Nye metoder: Innspill til metoder (forslag/metodevarsler/oppdrag)

Alle har anledning til å komme med tilleggsopplysninger til en metode som er foreslått for nasjonal metodevurdering. Det er ønskelig at innspill kommer inn så tidlig som mulig i prosessen, fortrinnsvis før behandling i Bestillerforum RHF.

Bruk dette skjemaet for å gi innspill til forslag, metodevarsler og oppdrag. På nyemetoder.no vil nye forslag/metodevarsler ha statusen «Forslag mottatt/åpent for innspill» før behandling i Bestillerforum RHF. Utfylt skjema sendes nyemetoder@helse-sorost.no.

NB: **Punkt 1-3 og 11 fylles ut av alle.** Punkt 4-9 fylles ut avhengig av rolle og kjennskap til metoden.

Jeg er klar over at skjemaet vil bli publisert i sin helhet på nyemetoder.no (kryss av): ☒
Har du informasjon du mener ikke kan offentliggjøres, ta kontakt med sekretariatet før innsending.

Jeg har fylt ut punkt 11 nedenfor «Interesser og eventuelle interessekonflikter» (kryss av): ☒

1.Hvilken metode gjelder innspillet?	
Metodens ID nummer*:	ID2021_139
Metodens tittel:	Triklosanbelagte suturer til forebygging av postoperativ sårinfeksjon

*ID-nummer finner du på metodesiden på nyemetoder.no og har formen ID2020_XXX

2. Opplysninger om den som gir innspill	
Navn	Emanuela Mauro
Eventuell organisasjon/arbeidsplass	Johnson & Johnson Medtech
Kontaktinformasjon (e-post / telefon)	emauro@its.jnj.com, +39 335 5900023

3. Oppsummert innspill til metoden (besvares av alle)
We would like to bring under the committee's attention some important remarks concerning the evaluation of the FHI Report "Triclosan coated sutures for prevention of SSI": 1. The type of subgroups explored in the Meta-Analysis are not relevant to the mechanism of action and overall efficacy, which is unaffected by surgery type, supported by NICE and WHO analyses [1-4]. 2. Falcon study is unfairly impacting the overall estimate for the Norwegian Healthcare System, considering: (a) it was mainly carried out in low-income countries, Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa, which differ from the Norwegian system [2,5] (b) triclosan-coated sutures were used only in the deep layer of the incisions, while superficial SSI were also recorded in the results [2,5].

3. The cost-consequence analysis should incorporate a probabilistic sensitivity analysis according to health-economics guidelines [6]. Our analysis, using UK costs and the Norwegian HTAs Confidence Interval estimates, shows very high probability of cost savings (the analysis is attached).
4. Triclosan does not have an impact to the environment, as it is metabolized in the human body and excreted via urine in a metabolized form [7,8]. Additionally, PLUS Antibacterial sutures were recognized by NICE Medical Technologies Guidance in June 2021, to have environmental benefits [3]. A sustainability impact for PLUS Antibacterial sutures is showing reduced emissions for Norway (is available if requested).
5. Antibiotic Resistance has not been proven in triclosan, based on the literature [12-36], especially for the low amount of Triclosan used in PLUS Antibacterial sutures compared to consumer products.

Please see point no. 10, for detailed information and references.

Nærmere informasjon om metoden og innspill til PICO*

*PICO er et verktøy for å formulere presise problemstillinger i metodevurderingsarbeid. PICO er en forkortelse for Population/Problem – Intervention – Comparison – Outcome. PICO brukes til å presisere hvilken populasjon/problem som skal studeres, hvilke(t) tiltak (metode/behandling) som skal vurderes, hvilket tiltak det er naturlig å sammenligne med, og hvilke utfall/endepunkter det ~~å~~ er relevant å måle/vurdere. PICO er viktig for planlegging og gjennomføring av en metodevurdering.

4. Kjenner du til om metoden er i bruk i Norge i dag?

Er metoden i bruk utenom kliniske studier i dag: Ja
Fra hvilket tidspunkt har den vært i bruk: 2005
Hvor er eventuelt metoden i bruk: Innen sårlukking etter kirurgi hvor absorberbare suturer benyttes.

5. Hvilken pasientgruppe i den norske spesialisthelsetjenesten er metoden aktuell for? (PICO)

Beskriv kortfattet:

6. Er du kjent med behandlingsalternativer til denne metoden og hvordan disse fungerer for pasientgruppen i dag? (PICO)
Beskriv kortfattet:

7. Har du innspill til hva som vil være viktig for pasienter som er aktuelle for behandling med metoden? (PICO)
Hva kan oppfattes som en fordel for pasienter og brukere med denne metoden sammenlignet med aktuelle alternativer? Hvilke endepunkter/resultater av behandlingen er det aktuelt å måle? Beskriv kortfattet:

8. Spesielt for medisinsk utstyr (besvares av leverandør): CE-merking
Foreligger det CE-merking for bruksområdet som beskrives i metoden? I så fall angi type og tidspunkt:

9. Spesielt for legemidler (besvares av leverandør): Markedsføringstillatelse (MT)
Har legemiddelet MT for indikasjonen som omfattes av metoden? Angi i så fall tidspunkt eller ventet tidspunkt for MT:

10. Andre kommentarer
We want to make the committee aware that we some comments on the methodology: We want to make the committee aware that we some comments on the methodology: 1. **The type of subgroups explored in the Meta-Analysis are not relevant to the mechanism of action and overall efficacy** a. PLUS Antibacterial Sutures Mechanism of action is unaffected by the surgery type. It is known that the presence of a suture in a wound lowers the inoculum burden required for infection by a factor of 10000 [1]; the triclosan coating of PLUS Antibacterial Sutures prevents bacterial colonisation and biofilm formation on the suture and thereby reduces this particular risk factor for SSI [2].

b. Other HTA bodies, like NICE [3] and WHO [4], have grouped together all types of surgeries in their Meta-Analyses, with the WHO meta-regression analysis 8 showing that "The effect of triclosan coating of sutures on reducing SSI was similar between braided and monofilament sutures (p = 0.380), clean wounds and other wounds (p = 0.690), cardiac and other surgery (p = 0.900), and abdominal and other surgery (p = 0.832).".

2. Falcon study is unfairly impacting the overall estimate for the Norwegian Healthcare System

a. We have observed that in the gastrointestinal / abdominal subgroup analysis, 41.8% of the weight was given to the FALCON trial [5] which was mainly carried out in low-income countries, Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa [5]. Ethicon PLUS Antibacterial Sutures are expected to perform as part of a bundle of care. However, we believe the Norwegian healthcare system is different to the countries in the Falcon study, thus the FALCON study is expected to have limited applicability.

b. In the FALCON trial, both superficial incisional and deep incisional wound infections were included as the primary outcome; however, triclosan-coated sutures in the treatment group were only used in the deep layer of the incision for closure of the fascia [2]. This means that triclosan-coated sutures could reduce the risk of deep incisional SSI but would not be expected to influence superficial incisional SSI outcomes. It is therefore our opinion that the wound closure methodology in the FALCON trial confounds the evaluation of triclosan-coated sutures [2].

3. The cost-consequence analysis should incorporate a probabilistic sensitivity analysis

a. The deterministic economic analysis does not incorporate the findings of the Meta-analysis, for example the upper and lower bounds of the Confidence Interval. It is best-practice for Health Technology Assessment to perform probabilistic sensitivity analysis [6].

b. To demonstrate this and provide additional economic evidence, we have utilized the cost consequence model we developed for NICE and that was critically apprised by them, and undertaken a probabilistic sensitivity analysis, to demonstrate the potential cost savings from utilizing PLUS Antibacterial sutures.

c. The findings of this analysis are in Attachment 1. We have utilized UK costs and presented cost estimates in 2020 UK Pounds (2020 Exchange rate: £1 UK = 12.07 NOK). Our analysis demonstrates the probability adopting PLUS Antibacterial sutures is cost saving, even when only including studies that were assessed a low risk of bias, to be 75.9% with the average cost saving per person to be approximately 2020 UK £2.84 (34.27 NOK in 2020 prices). If we consider, as is stated in the report, approximately 413,000 surgical procedures are performed annually in Norway, the estimated annual cost saving is 14.2million NOK. We would be willing to fully adapt our economic model for a Norwegian perspective.

4. **Triclosan does not have an impact to the environment impact, while the usage of PLUS Antibacterial sutures is expected to be positive**
    a. The Triclosan in PLUS Antibacterial sutures poses a negligible risk of environmental impact due to its lack of a pathway into the environment. This contrasts sharply with many consumer products that have contained triclosan for over six decades, including toothpastes, mouthwashes, and soaps; these products often enter waterways and landfills as they can be washed down drains or disposed of as household waste, introducing triclosan into the environment in its original, unmetabolized form [7, 8]. In the case of PLUS Antibacterial sutures, the triclosan is metabolized by the liver once implanted into patients and is subsequently excreted in the urine as a conjugated product; notably, this metabolized form has not been linked to bacterial resistance [7, 8]. Additionally, any unused sutures are managed as medical waste and are typically incinerated, further minimizing any potential environmental impact. It is also worth noting that even after the widespread and long-term use of consumer products containing triclosan, there has been no significant evidence to suggest adverse environmental effects [7, 8].

    b. We would also like to mention that a potential reduction of SSI incidence due to PLUS Antibacterial sutures can be estimated to positively affect the environment; we have run an ETHICON model based on the annual number of surgical procedures in Norway [9], which we are sharing in the attached report. “The environmental impact of an SSI was estimated to incur 0.58 tCO_2 e GHG emissions (equivalent to two return flights from London to Rome), 872 m^3 water use, and 0.06 tonnes of waste generation [10]. PLUS Antibacterial sutures were recognized by NICE Medical Technologies Guidance in June 2021, to potentially have environmental benefits [3]. The use of PLUS Antibacterial sutures, through the reduction of SSI risk, is estimated to result in environmental savings of 1,390 tCO2e (equivalent to 4,916 return flights from London to Rome), 2.1 million m^3 water use, and 156 tonnes of waste, per 800,000 surgical procedures per year [11].

5. **Bacterial Resistance has not been proven in triclosan**
    a. We would also like to share the following literature [12-36] that has important data, demonstrating that no resistance from robust data can be found following long-term triclosan exposure through hygiene products / stents, and there should be no reason to assume that resistance will develop through one-time exposure after suture implantation. Petri-dish studies should be taken as a worst-case scenario, as these effects have not been seen in patients over the 60 years of applications. We should also state that the amount of Triclosan used in PLUS Antibacterial sutures is miniscule compared to consumer products, while consumer products are used in daily practice, compared to counted number of surgeries in a human lifetime.

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11. Johnson & Johnson Plus Sutures Environmental Impact Model Report
12. De Jongeet al. 2016 Meta-analysis and trial sequential analysis of triclosan-coated sutures for the prevention of surgical-site infection
13. Barbolt2002 Chemistry and Safety of Triclosan, and Its Use as an Antimicrobial Coating on Coated VICRYL*Plus Antibacterial Suture (Coated Polyglactin910 Suture with Triclosan)
14. Gillock et al.2011Triclosan-resistant bacteria isolated from feedlot and residential soils
15. Kahn et al.2018 Distribution of triclosan-resistant genes in major pathogen microorganisms revealed by metagenome and genome-wide analysis
16. Levy et al.2001Antibacterial Household Products: Cause for Concern
17. Braoudakiet al.2004Low level of cross-resistance between triclosan and antibiotics in E.ColiK-12 and E.coli O55 to E. coli O147
18. Westfall et al. 2019 The Widely Used Antimicrobial Triclosan Induces High Levels of Antibiotic Tolerance In Vitro and Reduces Antibiotic Efficacy up to 100-Fold In Vivo
19. Ciusaet al. 2012 A novel resistance mechanism to triclosan that suggests horizontal gene transfer and demonstrates a potential selective pressure for reduced biocide susceptibility in clinical strains of Staphylococcus aureus
20. Lu et al. 2018 Non-antibiotic antimicrobial triclosan induces multiple antibiotic resistance through genetic mutation

21. Birosovaet al. 2009 Development of triclosan and antibiotic resistance in Salmonella enterica serovar Typhimurium
22. McBain et al. 2004 Selection for high-level resistance by chronic triclosan exposure is not universal
23. Marshall et.al 2012 The Frequency of Antibiotic-Resistant Bacteria in Homes Differing in Their Use of Surface Antibacterial Agents
24. Cole et.al 2003 Investigation of antibiotic and antibacterial agent cross-resistance in target bacteria from homes of antibacterial product users and nonusers
25. Sullivan et al. 2003 Will triclosan in toothpaste select for resistant oral streptococci?
26. Aiello et al. 2004 Relationship between Triclosan and Susceptibilities of Bacteria Isolated from Hands in the Community
27. Jones et al. 1988 The effect of long-term use of a dentifrice containing zinc citrate and a non-ionic agent on the oral flora
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30. Cullinan et al. 2014 No evidence of triclosan-resistant bacteria following long-term use of triclosan-containing toothpaste
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36. Davison et al. 2010 SCCS Opinion on Triclosan –Antimicrobial Resistance

11. Interesser og eventuelle interessekonflikter

Beskriv dine relasjoner eller aktiviteter som kan påvirke, påvirkes av eller oppfattes av andre å ha betydning for den videre håndteringen av metoden som det gis innspill på (for eksempel: økonomiske interesser i saken, oppdrag eller andre bindinger).

Beskriv kortfattet:
Johnson & Johnson Ethicon er en global produsent av suturer. Ethicon er representert i Norge av Ortomedic AS.