the strength of this recommendation should be conditional.

Ethicon's position on triclosan

In August 2018, Ethicon released the following statement, reaffirming the safety and efficacy of triclosan in Plus Antibacterial Sutures in response to the December 2017 FDA Final Rule.

https://www.jnjmedicaldevices.com/en-EMEA/mir

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Dear Customer,

Thank you for your question regarding the recent FDA Final Rule, published on December 20, 2017, establishing that 24 active ingredients used in 5 categories of over-the-counter (OTC) healthcare antiseptic products are not generally recognized as safe and effective (GRAS/GRAE). The five categories of healthcare antiseptic products are 1) healthcare personnel hand washes, 2) healthcare personnel hand rubs, 3) surgical hand scrubs, 4) surgical hand rubs, and 5) patient antiseptic skin preparations.

The FDA decision was based on a lack of sufficient safety and efficacy data provided by manufacturers of any products containing the 24 active ingredients in response to a request by FDA in 2015. The result of this final rule will be that as of December 20, 2018; any products incorporating any of the 24 antiseptic ingredients for the five uses above would now be classified as new drugs requiring approved new drug applications (NDAs) or abbreviated new drug applications (ANDAs) prior to marketing.

Since one of the 24 active ingredients cited in the final rule is triclosan, we have received questions about the impact of this final rule to ETHICON Plus Antibacterial sutures, which contain triclosan. This Final Rule applies ONLY to healthcare antiseptic washes and rubs, surgical scrubs and rubs, and skin preparation products. Therefore, the use of triclosan in Ethicon Plus Antibacterial sutures is not affected by this final rule.

While questions of safety and efficacy may exist regarding the use of triclosan in the covered healthcare antiseptic products, triclosan remains an important medical option in certain surgical applications. Ethicon Plus Antibacterial sutures from Ethicon, which contain triclosan (IRGACARE® MP*), address one of the risk factors associated with surgical site infections (SSIs)—the most common type of healthcare-associated infections among surgical patients. Sutures, while necessary to close a surgical incision and provide external support to maintain wound edge apposition during the critical healing period, do act as a foreign body. Small numbers of bacteria in the wound can colonize the suture surface. In this way, the suture although ubiquitous and necessary for surgical wound closure, also presents a risk factor for the development of surgical site infection. This risk factor can be addressed by coating the suture surface with an antibacterial agent that inhibits the growth of bacteria. Therefore, the innovation of ETHICON Plus Antibacterial sutures represents a targeted intervention to address the specific risk factor for SSI posed by the presence of suture as a foreign body in the wound.

Since the first FDA clearance in 2002, Ethicon Plus Antibacterial sutures have been clinically evaluated in multiple independent studies published in the peer reviewed medical literature. Numerous randomized clinical trials have been performed on the use of Ethicon Plus Antibacterial sutures to lower surgical site infection rates. Moreover, the use of triclosan coated sutures is recommended in recent evidence-based infection prevention guidelines published by The World Health Organization, the CDC and the American College of Surgeons and Surgical Infection Society.[5-7†]

As with all our products, we will continue to monitor scientific data, as well as global developments. To date, reviews by scientific advisory bodies have determined that triclosan is a safe and effective antimicrobial that has been used for over 40 years. We remain confident in its medically appropriate use based on its ability to address an important risk factor associated with surgical site infection. Ethicon has no plans to discontinue the use of triclosan in its portfolio of Plus Antibacterial Sutures.

If you would like additional information regarding this topic, please contact Ethicon's Medical Affairs department at https://www.jnjmedicaldevices.com/en-EMEA/mir

Sincerely,

Liza G. Ovington, PhD, FACCWS, FAPWCA
Franchise Medical Director,
Ethicon, Inc.

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†CDC, WHO, and ACS/SIS guidelines on reducing the risk of surgical site infections are general to triclosan-coated sutures and are not specific to any one brand.

The need for Plus Antibacterial Sutures

Prevalence of Surgical Site Infections (SSIs)

SSIs are the most common healthcare-associated infections (HAIs) among surgical patients, posing serious concern for patients and real consequences for physicians and healthcare organizations.[8]

- SSI in Europe affect more than 500,000 people per year

Surgical Site Infections (SSI)[9,10]

- 37% of hospital acquired infections in surgical patients are SSIs
- Patients with an SSI are twice as likely to spend time in an intensive care unit
- Patients with an SSI are five times more likely to be readmitted after discharge
- Patients with an SSI are twice as likely to die
- 40-60% of surgical site infections may be preventable

The suture as a site of infection

Reducing the risk of surgical site infection (SSI) requires an evidence-based surgical care bundle approach that includes management of patient risk factors for infection, proper skin antisepsis, instrument sterilization, environmental control within the operating room, and antibacterial devices.[5,6] Antimicrobial prophylaxis alone may not be adequately effective against surgical site infection; prophylactic antibiotics can't always reach the incision site.[11-12,24]

Generally, large numbers of bacteria are required for surgical site infection to occur. In a typical patient, the infective dose is >100,000 microorganisms per gram of tissue, although this number is dependent on the bacterial species and may be lower if the patient's immune system is compromised, or in the presence of a foreign body.[12]

Sutures, like all implanted materials, can be a nidus for infection, because they lower the infective threshold, i.e., they decrease the amount of bacteria needed to cause an SSI.[12,13] In the presence of a foreign body such as suture, it takes only 100 staphylococci per gram of tissue for an SSI to develop.[12]

Although every operation begins with an antiseptic preparation of the skin to kill superficial bacteria, some bacteria remain below the visible surface of the epidermis, in the lining of hair follicles, sweat glands, and other areas.[6,14] Once a suture is introduced into a surgical incision, bacteria on the surface of the epidermis, disrupted while making a skin incision, migrate from the surface to the foreign body, which is the site of SSI initiation.[15-16]

Bacteria can adhere to and colonize the suture during its implantation. Subsequently, the colonizing bacteria can develop into a polymicrobial biofilm on the suture.[15] Biofilm on implanted sutures can increase over time as the colonizing bacteria secrete a sticky polymeric matrix.[17-18] A biofilm matrix is difficult to penetrate by macrophages or local or systemic antimicrobials, therefore the likelihood of SSI is increased.[17]

Typical bacterial concentration required for SSI to develop

>100,000

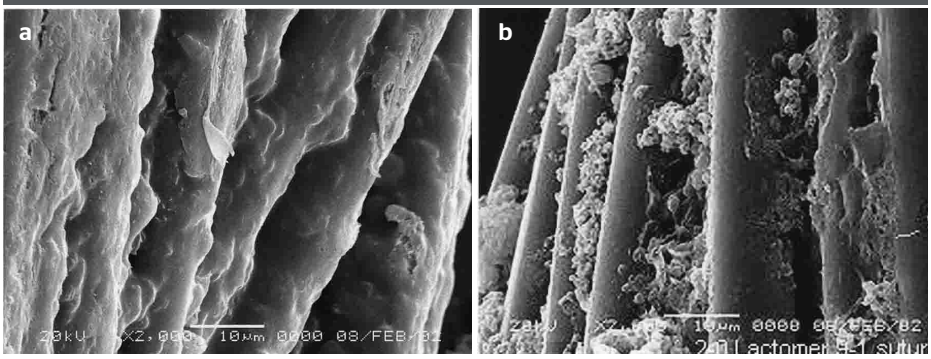
per gram of tissue[12]

In the presence of a foreign body such as suture, it takes only 100 staphylococci per gram of tissue for an SSI to develop[12]

100

per gram of tissue

Biofilm formation increases the difficulty of treating an infection, even in the presence of antibiotics[19]

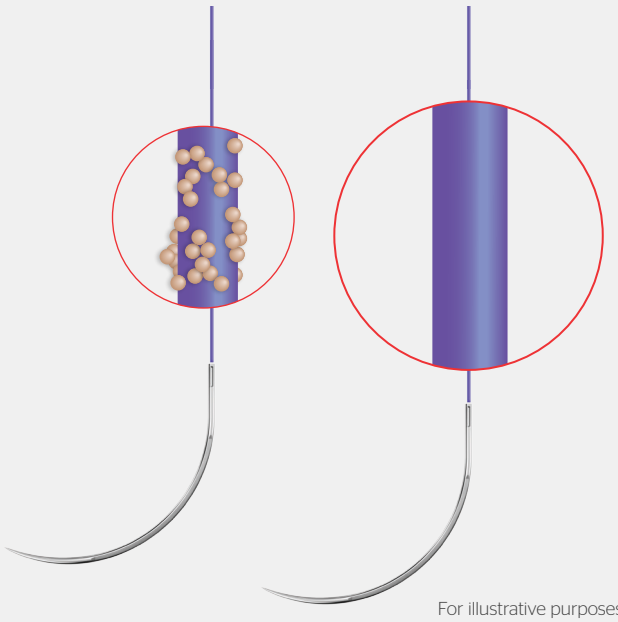


Suture material scanning electron microscope (SEMs). Suture material was exposed to MRSE for 24 h. (a) Coated polyglactin 910 suture with triclosan. (b) Braided lactomer 9-1. Note the absence of colonization on the triclosan-treated suture. Original magnification, x2,000.

Plus Sutures have been shown to reduce the risk of biofilm formation by inhibition of bacterial colonization of the suture[2-4,13,20¥] Plus Sutures – the only sutures with Triclosan available worldwide with antibacterial protection offered by IRGACARE®* MP (Triclosan)[21§]

Plus Antibacterial Sutures have been shown in vitro to inhibit bacterial colonization of the suture for 7 days or more and are effective against the most common organisms associated with SSIs:[2-4]

- ✓ *Staphylococcus aureus*
- ✓ *Staphylococcus epidermidis*
- ✓ MRSA
- ✓ MRSE
- ✓ *Escherichia coli*†
- ✓ *K pneumoniae*†



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†PDS™ Plus Antibacterial (polydioxanone) Suture and MONOCRYL™ Plus Antibacterial (poliglecaprone 25) Suture only.
¥Data generated in vitro and in animal models; Plus Sutures have been shown to inhibit bacterial colonization of the suture for 7 days or more (Staphylococcus aureus, Staphylococcus epidermidis, Methicillin-resistant Staphylococcus aureus (MRSA), Methicillin-resistant Staphylococcus epidermidis (MRSE), Escherichia coli† (E coli) and Klebsiella pneumoniae†).
§There are no competitive Triclosan coated sutures that have both FDA clearance and CE Mark as of June 2020.

Safety and efficacy

Ethicon Plus Antibacterial Sutures were granted clearance by the US Food and Drug Administration (FDA) in 2003 and approved/released outside the US in 2004. In the 5 years between 2016 and 2020 more than 500 million individual Plus Suture strands have been sold worldwide.[22]

- The IRGACARE® MP* triclosan used in Plus Antibacterial Suture is an antiseptic, not an antibiotic, with no proven clinical connection to antibiotic cross-resistance.[23,25-27]
- The small amount of triclosan used in Plus Antibacterial Sutures does not accumulate in the body and is metabolized and excreted in a neutralized form.[1,7]
- Sutures that go unused are destroyed as medical waste, so any residual triclosan-coated suture is not released into the environment.
- A lab study concluded that triclosan readily photodegraded in surface water and completely degraded in soil[69]
- The triclosan on Ethicon Plus Sutures has been shown in vivo and in vitro to be non-toxic, non-irritating, non-carcinogenic and non-teratogenic.[1]

Triclosan-coated sutures are supported by evidence-based recommendations from a number of global health authorities as part of the SSI prevention bundle.[5-6,16,28-29,68*]

Global Health Authorities

WHO

World Health organization 2016[6]: 'The panel suggests the use of triclosan coated sutures for reducing the risk of SSI, independent of the type of surgery. (conditional recommendation, moderate quality of evidence.)'

CDC

Center for disease control and prevention, 2017[5]: 'Consider the use of triclosan-coated sutures for the prevention of SSI.'

ACS/ SIS

American collage of surgeons/ Surgical infection society, 2016 SSI-guidelines[28]: 'Triclosan antibacterial sutures use is recommended for wound closure in clean and clean contaminated abdominal cases.'

Local Health Authorities (UK and Germany)

NICE Guidelines 2019 update

NICE Guidelines Update 2019[16]: 'When using sutures, consider using antimicrobial triclosan-coated sutures, especially for pediatric surgery, to reduce the risk of surgical site infection (2019).'

KRINKO

Commission for Hospital Hygiene and Infection Prevention 2018[29]: 'Antiseptically coated sutures only reduce the threat of infection where there are high baseline SSI rates, contamination class III and IV surgeries, and patients with multiple morbidities (Cat.II).'

European Network

EUnetHTA

European Network for HTA 2017:[68] 'A statistically significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSI was demonstrated in our systemic review /meta-analysis, based on moderate quality RCTs Data.'

Plus Sutures – the only sutures with Triclosan available worldwide with antibacterial protection offered by IRGACARE®† MP (Triclosan)[21*]

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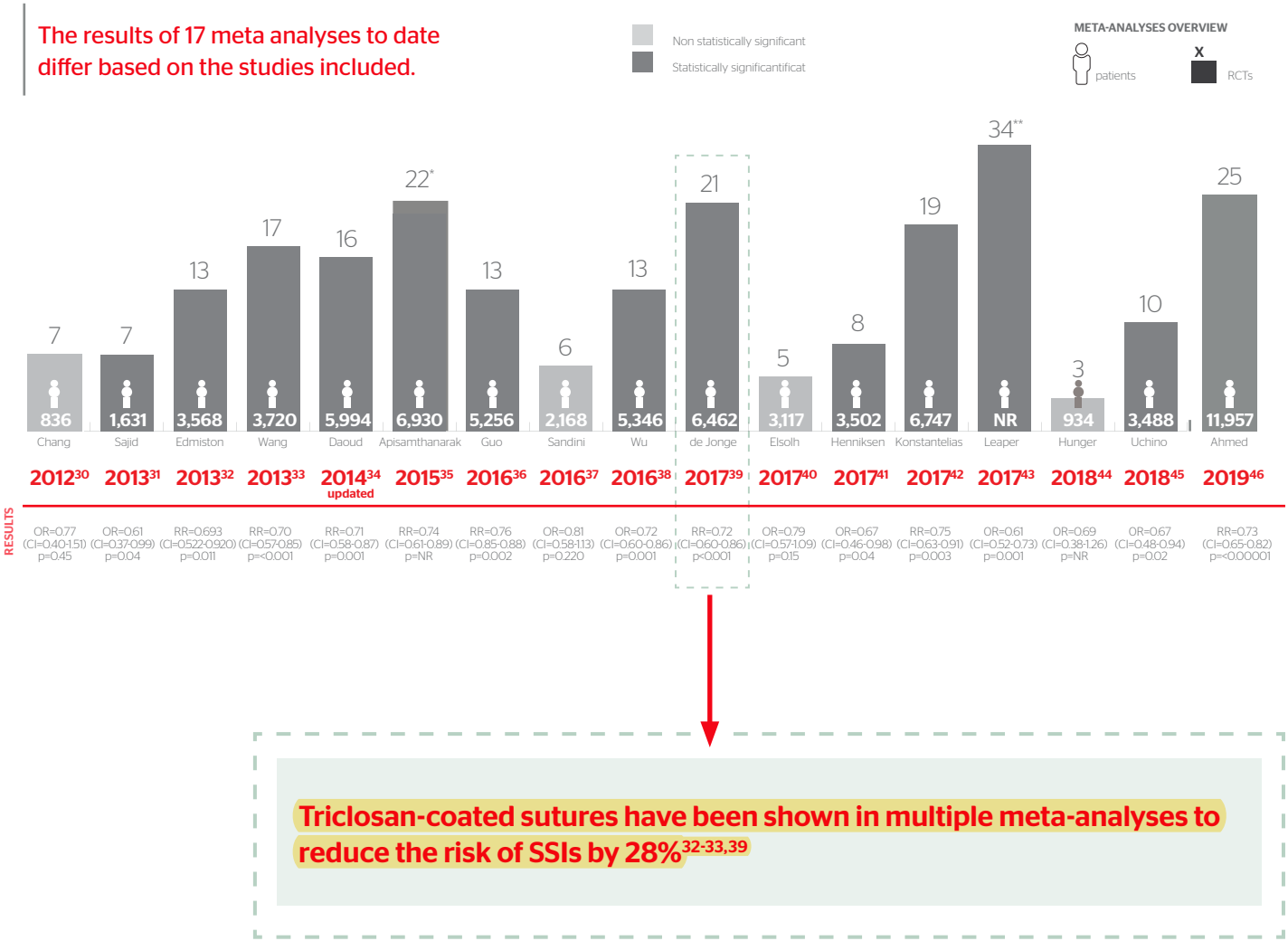
†CDC, WHO, and ACS/SIS guidelines on reducing the risk of surgical site infections are general to triclosan-coated sutures and are not specific to any one brand.

Clinical support for triclosan-coated sutures – meta-analyses overview

ETHICON Plus Antibacterial Sutures have been shown to significantly reduce the risk of Surgical Site Infection (SSI) in multiple meta analyses

The results of 17 meta analyses to date differ based on the studies included.



Triclosan-coated sutures have been shown in multiple meta-analyses to reduce the risk of SSIs by 28%[32-33,39]

* One publication is duplicated

**Leaper's meta analysis include both Observational studies and RCTs

Ethicon Plus Antibacterial Suture portfolio

Available in a range of absorbable polymers and sizes, in both monofilament and multifilament sutures

MONOCRYL™ Plus Antibacterial (Poliglecaprone 25) Suture

MONOCRYL™ Plus Antibacterial (poliglecaprone 25) Suture

- Ideal for subcuticular skin closure[47]
- MONOCRYL™ Plus Antibacterial Sutures are intended for use in general soft tissue approximation and/or ligation where an absorbable material is indicated.[48]

Coated VICRYL™ Plus Antibacterial (Polyglactin 910) Suture

Coated VICRYL™ Plus Antibacterial (polyglactin 910) Suture

- Predictable breaking strength retention profile to provide support for up to 28 days while tissues heal[49]
- Proprietary suture coating and polymer properties minimize drag force and elicit only a slight tissue reaction during absorption[47, 49]

PDS™ Plus Antibacterial (Polydioxanone) Suture

PDS™ Plus Antibacterial (polydioxanone) Suture

- Can be used for secure fascia closure.[50]
- Retains 60% of its original strength for 6 weeks, providing support to the fascia as it slowly heals[50*]

Also available in a range of absorbable polymers and sizes in barbed suture designs

Stratafix™ Spiral MONOCRYL™ Plus Knotless Tissue Control Device

STRATAFIX™ Spiral MONOCRYL™ Plus Knotless Tissue Control Device

- STRATAFIX™ Spiral Knotless Tissue Control Devices provide smooth tissue passage and a secure hold that helps control tension and achieve excellent tissue approximation.[51-58]
- 62% of its original strength remains after 7 days implantation and approximately 27% of its original tensile strength at 14 days post implantation. All of the original tensile strength is lost by 21 days post implantation.[59]

Stratafix™ Spiral PDS™ Plus Knotless Tissue Control Device

STRATAFIX™ Spiral PDS™ Plus Knotless Tissue Control Device

- STRATAFIX™ Spiral Knotless Tissue Control Devices provide smooth tissue passage and a secure hold that helps control tension and achieve excellent tissue approximation.[51-58]
- Retains 40%-70% of its original strength for 6 weeks, providing support to the fascia as it slowly heals[60*]

Stratafix™ Symmetric PDS™ Plus Knotless Tissue Control Device

STRATAFIX™ Symmetric PDS™ Plus Knotless Tissue Control Device

- STRATAFIX™ Symmetric PDS™ Plus Knotless Tissue Control Device provides greater holding strength than traditional sutures and can be used to close in high-tension areas, such as fascia** [56, 61-65]
- Retains 55% of its original strength for 6 weeks, providing support to the fascia as it slowly heals[66]

Shown in vitro to inhibit bacterial colonization of the suture for 7 days or more †, [2-4, 67]

Plus Antibacterial Sutures have been shown in vitro to inhibit bacterial colonization of the suture for 7 days or more and are effective against the most common organisms associated with SSIs:[2-4]

- Staphylococcus aureus
- Staphylococcus epidermidis
- MRSA
- MRSE
- Escherichia coli †
- K pneumoniae †

* For size (3-0)and larger, Please refer to IFU for details.

** Conclusions derived from pre-clinical data

† MONOCRYL™ Plus Antibacterial (poliglecaprone 25) Suture and PDS™ Plus Antibacterial (polydioxanone) Suture only.

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