Region Hovedstaden

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## NOTAT

Til: Miljø- og klimaudvalget

# Administrationens faktuelle bemærkninger til brug af antibakterielle suturer på Region Hovedstadens hospitaler

### Konklusioner

- En offentlig ordregiver som Region Hovedstaden kan ikke i sine udbud af indkøbsaftaler pege på et specifikt produkt fra en navngiven producent.
- Region Hovedstadens hospitaler har i de eksisterende indkøbsaftaler mulighed for at indkøbe antibakterielle suturer. I regionens igangværende udbud af suturer er der lagt op til, at antibakterielle suturer fortsat skal være en del af sortimentet.
- P.t. er gennemsnitsprisen pr. stk. højere for antibakterielle suturer end for konventionelle suturer.
- Det kan i visse tilfælde give mening at betale en højere gennemsnitspris pr. stk., hvis indkøbet af et dyrere produkt resulterer i et lavere samlet forbrug eller hvis indkøbet medfører positive effekter på for eksempel bæredygtighed.
- En positiv bæredygtighedseffekt isoleret til brugen af antibakterielle suturer frem for konventionelle suturer har nær sammenhæng med hvor meget brugen af antibakterielle suturer kan bidrage til at nedbringe antallet af sårinfektioner (og dermed forbruget af antibiotika, antallet af indlæggelsesdage og antallet af reoperationer).
- En nærmere analyse af effekter isoleret til brugen af antibakterielle suturer på Region Hovedstadens hospitaler er ikke simpel at gennemføre, fordi mange faktorer spiller ind på risikoen for sårinfektioner.

## Udbudsjuridiske bemærkninger

Region Hovedstadens forbrug af suturer har et økonomisk omfang, der betyder, at produkterne skal anskaffes via et EU-udbud. Den aktuelle tærskelværdi (grænse for EU-udbud) for regioner er ca. 1,6 mio. kroner. Region Hovedstadens forbrug belyses nærmere nedenfor under punkt 2 og 3.

Indledningsvis bemærkes det, at der i dette notat bruges betegnelsen ”antibakterielle suturer”, idet betegnelsen ”Plus sutur” er knyttet sammen med produkter fra virksomheden Johnson & Johnson.

Antibakterielle suturer har, sammenlignet med konventionelle suturer, den yderligere egenskab, at de er behandlet med en antibakteriel coating indeholdende triclosan eller klorhexidin.

Udbudsreglerne indebærer, at Region Hovedstaden skal udforme sine udbud i henhold til principperne om ligebehandling, gennemsigtighed og proportionalitet (jf. udbudslovens § 2), hvilket bl.a. betyder, at der i et EU-udbud ikke kan peges på en bestemt leverandør eller et bestemt produkt.

Derudover indebærer udbudsreglerne, jf. udbudsloven §2, stk. 2, at udbud ikke må udformes, så konkurrencen kunstigt begrænses, hvilket blandt andet vil være tilfældet, hvis en eller flere virksomheder favoriseres uretmæssigt. Det betyder, at krav, der opstilles som en del af udbuddet, skal være sagligt begrundet. I et udbud af suturer vil et krav om, at suturer skal have særlige antibakterielle egenskaber (sammenlignet med konventionelle suturer) derfor skulle være båret af saglige hensyn. Sådanne hensyn kan for eksempel kan handle om behandlingseffekten på patienter, den kliniske/faglige kvalitet, effektiv ressourceudnyttelse/økonomi eller bæredygtighed.

## Region Hovedstadens igangværende udbud

Region Hovedstaden har et igangværende udbud af en indkøbsaftale vedrørende suturer, hvor der som en del af udbuddet indgår en separat delaftale vedrørende antibakterielle suturer. Det er på alle udbuddets delaftaler muligt for tilbudsgiverne at tilbyde antibakterielle suturer i stedet for konventionelle suturer.

Der udbydes en 4-årig rammeaftale med en anslået samlet værdi på cirka 57 mio. kroner. Udbudsbekendtgørelsen kan ses her: https://udbud.dk/detaljevisning?noticeId=97ee94b9-14c7-43f7-8514-5c256c4b9710&noticeVersion=01&noticePublicationNumber=00001861-2025

Brugergruppen drøftede under forberedelserne til udbuddet specifikt suturer med antibakteriel coating både internt i brugergruppen og på dialogmøder med leverandører. En enig brugergruppe besluttede 1) at lade antibakterielle suturer indgå som en særlig delaftale i udbuddet, og 2) at der på udbuddets

øvrige delaftaler kan bydes ind med såvel antibakterielle som konventionelle suturer.

Brugergruppen repræsenterer alle relevante specialer i Region Hovedstaden.

**Region Hovedstadens nuværende aftale vedrørende suturer**

Region Hovedstadens nuværende indkøbsaftale om suturer består af et antal delaftaler, hvoraf nogle delaftaler indeholder både konventionelle og antibakterielle suturer. Derudover er der en delaftale, der udelukkende indeholder antibakterielle suturer.

På de delaftaler, der indeholder både konventionelle og antibakterielle suturer, ligger gennemsnitsprisen for de antibakterielle suturer over gennemsnitsprisen for de konventionelle suturer. Det kan i visse tilfælde give mening at betale en højere gennemsnitspris pr. stk., hvis indkøbet af et dyrere produkt resulterer i et lavere samlet forbrug eller hvis indkøbet medfører positive effekter på for eksempel bæredygtighed. Betaling af en merpris bør altid, af hensyn til regionens forpligtelse til at tage skyldige økonomiske hensyn ved brug af offentlige midler, ske på baggrund af en grundig vurdering af om fordelene står i rimeligt forhold til merprisen.

Antibakterielle suturer indkøbes og anvendes allerede flere forskellige steder i Region Hovedstaden, idet en enkelt ortopædkirurgisk afdeling dog tegner sig for ca. 30% af det samlede forbrug.

**Øvrige danske regioner**

De 4 øvrige regioners samlede indkøb af antibakterielle suturer er den 8. januar 2025 opgjort til ca. 16,7 mio. kroner. Region Syddanmark har det højeste forbrug, hvilket der ikke er nogen umiddelbar forklaring på det vil bero på en nærmere undersøgelse.

**Hospitalsinfektioner i Danmark**

Rigsrevisionen afgav i 2017 en beretning om ”forebyggelse af hospitalsinfektioner”. Statens Serum Institut vurderede ved den lejlighed, at antallet af hospitalsinfektioner kunne reduceres med op til 20 %, bl.a. gennem god hygiejne (primært håndhygiejne), rationel brug af antibiotika og overvågning af forekomsten af infektioner. Rigsrevisionen har årligt frem til 2023 fulgt op på 2017-beretningen og bemærkede i sit sidste opfølgningsnotat blandt andet:

> ”Rigsrevisionens opfølgning viser, at Indenrigs- og Sundhedsministeriet fortsat følger udviklingen i hospitalsinfektioner via de nationale mål ved 2 indikatorer, men at udviklingen ikke er entydig.”

Der er således gode argumenter for løbende at have fokus på hospitalsinfektioner (ikke bare de typer, der behandles i 2017-beretningen).

Mange faktorer, som kan påvirke risikoen for postoperative sårinfektioner: For eksempel antal personer på operationsstuen, operationsbeklædning, handsker, operationsafdækningen, de anvendte kirurgiske instrumenter, kirurgens kompetencer/erfaring, operationens længde, patientens almentilstand, operationspersonalets håndhygiejne

En af regionens nuværende leverandører, virksomheden Johnson & Johnson har fremlagt sit bud på dokumentation for sammenhængen mellem brugen af antibakterielle suturer og postoperative infektioner. I dette materiale henvises der blandt andet til en infektionshygiejnisk vurdering fra Statens Serum Institut samt en "medical technologies guidance" fra National Institute for Health and Care Excellence (NICE); begge vedlægges som henholdsvis Bilag 1 og Bilag 2. Såvel vurderingen fra Statens Serum Institut som vurderingen og anbefalingen fra NICE er udarbejdet på Johnson & Johnsons foranledning og handler derfor om, hvorvidt brugen af Plus-suturer fra Johnson & Johnson kan anbefales.

En mulig positiv effekt på sårinfektioner på Region Hovedstadens hospitaler isoleret til brug af antibakterielle suturer frem for konventionelle suturer vil dog skulle undersøges nærmere for at afdække i hvilke afdelinger / på hvilke procedurer potentialet er til stede. En sådan undersøgelse er ikke simpel at gennemføre, idet mange forskellige faktorer har indflydelse på risikoen for sårinfektioner. Dette understreges i også i vurderingen og anbefalingen fra NICE[1], ligesom der peges på, at en kirurgs beslutning om brugen af Plus-suturer afhænger af den enkelte patients tilstand[2].

**Bæredygtighed**

Afdækning af de bæredygtighedsmæssige effekter isoleret til brugen af antibakterielle suturer frem for konventionelle suturer vil, som nævnt ovenfor, kræve en nærmere analyse.

Det må antages, at eventuelle positive bæredygtighedseffekter i alt fald vil kunne opnås, hvis brugen af antibakterielle suturer isoleret set resulterer i 1) et fald i forbruget af antibiotika, 2) et fald i antal indlæggelsesdage pr. patient, 3) et fald i antal reoperationer.

**Bilag 1:** Opdateret infektionshygiejnisk vurdering af Plus Suturer®, Statens Serum Institut, 24. november 2024

**Bilag 2:** Plus Sutures for preventing surgical site infection, Medical technologies guidance Reference number: MTG59, National Institute for Health and Care Excellence, 28 June 2021

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[1] Plus Sutures for preventing surgical site infection, side 14, afsnit 4.4.

[2] Plus Sutures for preventing surgical site infection, side 14, afsnit 4.3.

# Opdateret infektionshygiejnisk vurdering af Plus Suturer®

CEI er blevet bedt om at opdatere den af CEI i 2010 udførte infektionshygiejniske vurdering af Plus Suturer af firmaet Johnson & Johnson. Baggrunden for, at der ønskes en opdatering, er dels udviklingen inden for området dels nye internationale anbefalinger vedr. anvendelse af triclosan-suturer samt nyere RCT-studier på området.
Vurderingen omfatter nu 3 forskellige suturtyper, der alle indeholder triclosan, nemlig Vicryl Plus, Monocryl Plus og PDS Plus.
Vurderingen er som tidligere baseret på: brugsanvisninger/brochurer på engelsk; gennemgang af relevant litteratur, herunder nyere internationale guidelines; opdateret miljøkemisk rapport fra Finland fra 2013 samt en EU-rapport om triclosan fra juni 2010.

## Generelt om triclosan

Triclosan er en klorholdig phenol med det kemiske navn 5-chloro-2-(2,4-dichlorophenoxy)phenol og formel $C_{12}H_7Cl_3O_2$.
Stoffet har i lighed med andre phenoler antibakterielle egenskaber, og det anvendes derfor i en lang række husholdningsprodukter såsom sæber, deodoranter, tandpasta, rengøringsmidler mm. (1,2,3).
Triclosan kan både virke biocidt og bakteriostatisk (1,2). Ved sædvanlige brugskoncentrationer virker det biocidt med flere angrebspunkter i mikroorganismers cytoplasma og membraner, hvorimod det i lavere koncentrationer virker bakteriostatisk og hæmmer bakteriers fedtsyresyntese og dermed dannelse af cellemembraner. For sidstnævnte findes en resistensmekanisme i flere bakterier, herunder *E. coli* og *S. aureus,* med udvikling af low-level resistens over for triclosan. Andre bakterier såsom *Pseudomonas aeruginosa* har medfødt resistens over for triclosan.
En bekymring - udover bakteriers udvikling af resistens over for selve stoffet - har været, om triclosan kan udvise krydsresistens til andre antimikrobielle midler (1,2).

## Miljøstyrelsens og EU-kommissionens rapporter, beslutninger og anbefalinger om brug af triclosan

Triclosanholdige suturer er medicinsk udstyr og derfor ikke omfattet af Biocidforordningen (4) eller Kosmetikforordningen (5), men derimod Forordningen om Medicinsk Udstyr (6), hvoraf det fremgår, at ”*Denne forordning har til formål at sikre et velfungerende indre marked for medicinsk udstyr med udgangspunkt i et højt sundhedsbeskyttelsesniveau for patienter og brugere… Denne forordning fastsætter samtidig høje standarder for medicinsk udstyrs kvalitet og sikkerhed for at imødegå fælles sikkerhedsbekymringer for så vidt angår sådanne produkter*.” (6).
Miljøstyrelsen blev af EU-kommissionen udpeget til at foretage en vurdering af triclosan, da alle aktivstoffer i desinfektionsmidler ifølge Biocidforordningen (4) skal godkendes på EU-niveau, og hvert land har derfor fået tildelt et antal aktivstoffer til vurdering. Miljøstyrelsens rapport og konklusion blev forelagt Kommissionen den 8. april 2013 og publiceret i 2015 (7). På baggrund af denne rapport har en Biocidal Product Commity under det Europæiske Kemikalie Agentur (ECHA) indstillet, at triclosan ikke kan godkendes på EU-niveau som biocid inden for produkttype 1 (PT1), dvs. produkter til humant brug såsom hud- og hånddesinfektion (8) med følgende begrundelse: ”Triclosan opfylder kriterierne for klassificering i henhold til forordning (EF) 1272/2008 som giftig for vandlevende organismer af akut kategori 1 og opfylder substitutionskriterierne i artikel 10. Derfor opfylder triclosan ikke betingelserne i artikel 28, stk. 2, for at tillade optagelse i bilag I til forordning (EU) 528/2012.” Endvidere har Kommissionen heller ikke godkendt triclosan under produkttype 2, dvs. produkter til desinfektion af overflader (9).
Miljøstyrelsen anbefaler desuden, at brugen af triclosan reduceres i sæbe, tandpasta og andre husholdningsprodukter, da det ikke er nødvendigt at anvende triclosan i disse produkter (3).

Ifølge konklusionen i EU-rapporten om triclosan fra 2010 (10) findes der ikke tilstrækkelig dokumentation for, at anvendelse af triclosan i kosmetiske produkter giver anledning til klinisk resistens og krydsresistens, men man anbefaler, at der foretages yderligere studier.

### Brugsanvisninger/brochurer

Oplysningerne i dette afsnit stammer fra de engelske brugsanvisninger/brochurer.
Der er 3 hovedtyper af Plus Suturer, der alle indeholder triclosan, men som hver især har særlige anvendelsesområder. Fordelen ved disse suturer frem for almindelige suturer er ifølge producenten, at de har antibakteriel effekt og derfor er i stand til at forhindre bakteriel kolonisering i og omkring suturen, hvorved postoperative sårinfektioner kan forebygges.
Det er absorberbare suturer, der i *in vivo* forsøg har vist sig at være af samme styrke som ikke-absorberbare suturer. Det antibakterielle spektrum omfatter følgende bakterier: *Staphylococcus aureus* (inkl. MRSA), *Staphylococcus epidermidis, Escherichia coli*, *Klebsiella pneumoniae og Enterobacter cloacae* (11).

**PDS Plus suturer** er indikeret til brug ved suturering af blødt væv, inklusiv anvendelse i pædiatrisk kardiovaskulært væv, hvor vævsvækst forventes at forekomme, samt ved oftalmisk kirurgi (bortset fra kontakt med hornhinde og sclera). PDS Plus suturer er ikke indikeret til kardiovaskulært væv hos voksne, heller ikke ved mikrokirurgi eller i neuralt væv. Disse suturer er særligt nyttige, hvor kombinationen af en absorberbar sutur og forlænget vævssupport (op til 6 uger) er ønskelig.
**MONOCRYL Plus suturer** er indikeret til brug i generel bløddelsapproximering og/eller -ligering, men er ikke egnet til brug i kardiovaskulært eller neurologisk væv, mikrokirurgi eller oftalmisk kirurgi.
**Coated VICRYL™ Plus suturer** er indikeret til brug ved generel bløddelsapproximering og/eller -ligering, undtagen i oftalmiske, kardiovaskulære og neurologiske væv.

### Anbefalinger vedr. anvendelse af triclosan-suturer i internationale retningslinjer

Der er nyere internationale retningslinjer, som anbefaler anvendelse af triclosan-suturer ved mange forskellige typer af operationer og ikke kun ved abdominalkirurgi, der tidligere var hovedindikationen.
CDC publicerede en retningslinje om forebyggelse af postoperative sårinfektioner i 2017 (12), og heri står: *Consider use of triclosan-coated sutures for the prevention of surgical site infections*.
I en retningslinje fra WHO fra 2018 med titlen:"Global guidelines for the prevention of surgical site infection" (13) findes følgende anbefaling vedr. triclosanholdige suturer: "*The panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of surgical site infections, independent of the type of surgery.*"
To nye guidelines fra UK National Institute for Health and Care Excellence (NICE) indeholder anbefalinger vedr. anvendelse af triclosan-suturer – den første er fra april 2019 og er en generel retningslinje for forebyggelse af postoperative sårinfektioner (14). Heri er følgende anbefaling vedr. lukning af sår: "*When using sutures, consider using antimicrobial triclosan-coated sutures, especially for paediatric surgery, to reduce the risk of surgical site infection.*
Den anden NICE-guideline er fra juni 2021 med titlen:"*Plus Sutures for preventing surgical site infection*" (15). Denne guideline omhandler således kun Plus suturer og har følgende hovedanbefaling: "*Evidence supports the case for adopting Plus Sutures as part of a bundle of care for preventing surgical site infection in the NHS for people who need wound closure after a surgical procedure when absorbable sutures are an appropriate option.*" Anbefalingen er baseret på 31 RCT-studier samt metaanalyser, der har vist en næsten 30% reduktion i risiko for postoperative sårinfektioner ved anvendelse af disse suturer.

### Nyere dokumentation for anvendelse af triclosan i suturer

Firmaet Johnson & Johnson har udarbejdet en oversigt over samtlige studier til og med 2021, hvor triclosanholdige suturer sammenlignes med suturer uden triclosan (16). Den omfatter bl.a. 38 RCT-studier, 17 metaanalyser/systematiske reviews samt 30 andre videnskabelige studier. Før 2010 var der kun få studier, og disse var hovedsageligt foretaget inden for abdominalkirurgien, men i de senere år er der publiceret en del studier inden for en række andre kirurgiske specialer, fx

hjertekirurgi, ortopædkirurgi og kirurgi på børn. Hovedparten af disse studier er ikke finansierede af sutur-producenter, og de viser, at der er en signifikant reduktion i postoperative sårinfektioner i størrelsesordenen 30% (15), når der anvendes triclosanholdige suturer sammenlignet med almindelige suturer uden triclosan.
En helt ny metaanalyse fra maj 2022 (17), der sammenlignede forekomsten af postoperative sårinfektioner efter operation med brug af triclosanholdige suturer versus almindelige suturer uden triclosan viste, at der ikke var nogen signifikant forskel på de to suturtyper. Denne metaanalyse, som opstiller en ny ikke valideret definition for højkvalitets RCT, er baseret på 5 RCT-studier, og studiet konkluderer, at anbefalingerne i internationale guidelines vedr. anvendelse af triclosanholdige suturer bør trækkes tilbage. Det er dog indtil videre den eneste metaanalyse, som ikke har kunnet påvise evidens for, at triclosanholdige suturer reducerer forekomsten af postoperative sårinfektioner mere end almindelige suturer uden triclosan. Yderligere stammer 61% af data i metaanalysen fra lav- og middelindkomstlande med meget høje infektionsrater (22%), som ikke kan generaliseres til det danske sundhedsvæsen.

## Anvendelse af triclosan i suturer ud fra et miljømæssigt perspektiv

Jukka Pellinen, miljøkemiker fra Helsingfors Universitet, har på foranledning af Johnson & Johnson foretaget en miljøkemisk vurdering af PDSPS i marts 2009 (18). Denne rapport konkluderer, at den mængde triclosan, der overføres fra suturtråd til patient er meget lille og ikke udgør helbredsmæssige risici for patienten. Hvad miljøforurening angår, så vil overskydende triclosan-suturmateriale efter en operation bortskaffes som klinisk risikoaffald eller restaffald, der bortskaffes ved forbrænding. Det anføres endvidere, at den mængde triclosan, der kan påvises i miljøet fortrinsvis stammer fra kosmetiske produkter. Rapporten konkluderede, at der hverken var helbredsmæssige eller miljømæssige problemer forbundet med anvendelse af disse suturer.
En anden rapport af samme miljøkemiker fra 2013 (19) havde til formål at undersøge de miljømæssige konsekvenser af antibiotika og triclosan i spildevand på fx alger og fisk. Konklusionen på denne rapport var, at koncentrationerne af antibiotika (anvendt til behandling af fx sårinfektioner) i spildevand var betydeligt højere end koncentrationerne af triclosan (anvendt i suturer). Ud fra en økologisk risikovurdering er det derfor mindre miljøbelastende at anvende triclosan-suturer til forebyggelse af postoperative sårinfektioner end at behandle postoperative sårinfektioner med antibiotika (som kunne have været undgået, hvis der havde været anvendt triclosanholdige suturer ved operationerne).

## Sammenfattende vurdering

Triclosan har haft udbredt anvendelse de sidste 30 år i diverse husholdningsprodukter, og i de senere år har flere miljøundersøgelser vist udbredt forekomst i naturen, hvilket er bekymrende, da man ikke fuldt ud kender til konsekvenserne for dyre- og planteliv. De senere år er anvendelsen af triclosan i Danmark dog reduceret til primært kosmetiske produkter, men også her er der set en nedgang i anvendelsen, så det kun forefindes i nogle få produkter som tandpasta og deodoranter (3).
For mennesker gælder den største bekymring udvikling af resistens i bakterier samt triclosans mulige krydsresistens med de antibiotika, vi anvender til behandling af infektioner hos mennesker. Det er vist, at triclosan kan inducere resistens i mange bakterier, men den kliniske betydning heraf er ikke endeligt afklaret. Det samme gør sig gældende mht. krydsresistens. Derudover har der været en bekymring for, om triclosan kunne være hormonforstyrrende, men dette er endnu ikke fuldt belyst. Ukritisk anvendelse af triclosan i sundhedssektoren bør undgås.
Af ovennævnte grunde bør anvendelsen af triclosan begrænses til nogle få veldefinerede områder, hvor det er vist, at det har en gavnlig effekt, og hvor miljøbelastningen er minimal, som fx suturer.

## Konklusion

På basis af ovenstående oplysninger fra firmaet, rapporter, internationale retningslinjer og nyere RCT-studier samt metaanalyser, kan CEI konkludere, at

- triclosan har antibakteriel effekt over for især stafylokokker og *E. coli,* og siden seneste CEI-vurdering fra 2010 har nyere RCT-studier og metaanalyser inden for en række

kirurgiske specialer vist signifikant færre postoperative sårinfektioner ved anvendelse af disse suturer sammenlignet med almindelige suturer uden triclosan.

- internationale retningslinjer for forebyggelse af postoperative sårinfektioner, herunder NICE-guideline fra 2021, anbefaler anvendelse af triclosanholdige suturer som led i en generel "bundle of care" for at forebygge postoperative sårinfektioner.
- koncentrationerne af triclosan i de triclosanholdige suturer til humant brug er meget små og derfor ikke udgør nogen helbredsmæssig risiko for den enkelte patient.
- triclosan anvendt i suturer ikke udgør en miljømæssig belastning, da koncentrationerne i spildevand er meget små.

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NICE National Institute for Health and Care Excellence

NICE guidance

# Plus Sutures for preventing surgical site infection

Medical technologies guidance
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www.nice.org.uk/guidance/mtg59

# Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

# Contents

This guidance replaces MIB204.

# 1 Recommendations

1.1 Evidence supports the case for adopting Plus Sutures as part of a bundle of care for preventing surgical site infection in the NHS for people who need wound closure after a surgical procedure when absorbable sutures are an appropriate option.

1.2 Cost modelling shows that Plus Sutures is cost saving compared with non-triclosan absorbable sutures by an average of £13.62 per patient. These savings are from reduced surgical site infections. Cost savings will vary by surgery type and baseline risk of surgical site infection. For more information on the cost impact to the NHS please see the NICE resource impact summary report.

**Why the committee made these recommendations**

Plus Sutures is a range of synthetic, absorbable sutures with triclosan (Irgacare MP), a purified medical grade antimicrobial.

Clinical evidence shows that using Plus Sutures instead of standard absorbable sutures reduces the chance of a surgical site infection.

Even though Plus Sutures is more expensive than standard sutures, cost analyses show that it still leads to cost savings because of the reduction in surgical site infections.

# 2 The technology

## Technology

2.1 Plus Sutures (Ethicon, Johnson & Johnson Medical) is a range of synthetic, absorbable sutures that are either impregnated with or coated with triclosan (Irgacare MP), a purified medical grade antimicrobial, depending on the suture type. Absorbable sutures are absorbed by tissue over a period of time and do not need removing. The 3 sutures considered in this evaluation are indicated for general soft tissue approximation and ligation. Each has different physical properties and absorption rates, which affects which tissue types it is best suited to:

- Coated VICRYL Plus Antibacterial (polyglactin 910) Suture is a multifilament suture (multiple braided threads). VICRYL Plus retains 75% of its original tensile strength at 2 weeks after implantation; 40% to 50% at 3 weeks and 25% at 4 weeks. Complete absorption happens between 57 days and 70 days.

- MONOCRYL Plus Antibacterial (poliglecaprone 25) Suture is a monofilament suture (solid and smooth thread). MONOCRYL Plus retains 50% to 60% of its original tensile strength at 1 week and 20% to 30% at 2 weeks. Complete absorption happens between 91 days and 119 days. This suture is also available in a barbed design for knotless suturing (STRATAFIX Plus) but this version of the technology was not included in the evaluation.

- PDS Plus Antibacterial (polydioxanone) Suture is a monofilament suture (solid and smooth thread). PDS Plus Antibacterial retains 60% to 80% of its original tensile strength at 2 weeks, 40% to 70% at 4 weeks, and 35% to 60% at 6 weeks. Complete absorption happens between 182 days and 238 days. This suture is also available in a barbed design for knotless suturing (STRATAFIX Plus) but this version of the technology was not included in the evaluation.

  PDS Plus and MONOCRYL Plus contain no more than 2,360 micrograms/metre triclosan. VICRYL Plus has a coating of copolymer and calcium stearate as well as up to 472 micrograms/metre triclosan. The absorption rates and handling

properties are the same as non-triclosan sutures.

# Innovative aspects

2.2 Plus Sutures is innovative because sutures are coated or impregnated with triclosan (Irgacare MP). Triclosan is a broad-spectrum antibacterial agent. It helps reduce biofilm formation and bacterial colonisation, preventing the growth of most common organisms associated with surgical site infection for at least 7 days. Plus Sutures is already used in the NHS.

# Intended use

2.3 Plus Sutures would replace using non-triclosan absorbable sutures for wound closure in people that have had a surgical procedure, when absorbable sutures are an appropriate option. Plus Sutures should be used as part of a locally agreed bundle of care to reduce surgical site infections. Clinical experts reported that the handling properties of Plus Sutures were identical to non-triclosan sutures. Adopting Plus Sutures would not alter the current care pathway or need any additional training. The technology is already used extensively within the NHS.

# Costs

2.4 The cost of Plus Sutures is around £4.25 per suture, based on average prices of the 3 suture types.

For more details, see the Johnson & Johnson webpage on Plus Sutures.

# 3 Evidence

NICE commissioned an external assessment centre (EAC) to review the evidence submitted by the company. This section summarises that review. Full details of all the evidence are in the project documents on the NICE website.

## Clinical evidence

### The clinical evidence comprises 31 randomised controlled trials

3.1 The evidence assessed by the EAC included 31 randomised controlled trials including over 14,000 people. For full details of the clinical evidence, see section 3 of the assessment report in the supporting documentation on the NICE website.

### The evidence for reducing surgical site infection incidence is of good quality

3.2 The evidence base for Plus Sutures is extensive, of relatively high quality and is generalisable to the UK NHS. The EAC used the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology for appraising the quality of evidence for each outcome and said that the quality of evidence for surgical site infection incidence was high. This was considered the most important outcome and was reported by nearly all the included studies, with most of them using the same definition. None of the other outcomes listed in the scope had sufficiently robust empirical evidence to show Plus Sutures was statistically superior to standard sutures. However, some other outcomes can be inferred or extrapolated from the established reduction in incidence of surgical site infection, such as a shorter hospital stay, and lower readmission rates and healthcare costs. The EAC concluded that Plus Sutures use is associated with a causative reduction in the incidence of surgical site infection.

### Device-related adverse events reported in the evidence suggest

## using Plus Sutures is safe

3.3 To assess device-related adverse events, the EAC reviewed the randomised controlled trial data included in the assessment and also did a dedicated literature review to assess the nature of adverse events after using Plus Sutures. Studies that reported adverse events included 18 of the randomised controlled trials that were included in the assessment and an additional 17 randomised and non-randomised studies. Triclosan allergy was noted in a published case report that referenced a retrospective analysis of 113,162 patients who had been patch tested with triclosan 2% petroleum. A positive reaction was seen in only 363 patients (0.32%) but 54% of positive reactions were considered clinically relevant. The EAC concluded that there is no discernible safety signal from using Plus Sutures. The EAC noted that this conclusion was supported by information from the company (on the very low amounts of triclosan used in the sutures and on the rapid metabolism of triclosan) and by the clinical experts, who had not seen any cases of triclosan reactions. For full details of the adverse events, see section 6 of the assessment report in the supporting documentation on the NICE website.

## Results of company meta-analyses show that Plus Sutures is associated with a 30% reduction in the risk of surgical site infection

3.4 The company did 6 de novo meta-analyses to establish the overall pooled effect size associated with Plus Sutures on the incidence of surgical site infections. The primary outcome was the relative risk of developing a surgical site infection between Plus Sutures and control groups. The 6 separate meta-analyses were done using:

- all studies that provided enough data (base case, 28 studies)
- a subset of studies in adults (25 studies)
- a subset of studies in children (2 studies)
- a subset of studies in patients with clean wounds (15 studies)

- a subset of studies in patients with non-clean wounds (12 studies)
- all studies of Plus Sutures including STRATAFIX Plus that provided enough data, as a sensitivity analysis (31 studies).

  The results of the meta-analyses showed that Plus Sutures is associated with a nearly 30% reduction in the risk of surgical site infection in the base case and all results were considered statistically significant (with a 95% confidence interval of 0.59 to 0.85). The EAC noted that the company meta-analyses are of a high quality and at a low risk of bias. The methodology and results are transparent and clearly reported.

## The EAC did additional meta-analyses

3.5 The EAC validated the company's meta-analyses by replicating the analysis, and did 3 additional analyses. The EAC noted that because of heterogeneity the studies were not similar enough for fixed effects analysis, and the analysis should primarily be reported using a random effects model. However, this variation had minimal effects on the results. The additional analyses included stratifying the evidence by study quality, sample size and location. The results of the additional analyses indicated that Plus Sutures reduced the risk of surgical site infection, but the size of the effect appeared to be related to study quality and sample size. When only high-quality studies were included in the analysis the difference was not statistically significant. However, the EAC advised that this should be interpreted with caution because the smaller sample sizes and varied event rates will affect the precision and impact of the analysis.

## The company submitted additional analyses suggesting sustainability benefits

3.6 Based on the Sustainable Care Pathways Guidance, the company provided an analysis of the environmental impact of surgical site infections to NHS England. Environmental impact is presented in the guidance document in terms of 3 main environmental metrics: greenhouse gas emissions, fresh water use and waste generation. The report indicates that by preventing surgical site infections, using Plus

Sutures results in potential environmental benefits to the NHS in England.

# Cost evidence

## The company identified 8 economic studies

3.7 The company identified 8 studies that were relevant to the economic submission. The EAC concluded that the literature search was satisfactory and agreed that the 8 studies were relevant to the evaluation. The company said that all of the studies reporting on introduction of Plus Sutures resulted in cost savings but that none of the parameters in the company's de novo model were informed by the economic literature. For full details of the cost evidence, see section 9.1.2 of the assessment report in the supporting documentation on the NICE website.

## The company's model structure and time horizon are appropriate

3.8 The company submitted a simple decision tree which models a population of adults and children who need wound closure after a surgical procedure. The model assesses the cost of wound closure plus the cost of treatment for people who develop a surgical site infection. An additional branch of the decision tree modelled the mortality of people with a surgical site infection and was used by the company to calculate a cost per death avoided using cost-effectiveness methodology. The EAC considered the model structure to be appropriate, except for the mortality branch of the decision tree which complicates the model for the purposes of a cost-consequence modelling approach. The time horizon modelled was 1 year. The EAC noted that this aligns with published economic evaluations of Plus Sutures.

## The EAC accepted all assumptions in the company model

3.9 The company model made the following assumptions:

- Risk of surgical site infection relates only to those detected and treated during the initial inpatient episode or on readmission.

- The average surgical site infection episode cost does not include the cost of treating surgical site infections in the community.
- The risk of infection with Plus Sutures is calculated by applying the relative risk of surgical site infection associated with using Plus Sutures reported in the meta-analyses to a baseline risk of surgical site infection. The baseline risk of surgical site infection is based on UK data.
- Adverse events were not included in the model.

  The EAC concluded that the model assumptions were appropriate, conservative and supported by the evidence.

## The EAC made some minor changes to the costs of the technology

3.10 The company provided an estimate of the cost of Plus Sutures based on a weighted average of sales, including knotless, barbed sutures, and STRATAFIX Plus. The EAC reported that the company's estimation of the cost was not sufficiently transparent or reproducible, and included STRATAFIX Plus, which the EAC did not include in their analysis. The EAC amended the cost of the technology by calculating a mean cost of £3.63 to £4.94 depending on Plus Suture type.

## The EAC's changes to the model have a minimal effect on results

3.11 Because there were so few changes to the model parameters the EAC and the company's results were similar. In the EAC's base-case analysis Plus Sutures was found to be cost saving by a mean of £13.62 per person compared with the company's £13.88 per person.

## The company's extensive sensitivity analyses suggest that using Plus Sutures is cost saving

3.12 The company reported results of a 1-way deterministic sensitivity analysis that showed that the model was most sensitive to changes in the incidence of surgical site infection. However, the model was still cost saving even when the lowest plausible surgical site infection incidence was used (0.5%). Two-way deterministic sensitivity analyses were used

to explore the combined effect of surgical site infection incidence and relative risk, and surgical site infection incidence and cost of surgical site infection. The results were cost saving in all cases. This was further supported by threshold analyses that reported the following break-even points (deemed by the company and the EAC to be unlikely or implausible):

- a cost of surgical site infection of less than £1,410
- incidence of surgical site infection of less than 0.24%
- a relative risk of 0.93
- at least 21 sutures.

The results of the probabilistic sensitivity analysis, reported for the base case only, showed that Plus Sutures was cost saving in 99.8% of iterations (out of 1,000 iterations). The summary result was that Plus Sutures was associated with cost savings of £13.96 (95% credible intervals £4.97 to £22.22) per person.

## Plus Sutures remains cost saving in the EAC's additional sensitivity analyses

3.13 The EAC did additional sensitivity analyses that explored the uncertainty in the cost savings associated with each subgroup (adults, children, clean wounds and non-clean wounds) and the effect of different relative risk values reported in the EAC's meta-analyses of the clinical evidence (study quality, sample size and location). Plus Sutures was cost saving in all subgroups investigated. The most uncertainty was in the clean wound subgroup (£9.30; 95% credible intervals -£2.24 to £19.26; 94.6% probability of cost saving). The meta-analysis showed that the size of the effect of using Plus Sutures (lowering the risk of surgical site infection) diminished when only studies of a high quality, or large sample size, were included in the analysis (see section 3.5). The sensitivity analyses showed that using Plus Sutures remains cost saving when the relative risk from the higher quality studies and studies with larger samples sizes was adopted, but there was more uncertainty in the results.

# 4 Committee discussion

## Clinical-effectiveness overview

### The evidence shows that Plus Sutures is effective in reducing the incidence of surgical site infection

4.1 The evidence base for Plus Sutures is large, of relatively high quality and is likely to be generalisable to the NHS. Some of the individual studies did not show a significant reduction in surgical site infection incidence for Plus Sutures. However, when all results were combined in the meta-analyses, the effect was significant. Additional analyses done by the external assessment centre (EAC) showed that the size of effect was smaller when studies were stratified by quality or sample size. But it was not possible to determine if this was because of the effect measured in the studies or because of the small number of studies included in the analyses. The committee concluded that, although the effect size may vary depending on population and type of procedure, the evidence showed that Plus Sutures is likely to lead to overall reductions in surgical site infections.

## Side effects and adverse events

### Using Plus Sutures is safe and allergies to triclosan are very rare

4.2 No significant device-related adverse events were identified from the published evidence. The clinical experts noted that triclosan is safe and is used in many consumer products, at much higher concentrations and amounts than in Plus Sutures. None of the clinical experts had encountered anyone who had an allergic reaction to triclosan in Plus Sutures. The committee concluded that using Plus Sutures is safe and that adverse or allergic reactions to triclosan are likely to be very rare. The committee discussed antimicrobial stewardship considerations and concluded that neither the product nor concentration of triclosan raised

concerns about resistance.

# Equality considerations

## Surgeons consider a number of factors when choosing the appropriate suture

4.3 The committee discussed equality considerations for the use of Plus Sutures in the general population. The instructions for use highlight that 'absorbable sutures, including Plus Sutures may not be appropriate for older people, those who are malnourished, debilitated or have conditions that may prevent wound healing'. The clinical experts explained that a number of factors must be taken into consideration by the surgeon choosing the suture, including comorbidities, surgery type, tissue type and condition. The committee concluded that these were factors that surgeons would consider within the patient assessment for appropriate management plans. It did not consider there to be any equality issues as a result of its recommendations.

# Relevance to the NHS

## Plus Sutures should be used as part of a bundle of care to reduce surgical site infections

4.4 The clinical experts noted that, in their experience, Plus Sutures was most effective at reducing infections in deep and superficial tissue layers, rather than deep organ space tissues. However, the experts stated that while using Plus Sutures has been shown to reduce surgical site infection risk, to maximise their effect, they should be used alongside an appropriate care bundle for surgical site infection prevention, including antibiotic use, appropriate hair removal, glycaemic control and normothermia. The clinical experts reported their experience that introducing Plus Sutures to the surgical site infection prevention care bundle had resulted in fewer surgical site infections. The committee concluded that Plus Sutures should be used as part of a bundle of care to reduce surgical site infections.

# NHS considerations overview

## GPs with minor surgery clinics may also benefit from using Plus Sutures

4.5 The evidence on Plus Sutures was from hospitals. However, the committee noted that some GP clinics provide minor surgery services and use broadly the same care bundles for infection prevention as used in hospitals. The committee stated that the evidence collected in secondary care is likely to be largely generalisable to primary care settings. The committee concluded that Plus Sutures could be considered in GP minor surgery clinics.

# Training

## No additional training is needed to use Plus Sutures

4.6 The clinical experts advised that no further training is needed to use Plus Sutures compared with non-triclosan sutures. The addition of triclosan does not change the absorption profile when identifying the appropriate suture or change the handling of the suture itself. Clinical experts reported that the handling properties of Plus Sutures were identical to non-triclosan sutures and no modification of existing procedures is needed. The committee concluded that adopting Plus Sutures would not need a change to services.

# Cost-modelling overview

## The EAC's changes to the cost model are appropriate

4.7 The committee noted that the EAC made minor changes to the cost model, which were appropriate and accepted. The committee concluded that the comprehensive subgroup and sensitivity analyses supported cost savings in all subgroups.

# Main cost drivers

## Reduction in surgical site infection incidence is the main cost driver in the model

4.8 The committee discussed the estimated cost of surgical site infections and accepted the use of a UK study, which reported the cost savings associated with surgical site infections in hospitals (Jenks et al. 2014). Reduction in surgical site infection was the main driver for the cost savings. The committee concluded that the cost savings were likely to be realised in practice and were supported by the evidence and experience of the clinical experts.

# Scenario analyses

## Plus Sutures is cost saving in all likely scenarios

4.9 The committee discussed the comprehensive scenario analyses completed by the company and EAC, which showed Plus Sutures reduced the risk of surgical site infections in most scenarios. It accepted that results from the subgroups in which statistical significance was reduced should be interpreted with caution because the smaller sample sizes affect the analysis. The committee concluded that Plus Sutures is likely to save costs in most scenarios and that the scenarios at which costs break even are clinically unlikely.

# Cost savings

## The true cost of treating surgical site infections in the community is likely to be underestimated

4.10 The committee discussed the potential for further cost savings in the community as a result of fewer hospital-acquired surgical site infections and therefore less need for follow-up care, which was not captured in the economic model. The committee agreed with the company and the EAC

that the cost savings in the cost modelling are likely to be conservative.

## Plus Sutures is likely to be cost saving across all groups

4.11 The committee was satisfied that the cost-modelling evidence indicates that Plus Sutures is cost saving compared with non-triclosan absorbable sutures by an average of £13.62 per patient. The committee concluded that the sensitivity analyses showed that Plus Sutures remained cost saving across all subgroups.

# 5 Committee members and NICE project team

## Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technologies advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

## NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more health technology assessment analysts (who act as technical leads for the topic), a health technology assessment adviser and a project manager.

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