Input from external experts and manufacturer on the **2nd draft assessment - "Antibacterial-coated sutures versus non-antibacterial-coated sutures for the prevention of abdominal, superficial and deep incisional, surgical site infection"** - with author's replies

EUnetHTA JA3 WP4 - Other technologies

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February 2017

Content

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Comment from *Insert your name and organisation*	**Page number** *Insert 'general' if your comment relates to the whole document*	**Line or section number**	**Comment and suggestion for rewording** *Please insert each new comment in a new row.*	**Character of comment** • 'major'[a] =1 • 'minor'[b] = 2 • 'linguistic'[c] =3 *Please indicate your choice by writing the according number in this field, e.g. for major choose "1".*	**Author's reply**
			GENERAL		
Stephan Kriwanek, Austria			There are many repetitions in the text, but this may be due to the required format.		Thank you, we tried to avoid any repetitions, but some are related to the required predifened format of the assessment report.
Stephan Kriwanek, Austria			In summary I understand that a meta-analysis has the intention to follow other analyses and the recommendation of the WHO and the CDC. The problem with triclosan coated sutures is the minor quality of many studies and the fact, that the best study performed until now by Diener could not demonstrate a beneficial effect.		Thank you for your comments. We provided new SR and MA based on request of national decision-maker (please see the Project plan also); scientific conclusion were made according available studies results with appropriate explanation on risk of bias and data quality. Each national HTA doer and decision maker will make their own reccomendations and final decision.

Johnson & Johnson Medical			All braided (multi-filament) suture materials are coated with various material in order to make the suture smoother and allow it to be dragged through tissue and to tie down the knots. For this reason, we suggest modifying in the document *"noncoated"* to *"non-antibacterial coated".*	1	Accepted. Change made.
			Summary		
Stephan Kriwanek, Austria	16	214-218	PDS plus indications: include laparotomy closure		We listed indications according the Instructions for use: „INDICATIONS: PDS Plus Antibacterial sutures are indicated for use in soft tissue approximation, including use in pediatric cardiovascular tissue where growth is expected to occur and ophthalmic surgery (other than contact with cornea and sclera). PDS Plus Antibacterial suture is not indicated in adult cardiovascular tissue, microsurgery, and neural tissue. These sutures are particularly useful where the combination of an absorbable suture and ex tended wound suppor t (up to six week s) is desirable.“
Stephan Kriwanek, Austria	17	248	Change "the majority" to " a relevant number" of SSIs are preventable		Accepted. Change made. Thank you.

Ivana Mareković, Croatia	14	140,141	The title "Summary of relative effectiveness of triclosan-coated sutures" is not adequate since the title of the whole draft includes the term "antibacterial-coated sutures". Maybe the title should be reconsedered as there are no RCT for antibacterial-coated sutures other than those coated with triclosan.	2	Accepted. Change made. Thank you.
Ivana Mareković, Croatia	14	144	Not only prevention of incisional but also prevention of deep surgical site infections is evaluated.	2	No, only superficial and deep incisional SSIs were evaluated, please see the precise Title also.
Johnson & Johnson Medical	14	160-162	Presenting the technology, we believe it is important to clarify the mechanism of action of Triclosan coated sutures and the zone of inhibition according what is reported in the IFU. Therefore, we suggest rewording the following: "*By providing an area of 10-20 mm around the suture, triclosan prevents bacterial growth which prevents bacterial growth which is commonly associated with SSI development. The duration of the zone of inhibition in vitro can last up to 23 days,…."* Proposed rewording: *"Triclosan prevents/reduces colonization of the suture by bacteria commonly associated with SSI development. In vitro studies have shown that triclosan coated sutures placed in an agar plate create a zone of inhibition,which can last up to 23 days. Furthermore, in animal studies the antibacterial sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria."* (IFUs)	1	Accepted. Change made. Thank you.
Johnson & Johnson Medical	15	183-184	The statement is applicable to all absorbable sutures: we suggest adding "as with all absorbable suture"	1	Accepted. Change made. Thank you.

Johnson & Johnson Medical	19	293	Even though the WHO recommendation is conditional and with moderate quality of evidence, there are no higher pre/perioperative recommendations in the guidelines than this. We suggest completing the paragraph giving this additional information.	2	Thank you, but we only presented the facts.
Johnson & Johnson Medical	28	536	The source of evidence should be explicitly clarified in the conclusion section. For this reason, we suggest adding the following statement: "All the clinical data assessed in this report are related to Triclosan coated sutures. No published clinical studies have been identified on chlorhexidine-coated sutures"	1	Accepted. Change made. Thank you.
Johnson & Johnson Medical	28	543	Even though relative safety of triclosan coated suture could not be confirmed due ot a lack of reporting of AEs in RCTs and non-RCTs included in the assessment, it should also be recognised that there is a great deal (over 10 years) of clinical experience with triclosan coated sutures. Within that context, Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures. We remain confident in the medically appropriate use of antibacterial sutures and need for this product. Proposed rewording*"Even though relative safety of triclosan coated suture could not be confirmed from the AEs reported in the RCTs and non-RCTs included in our assessment, 10 years since the launch ,Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures ."*	1	We reformulated the text in: "The relative safety of triclosan-coated sutures could not be confirmed due to a lack of reporting of AEs in RCTs and non-RCTs included in our assessment. The same is true for chlorhexidine-coated sutures because no clinical studies were found during our literature search. Ten years after the launch, the manufacturer Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures."
Description and technical characteristics of the technology					

Stephan Kriwanek, Austria	46	796	Vicryl plus is not effective against E.coli and K.pneumonia while Monocryl plus and PDS plus are effective. This is not easy to understand as all materials include Triclosan as anti-infective agent.		Triclosan coated sutures: Vicryl Plus, Monocryl Plus and PDS Plus contain different concentrations of Irgacare (triclosan). Monocryl Plus and PDS Plus sutures contain 2360µg/m while Vicryl Plus contains 275 µg/m. List of microrganisms which are inhibited by the sutures according to the results of the zone inhibition test are listed in the Instructions for use of each suture and the same antibacterial effect was listed in the table from the evidence submission file given by manufacturer (Johnson and Johnson).
Johnson & Johnson Medical	45	773-775	In the description of the technology, we believe It is important to clarify the mechanism of action of Triclosan coated sutures and the zone of inhibition according what is reported in the IFU. Therefore, we suggest rewording the following: "*By providing an area of 10-20 mm around the suture, triclosan prevents bacterial growth which prevents bacterial growth which is commonly associated with SSI development. The duration of the zone of inhibition in vitro can last up to 23 days,…."* Proposed rewording: *"Triclosan prevents/reduces colonization of the suture by bacteria commonly associated with SSI development. In vitro studies have shown that triclosan coated sutures placed in an agar plate create a zone of inhibition, which can last up to 23 days. Furthermore, in animal studies the antibacterial sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria."* (IFUs)	1	Accepted. Change made. Thank you.

Johnson & Johnson Medical	47	815	We suggest clarifying the mechanism of action adding a missing information, as reported in the IFU *"Furthermore, in animal studies Vicryl Plus sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria"* (IFU)	2	Accepted. Change made. Thank you.
Johnson & Johnson Medical	47	842	We suggest clarifying the mechanism of action adding a missing information, as reported in the IFU: *"Furthermore, in animal studies Monocryl Plus sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria"* (IFU)	2	Accepted. Change made. Thank you.
Johnson & Johnson Medical	48	855	We suggest clarifying the mechanism of action adding a missing information, as reported in the IFU: *"Furthermore, in animal studies PDS Plus sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria"* (IFU)	2	Accepted. Change made. Thank you.
Johnson & Johnson Medical	52	948	This paragraph presents the comparators: we suggest removing *"coated"* to avoid confusion.	1	Accepted. Change made. Thank you.
Johnson & Johnson Medical	53	993	The papragraph mentions Triclosan coated suture but the reference in the parenthesis is "*Assufil Plus- instruction for use"*: please modify it with *"Vicryl Plus, Monocryl Plus, PDS Plus-Instruction for use"*	1	Accepted. Change made. Thank you.

Johnson & Johnson Medical	54	1011-1013	The relevance and applicability of this statement extracted from the WHO guidelines is questionable: First, the report quotes the first half of a paragraph from the WHO report, thus removing the broader context from the WHO report. In the EUnetHTA report it is positioned as a stand-alone paragraph. Interestingly the authors have decided to exclude any positive perspectives from the WHO statement. Second, and more relevant, this text is within the reimbursement section of the report. Without prejudice, we feel this section is out of scope. However, the authors quote the WHO statement "*Moreover, the availability of antimicrobial-coated sutures is limited in low and middle 1009 income countries*". Given we indicated our technology is available throughout the EU we request the authors clarify which LMICs they are specifically referencing. Triclosan coated sutures have been available within the EU for over 10 years. Third, quoting that "sutures are expensive in general" – is not contextualised, nor evidence-based. We believe this comment to be out of scope for an REA, and unsubstantiated within the context of the report. Expensive compared to the cost of the total surgery? The cost of a day in in hospital? the cost of other wound closure option such as glue? Overal, we consider this paragraph is out of scope: the aim of this report is to perform a Relative Effective Assessment for EU members: any economic consideration, including price, should be excluded from this report. We suggest removing this paragraph.	1	Accepted. Change made. Thank you.

Johnson & Johnson Medical	54	1039-1040	Several studies assessed the bacterial resistance to Triclosan: there is not sufficient evidence to support claims of antibiotic resistance or bacterial resistance to triclosan in patients. We suggest adding the following references to the report: *Gilbert P, and McBain AJ. Literature-Based Evaluation of the Potential Risks Associated With Impregnation of Medical Devices and Implants With Triclosan. Surg Infect J. 2002;3(suppl 1):S55-S64; Goodfellow G, Lee-Brotherton V, Daniels J, Roberts A, Nestmann E. (2003) Antibacterial resistance and triclosan. Society of Toxicology Annual Meeting, Salt Lake City, UT; Aiello AE, Marshall B, Levy SB, et al. Relationship between triclosan and susceptibility of bacteria isolated from hands in the community. Antimicrob Agents Chemother 2004;48:2973-2979*	1	Text was reformulated and references added, thank you.
			Health problem and current use		
Stephan Kriwanek, Austria	64	1416	"contamination of suture materials appears to be one of the most frequent causes of SSI" This could mean that the materials we implant are not sterile. I would therefore suggest to change the sentence to "intra or postoperative contamination of suture materials…."		Accepted. Change made. Thank you.
Stephan Kriwanek, Austria	71	1683	"the cost of treating superficial SSi is relatively low" This is not what we experience. Patients may need many treatments and even underpressure therapy. I would suggest to give numbers or change the sentence to "relatively low when compared to intra-abdominal infections"		Accepted. Change made. Thank you.

Johnson & Johnson Medical	84	2266	Please add a footnote to the table stating it is not appropriate to compare procedure volume year by year: Proposed statement *"the table provides a general indication of the volume of procedures across Europe. Year on year comparison cannot be done because the mix of country providing data varies."* Apologies for missing it in our submission.	1	Text was reformulated according the original report: "The table provides a general indication of the volume of procedures across Europe. The extent to which this is performed is influenced by a number of factors: the size of the population, the incidence of the underlying disease, differences in medical practices between countries and the availability of financial and human resources."
Johnson & Johnson Medical	87	2362	Modify *"sit"* to *"site"*	3	Accepted. Change made. Thank you.
Johnson & Johnson Medical	87	2366	Add *"of"* between *"adherence"* and *"bacteria"*	3	Accepted. Change made. Thank you.
			Clinical effectiveness		

Stephan Kriwanek, Austria	111	2858	"mass closure was associated with lower incidence of incisional hernia" This meta-analysis is outdated. The technique that is recommended today is the "small bite " technique.		Thank you for your comment: We transparently provided literature data, data from evidence-based resources like UpTodate and then specifies that "Principles of abdominal wall closure and recommendations could be found in different literature sources." In European Hernia Society guidelines on the closure of abdominal wall incisions (Muysoms et al. Hernia. 2015;19(1):1-24), for many key questions only weak reccomendations or no recommendation was made due to lack of sufficient evidence (weak reccomendation was given for "small bites technique" also). An update is planned for 2017.
Johnson & Johnson Medical	108	2730	Remove *"just"*	3	Accepted. Change made. Thank you.
Johnson & Johnson Medical	109	2754	Modify *"Dienere"* with *"Dienier"*	3	Accepted. Change made. Thank you.
			Safety		

Johnson & Johnson Medical	119	3008	Even though relative safety of triclosan coated suture could not be confirmed due ot a lack of reporting of AEs in RCTs and non-RCTs included in the assessment, Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures. We remain confident in the medically appropriate use of antibacterial sutures and need for this product. Proposed rewording: *"Even though relative safety of triclosan coated suture could not be confirmed from the AEs reported in the RCTs and non-RCTs included in our assessment, 10 years since the launch, Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures."*		Please see answer already provided above, on page 5, thank you.
Johnson & Johnson Medical	120	3054	Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures. We remain confident in the medically appropriate use of antibacterial sutures and need for this product. Proposed rewording suggested to follow *"In conclusion, the RCTs and non-RCTs were not sufficient to answer the questions related to relative safety due to the fact that little evidence was identidied on the potential harms of triclosan coated sutures. However, 10 years since the launch, Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures.*		Please see answer already provided above, on page 5, thank you.
			Potential ethical, organisational, pateint and social and legal aspects		
Ivana Mareković, Croatia	122	3079	Research questions, results and discussion for "Potential ethical, organiational, patient social and legal aspects" is not completed.		Results and discussion section were merged and only brief answers were provided. HTA doers on national levels could go in detailes if needed.

Johnson & Johnson Medical	122	3086-3087	Several studies assessed the bacterial resistance to Triclosan: there is not sufficient evidence to support claims of antibiotic resistance or bacterial resistance to triclosan in patients. We suggest adding the following references to the report: Gilbert P, and McBain AJ. Literature-Based Evaluation of the Potential Risks Associated With Impregnation of Medical Devices and Implants With Triclosan. *Surg Infect J.* 2002;3(suppl 1):S55-S64; Goodfellow G, Lee-Brotherton V, Daniels J, Roberts A, Nestmann E. (2003) Antibacterial resistance and triclosan. Society of Toxicology Annual Meeting, Salt Lake City, UT; Aiello AE, Marshall B, Levy SB, et al. Relationship between triclosan and susceptibility of bacteria isolated from hands in the community. *Antimicrob Agents Chemother* 2004;48:2973-2979	1	Text is reformulated and references added.
			References		
Ivana Mareković, Croatia	123	Line 3100	Reference list is not formatted.		Reference list will be formated at the end of assessment process, in the final version of the document.
			Appendix		
			No comments received.		Not applicable.