National Institute for Health and Care Excellence

Guideline - LARC
Guideline Consultation Table
Consultation 11th June 2014 -9th July 2014

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Royal College of General Practitioners (RCGP)	1	Addendum	General	General	I have only read sections 1, 2 and 3 as the summary of the guideline addendum	Thank you. Noted.
SH	Merck Sharp & Dohme Ltd (MSD)	1	Addendum	General	General	Thank you for the opportunity to consult on the addendum, which represents the proposed replacement of the current Chapter 7: Progestogen-only subdermal implants (POSDIs) in the full version of clinical guideline 30 (Ref 1). We note that the addendum that is proposed to replace chapter 7 is the only document subject to consultation. During a stakeholder consultation phase of a standard guideline update (as opposed to a rapid update), all versions of the guideline are made available for stakeholder review (i.e. full version and NICE version). We note than in this instance the proposed replacement text concerning the implant for the NICE version of CG30 (Ref 2) is not available for consultation; consequently we are unable to comment on any potential wording which may be subsequently published in an updated version of NICE guideline CG30. Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014] Ref 2: NICE (2005) NICE Clinical guideline 30 Long-acting reversible contraception. October 2005 (Available at: https://www.nice.org.uk/guidance/cg30/resources/guidance-longacting-reversible-	Thank you. The NICE version will be updated and published alongside the addendum. The guidelines update process is currently a pilot process, and it is the intention to make the NICE version available for consultation for some future guideline updates, before deciding whether or not a NICE version of the guideline will be routinely available for consultation.

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						contraception-pdf) [Accessed 25 June 2014]	
SH	Digital Assessment Service, NHS Choices	1	Addendum	General	General	No comments on the consultation. Welcome the advice.	Thank you
SH	Royal College of Paediatrics and Child Health (RCPCH)	1	Addendum	General	General	Thank you for inviting the Royal College of Paediatrics and Child Health to comment on the Long Acting Reversible Contraception addendum consultation. We have not received any responses for this consultation.	Thank you
SH	Primary Care Women's Health Forum	1	Addendum	General	General	The PCWHF members are satisfied with this addendum and had no recommendations to make. We are supportive of this work.	Thank you
SH	NHS England	1	Addendum	General	General	Thank you for the opportunity to comment on the draft scope for the above clinical guideline. I wish to confirm that NHS England has no substantive comments to make regarding this consultation.	Thank you
SH	Bayer Plc	1	Addendum	1.1	6	The recommendations included in the addendum appear to relate exclusively to the information that should be given to women, whereas the previous guideline also covered 'other issues to consider before fitting an implant' e.g. specific groups, medical conditions and contraindications, 'practical details of fitting implants' and 'follow-up and managing problems'. It is not clear why these other areas of the guideline have not been updated. We suggest that if previous recommendations are not updated, guideline users are referred to an appropriate source of information for these issues.	Thank you. The style of current NICE guidance is to be as clear and succinct as possible, and to omit information that can be found elsewhere (for example, in medical textbooks, or the summary of product

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							characteristics for a device or drug). This is why the sub sections on 'other issues to consider before fitting an implant', 'practical details of fitting implants' and 'follow-up and managing problems' are not included in the update. Guideline users are not expected to use guidelines in isolation, but to consult other sources where needed. This is highlighted in the 'linking evidence to recommendations' table: 'The Committee noted that the summary of product characteristics for Nexplanon contains important information on contraindications, adverse effects and instructions for fitting and removal that should be consulted by clinicians advising women on contraception' The summary of product characteristics includes all of the headings mentioned above.

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SH	British Medical Association	1	Addendum	1.1	6	The summary of recommendations says "tell women..." but in the actual paper (paragraph 2.1.6) it says "advise women..." As the evidence for every recommendation is graded as low or very low we would suggest that "advise women" or perhaps "discuss with the patient" would be more suitable.	Thank you. The Committee discussed the wording of the recommendation in response to your comment, and decided that 'inform' implied a more patient-centred approach than 'tell' and so the wording has been changed accordingly. Note that for this type of recommendation (about providing information), NICE does use different words to signify a recommendation's strength.
SH	Merck Sharp & Dohme Ltd (MSD)	2	Addendum	General	General	We request that updated recommendations from the finalised addendum are reflected in an update to the section on progestogen-only subdermal implants in the NICE version of CG30. We suggest it would be appropriate to ensure updated information is provided under the same headings as currently appear in the NICE version of CG30 (listed below) (Ref 2), to permit appropriate comparisons against recommendations concerning other LARC methods. • "Decision making – women should be given the following information" • "Other issues to consider before fitting an implant" • "Practical details of fitting the implant" • Follow-up and managing problems" Ref 2: NICE (2005) NICE clinical guideline 30 Long-acting reversible contraception. October 2005 (Available at: https://www.nice.org.uk/guidance/cg30/resources/guidance-longacting-reversible-contraception-pdf) [Accessed 25 June 2014]	Thank you. The NICE version of the guideline will be updated and published alongside the addendum. However, the suggested subheadings will not be used. NICE guidelines have evolved over the 12 years that they have been produced, and the methodology used and style of presentation has changed substantially since the original long-acting reversible contraception guideline

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							was published in 2005. Therefore, the topics covered by the update are not identical to those in the original guideline, as much of this information is available elsewhere (for example, the summary of product characteristics for Nexplanon). Therefore, the suggested subheadings are no longer possible.
SH	Royal College of General Practitioners (RCGP)	2	Addendum	2.1.2 line 18		"Comparing etonogestrel subdermal implants to other etonogestrel subdermal implant" is very confusing. I think you mean Nexplanon with Implanon, so isn't it better just to say that or at least to clarify.	Thank you. We have provided Implanon and Nexplanon as examples in brackets to make this clearer.
SH	Bayer Plc	2	Addendum	2.1.5	11	**Relative value of different outcomes** In the original guideline, the effectiveness of the contraceptive methods was assessed against outcomes agreed by the guideline development group on the basis of their relevance to patients and professionals. Amongst these outcomes was '*discontinuation and acceptability of method*.' This outcome is of critical importance when evaluating methods of contraception as acknowledged in the 'contraception use and principles of care' section of the full LARC guideline: "*continuation rates influence the effectiveness of contraception, since women often change to a less effective method or spend some weeks or months using no method while they decide what to use next," and also that "continuation rates of LARC are also fundamental to cost effectiveness*." It is not clear therefore, why '*discontinuation and acceptability of method'* was not considered to be an outcome relevant to decision making when reviewing the	Thank you. The outcomes that were considered in the evidence review were prioritised by the topic-specific committee members. The GRADE process for evaluating research evidence requires that only outcomes that are important for decision making for clinicians and

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						evidence for the guideline addendum relating to progestogen-only subdemal implants (POSDIs). The interim process and methods guide for the clinical guideline updates using standing committees pilot programme 2013, states that "*updates [are] limited to the existing guideline scope and review questions*". As such this important outcome should not have been omitted from the update without consultation with stakeholders. If this addendum were to be incorporated as it stands, the guideline would suggest that women should be given information about the discontinuation rate and reasons for discontinuation for the other LARC methods, but not for POSDIs. This would give the unbalanced impression that discontinuation is not a concern for this method, while on the contrary it is in fact recognised in the addendum that "*an important possible source of bias for many studies was that the dropout rate was often very high (typically 30-40% over 3 years). Most studies reported that the majority of women who left the study did so because they wished to have their implant removed. The committee noted that women with adverse side effects such as unacceptable bleeding pattern changes might be more likely to wish to have their implant removed…*" We strongly recommend that the evidence for this important outcome be reviewed for the POSDI, and that a recommendation should be included to 'tell' women the discontinuation rate along with the most common reason for discontinuation, in line with the sections for all other interventions included in the clinical guideline. This is important to ensure that women are presented with a balanced overview of all LARC methods when making decisions. We have undertaken a systematic review to identify literature reporting the efficacy and discontinuation rate of contraceptive methods, including the POSDI, in Europe, the USA, Canada and Australia, published since the date of the original NICE guideline in 2005 (searches were run in January 2014, and subsequently published literature was also checked to date). This review identified 16 publications relating to 12 unique studies and one integrated clinical trial analysis reporting the discontinuation rate of POSDIs, including studies from the UK. Please find below a list of citations identified in this review. Further details of the systematic review methodology are available from Bayer plc on request. (1) Agrawal A, Robinson C. An assessment of the first 3 years' use of Implanon in Luton. J Fam Plann Reprod Health Care 2005 Oct;31(4):310-2. (2) Arribas-Mir L, Rueda-Lozano D, Agrela-Cardona M, Cedeno-Benavides T, Olvera-Porcel C, Bueno-Cavanillas A. Insertion and 3-year follow-up experience of	patients are used for decision making. This approach was not used in the original guideline (and also, the priorities of clinicians and patients may have changed in the intervening years). Stakeholders are not consulted on the outcomes that are included each review question, even for original guidelines – this is a matter for the guideline development group. The Committee discussed the reasons that discontinuation was not prioritised as an outcome in response to this comment. Discontinuation was not included in the review because discontinuation rates are difficult to interpret – discontinuation of a method of contraception does not necessarily imply dissatisfaction, and may be rather different in

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						372 etonogestrel subdermal contraceptive implants by family physicians in Granada, Spain. Contraception 2009 Nov;80(5):457-62. (3) Blumenthal PD, Gemzell-Danielsson K, Marintcheva-Petrova M. Tolerability and clinical safety of Implanon. Eur J Contracept Reprod Health Care 2008 Jun;13 Suppl 1:29-36. (4) Cea-Soriano L, Garcia Rodriguez LA, Machlitt A, Wallander MA. Use of prescription contraceptive methods in the UK general population: a primary care study. BJOG 2014 Jan;121(1):53-60. (5) Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, et al. Continuation and satisfaction of reversible contraception. Obstet Gynecol 2011 May;117(5):1105-13. (6) O'neil-Callahan M, Peipert JF, Zhao Q, Madden T, Secura G. Twenty-four-month continuation of reversible contraception. Obstet Gynecol 2013 Nov;122(5):1083-91. (7) Rosenstock JR, Peipert JF, Madden T, Zhao Q, Secura GM. Continuation of reversible contraception in teenagers and young women. Obstet Gynecol 2012 Dec;120(6):1298-305. (8) Harvey C, Seib C, Lucke J. Continuation rates and reasons for removal among Implanon users accessing two family planning clinics in Queensland, Australia. Contraception 2009 Dec;80(6):527-32. (9) Jeffreys LA, Clark AL. A successful approach to long-acting contraceptive implants in primary care. Contraception 2012 Apr;85(4):381-3. (10) Lakha F, Glasier AF. Continuation rates of Implanon in the UK: data from an observational study in a clinical setting. Contraception 2006 Oct;74(4):287-9. (11) Short M, Dallay D, Omokanye S, Hanisch JU, Inki P. Acceptability of the levonorgestrel releasing-intrauterine system and etonogestrel implant: one-year results of an observational study. Eur J Contracept Reprod Health Care 2012 Feb;17(1):79-88. (12) Short M, Dallay D, Omokanye S, Stauch K, Inki P. Acceptability of long-acting, progestin-only contraception in Europe: a two-year prospective, non-interventional study. Eur J Contracept Reprod Health Care 2014 Feb;19(1):29-38. (13) Teunissen AM, Grimm B, Roumen FJ. Continuation rates of the subdermal contraceptive Implanon((R)) and associated influencing factors. Eur J Contracept Reprod Health Care 2014 Feb;19(1):15-21. (14) Trussell J. Contraceptive failure in the United States. Contraception 2011	research trials than in everyday practice.

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						May;83(5):397-404. (15) Weisberg E, Fraser I. Australian women's experience with Implanon. Aust Fam Physician 2005 Aug;34(8):694-6. (16) Weisberg E, Bateson D, McGeechan K, Mohapatra L. A three-year comparative study of continuation rates, bleeding patterns and satisfaction in Australian women using a subdermal contraceptive implant or progestogen releasing-intrauterine system. Eur J Contracept Reprod Health Care 2014 Feb;19(1):5-14.	
SH	British Medical Association	2	Addendum	2.1.5	13	It is sensible to highlight that Nexplanon is the only licensed for women aged 18-40 years however it is in common clinical use in the UK outside of this age range, particularly in younger females.	Thank you. This has been highlighted in the 'other considerations' section of the 'linking evidence to recommendations table'.
SH	Merck Sharp & Dohme Ltd (MSD)	3	Addendum	General	General	Currently, no information concerning the contraceptive implant is provided in the table "Long-acting contraception: how the methods compare" available on the "information for the public" page of CG30 available on the NICE website (Ref 3) or the table appearing within Appendix E: "Features of the LARC methods to discuss with women" within the NICE version of CG30 (Ref 2). We request that upon publication of the finalised addendum, the abovementioned tables are updated in a timely manner to reflect the updated information and recommendations concerning etonogestrel implants, in line with process set out in the interim process guide for rapid updates (Ref 4). Ref 2: NICE (2005) NICE clinical guideline 30 Long-acting reversible contraception. October 2005 (Available at: https://www.nice.org.uk/guidance/cg30/resources/guidance-longacting-reversible-contraception-pdf) [Accessed 25 June 2014] Ref 3: NICE (2005) Long-acting contraception: how the methods compare: Available at: https://www.nice.org.uk/guidance/CG30/IFP/chapter/Long-acting-contraception-how-the-methods-compare [Accessed 24 June 2014] Ref 4: NICE (2013) Interim process and methods guide for the clinical guideline updates using standing committees pilot programme 2013. Available at:	Thank you. The NICE version and information for the public versions of the guideline will be updated and published alongside the addendum (scheduled for publication in September 2014). The tables that you refer to in your comment will be updated before publication, in line with the information in the addendum.

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						http://publications.nice.org.uk/interim-process-and-methods-guide-for-the-clinical-guideline-updates-using-standing-committees-pilot-pmg17/process#close [Accessed 30 June 2014]	
SH	British Medical Association	3	Addendum	2.1.3	9	We are concerned that there were no studies identified that assess the cost-effectiveness or cost-utility of etonogestrel implants, especially as their use is advocated in preference to combined oral contraceptive pill	Thank you. Although we did not find any studies that met the inclusion criteria for the health economic search, as noted in the linking evidence to recommendations table, it is likely that subdermal implants are cost effective. Health economic modelling was conducted when the guideline was originally written, and concluded that all forms of long-acting reversible contraception were cost-effective. The cost of Nexplanon is actually slightly lower than the cost of Implanon (which the previous analysis was based on). Therefore it is very likely that subdermal implants remain a cost-effective option.
SH	Merck Sharp & Dohme Ltd	4	Addendum	General	General	As mentioned previously, the addendum which is the subject of this consultation is proposed to replace Chapter 7: POSDIs in the full version of CG30 (Ref 1). We note that the format of the addendum is substantially different to the current version of chapter 7, as well as chapters 4-6 (concerning alternative LARC methods) appearing	Thank you. You are correct that the format of the addendum is rather different to that of the

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	(MSD)					in the current full version of CG30. Due to these differences, which include changes to the layout, ordering and sub-headings used, we are concerned that it may be difficult for readers to compare and contrast the evidence and recommendations in the addendum on etonogestrel implants against information on alternative LARC methods available in the other chapters of the full version of CG30 which will remain current. We suggest the information should be provided following the existing format as per the current chapter 7: • 7.1 Introduction • 7.2 Effectiveness • 7.3 Discontinuation and reasons for discontinuation • 7.4 AEs • 7.5 Common concerns and symptoms • 7.6 Risks • 7.7 Return to fertility • 7.8 Details of method use • 7.9 training of HCPs • 7.10 specific groups • 7.11 Medical conditions and CIs • 7.12 Drug interactions • 7.13 Follow-up Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014]	original guideline. NICE guidelines have evolved over the 12 years that they have been produced, and the style of presentation has changed substantially since the original long-acting reversible contraception guideline was published in 2005. Therefore it is inevitable that there will be inconsistencies in format between the addendum and the old guidance, especially when the original guidance was produced many years ago. Making the format the same as the original would mean that every update that NICE produced would have a different format, and that guidance would never be brought in line with the current NICE style. Consequently, we have decided to take the approach of producing updates as addenda that are consistent with current style, but this

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							does mean that there will be some differences with the original guidelines. The section of the guideline on subdermal implants does not contain some of the information in the original, it is therefore not possible to use the subheadings suggested here.
SH	Bayer Plc	4	Addendum	1.1	6	The 2005 guideline also recommended that women should be given information about risks and possible side effects, and previously covered 'common concerns and symptoms' such as weight change, altered mood, altered libido, headache and acne. As suggested in order number 3 for discontinuation, 'risks and possible side effects' should also be covered under 'what to tell women' as for other the other LARC methods to ensure that the guideline is fair and balanced.	Thank you. Information about risks and side effects (such as the ones listed here) can be found in the summary of product characteristics for Nexplanon. Guideline users are not expected to use guidelines in isolation, but to consult other sources where needed. NICE does not wish to replicate information that is available elsewhere, as it may be updated more frequently than NICE guidance, and adding extra information may make NICE guidance less succinct and clear.

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SH	Merck Sharp & Dohme Ltd (MSD)	5	Addendum	1.1		Section 1.1: Recommendations: Within the proposed addendum, classifications have not been assigned against the proposed recommendations concerning etonogestrel implants. However in the current chapter 7 in the full version of CG30, as well as in all other chapters on alternative LARC methods, classifications against each recommendation are provided (from class A to D(GPP)) (Ref 1). The lack of classification against proposed recommendations in the addendum may cause ambiguity when comparing against existing recommendations on alternative LARC methods in the other chapters of the full version of CG30. Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014]	Thank you. NICE (and other international guidance producers) no longer uses classifications for recommendations, as they are difficult to understand, and sometimes lead to the erroneous interpretation that recommendations with higher classifications are more important for implementation. Making the methods consistent with the original would mean that guidance would never be brought in line with current methods. We therefore are adopting a consistent approach across all guideline updates, in line with the current NICE manual for the production of clinical guidelines. This means that a classification approach no longer used, and instead, the strength of recommendations is

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							indicated in the wording. Although this might cause some confusion when comparing between chapters, this is in line with the guidelines manual.
SH	Bayer Plc	5	Addendum	1.1	6	The previous guideline stated that women should be informed that "*bleeding patterns are likely to remain irregular over time*". It is not clear why this recommendation has not been included in the addendum. It does not appear to be reported that evidence was considered showing this to no longer be the case with Nexplanon. Indeed, the SmPC states that "*The bleeding pattern experienced during the first three months is broadly predictive of future bleeding patterns for many women*."17 We suggest that it is important that women be informed of this potential change to their bleeding pattern. (17) Merck Sharp & Dohme Limited. Nexplanon 68 mg implant for subdermal use. Summary of Product Characteristics. 12 Dec. 2013. Available from: https://www.medicines.org.uk/emc/medicine/23824/SPC/Nexplanon+68+mg+implant+for+subdermal+use/. (Last accessed: 3/7/2014).	Thank you. The Committee discussed this comment, and agreed that bleeding patterns were likely to remain changed while the implant was being used. This is reflected in the recommendation which states that bleeding pattern changes are likely 'during implant use'. This is now also emphasised in the linking evidence to recommendations table. The topic-specific members noted that it was still important that women alerted their health-care provider to a change in bleeding pattern that occurred during implant use, and thought that using the term 'irregular' to describe bleeding

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							patterns might discourage women from seeking advice if bleeding patterns changed. This is now also noted in the 'linking evidence to recommendations' section of the addendum.
SH	Merck Sharp & Dohme Ltd (MSD)	6	Addendum	2.1.4		Section 2.1.4: Evidence statements: In the proposed addendum, evidence statements have been graded according to a modified GRADE profile (high, moderate, low, very low), which differs from the approach taken in the current full version of CG30, in which evidence is graded according to table 1.1 (Levels of evidence in included studies; page 19 of full version of CG30) (Ref 1) which assigns levels from 1++ (highest quality) to 4 (lowest quality). The different approach taken to grading evidence in the addendum may cause ambiguity when readers wish to compare quality of evidence on etonogestrel implants within the addendum against evidence concerning alternative LARC methods in other existing chapters of CG30. We appreciate that the classification of evidence according to the GRADE criteria is consistent with the process proposed in the draft version of the guideline manual which was recently subject to public consultation (Ref 5). Whilst such an approach would be appropriate in the context of updating/creating an entire guideline, we feel it is inappropriate to change the system of classification during a rapid update. It is important that the same format/structure and classification systems are used, to allow readers to review the addendum (replacement chapter) in the same context as other chapters of the full guideline which are to be retained. Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014] Ref 5: NICE 2014 Developing NICE guidelines manual 2014 for consultation.	Thank you. NICE guidelines have evolved over the 12 years that they have been produced, and the methodology used has changed substantially since the original long-acting reversible contraception guideline was published in 2005. Making the methods consistent with the original would mean that guidance would never be brought in line with current methods. We therefore are adopting a consistent approach across all guideline updates, in line with the current NICE manual for the production of clinical guidelines.

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						Available at: https://www.nice.org.uk/proxy/?sourceUrl=http%3a%2f%2fwww.nice.org.uk%2fgetinvolved%2fcurrentniceconsultations%2fniceguidelinesthemanual.jsp%3fdomedia%3d1%26mid%3d095EBAAF-E93D-FAC1-4E0B082CEE7B23F7 [Accessed 27 June 2014)	The GRADE approach is recognised internationally (it is used by many organisations worldwide, including the world health organisation), and provides a transparent and robust way of evaluating evidence to support recommendations.
SH	Bayer Plc	6	Addendum	Appendix C	23	We note that retrospective non-comparative studies were excluded from the systematic literature review if higher quality evidence was available for all reported outcomes. However, as recognised in the original LARC guideline, "discontinuation rates from countries where access to contraception is limited and/or expensive may differ from those in the UK, for example, in developing countries." Therefore we suggest that consideration should be given to all UK studies when reviewing the evidence relating to the discontinuation rate of POSDIs regardless of study design.	Thank you. Discontinuation was not included in the review because discontinuation rates are difficult to interpret – discontinuation of a method of contraception does not necessarily imply dissatisfaction, and may be rather different in research trials than in everyday practice.
SH	Merck Sharp & Dohme Ltd (MSD)	7	Addendum	General	General	Full details of the evidence supporting the evidence statements in the draft addendum are provided in the appendices. This again differs from the format which applies to all other chapters of the full version of CG30, which will be retained (Ref 1). We suggest a consistent approach should be taken to allow easy comparison between chapters. Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014]	Thank you. NICE guidelines have evolved over the 12 years that they have been produced, and the methodology used and style of presentation has changed substantially since the original long-

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							acting reversible contraception guideline was published in 2005. Therefore, as you note, there are inconsistencies in format between the addendum and the old guidance (and therefore between chapters). Making the format the same as the original would mean that every update that NICE produced would have a different format, and that guidance would never be brought in line with current methods. We therefore are adopting a consistent approach across all guideline updates, in line with the current NICE manual for the production of clinical guidelines.
SH	Merck Sharp & Dohme Ltd (MSD)	8	Addendum	1.1		We support the proposed updated recommendations, which reflect the current evidence base for Nexplanon. We note that the proposed recommendations reflect the areas covered under the "Decision Making" sub-section of the current section concerning POSDI in the NICE version of CG30 (Ref 2) and Section 2 (Summary of Recommendations) within the current full version of CG30 (Ref 1). To ensure consistency with information present on other LARC methods, we suggest	Thank you. The recommendations in the sections highlighted here contain information that can be found in the summary of product characteristics for Nexplanon. NICE does

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						it is also important for specific recommendations to be made under the following sub-headings. Although evidence may be presented in the addendum which fits within the below categories, this has not been reflected in new/updated recommendations in the draft addendum: • Other issues to consider before fitting an implant • Practical details of fitting implants • Advice for women at time of fitting • Follow-up and managing problems Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014] Ref 2: NICE (2005) NICE clinical guideline 30 Long-acting reversible contraception. October 2005 (Available at: https://www.nice.org.uk/guidance/cg30/resources/guidance-longacting-reversible-contraception-pdf) [Accessed 25 June 2014]	not wish to replicate this information, as it likely to be updated more frequently than NICE guidance. The style of current NICE guidance is to be as clear and succinct as possible, and to omit information that can be found elsewhere (for example, in medical textbooks, or the summary of product characteristics for a device or drug). Guideline users are not expected to use guidelines in isolation, but to consult other sources where needed. This is highlighted in the 'linking evidence to recommendations' table: 'The Committee noted that the summary of product characteristics for Nexplanon contains important information on contraindications, adverse effects and instructions for fitting and removal that should be

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							consulted by clinicians advising women on contraception'
SH	Merck Sharp & Dohme Ltd (MSD)	9	Addendum	2.1.5		Table 1, section "Trade-off between net health benefits and resource use": The proposed wording currently states that "Given that Nexplanon….is bioequivalent to Implanon, and has a similar cost, the committee agreed that it was reasonable to assume that etonogestrel implants are likely to remain a cost effective option". We request the word "likely" should be removed from the above sentence, as this introduces ambiguity. The current cost of Nexplanon (£83.43) is lower than the cost of Implanon in 2005 (£90.00), when the cost effectiveness analysis for CG30 was conducted. Consequently Nexplanon remains a cost effective option.	Thank you. The cost-effectiveness of subdermal implants is not known with absolute certainty, as a cost-effectiveness analysis was not conducted with the updated effectiveness and cost data. However, we acknowledge that subdermal implants are very likely to be cost effective, and have changed the wording accordingly.
SH	Merck Sharp & Dohme Ltd (MSD)	10	Addendum	2.1.5		Table 1, section "Quality of evidence": This section currently states "The Committee noted that women with adverse side effects such as unacceptable bleeding pattern changes might be more likely to wish to have their implant removed, so estimates of adverse outcomes might be underestimated due to the high dropout rate. We would like to comment that we feel the "high dropout rate" referred to above is inaccurate. When compared to other LARC methods, the etonogestrel implant has a similar year 1 discontinuation rate as IUS and IUD, and a substantially lower discontinuation rate than the Injectable (Ref 1). As the discontinuation rate for the etonogestrel implant should be considered in the context of discontinuation rates for all LARC methods, reference to "high dropout rates" is potentially misleading. Ref 1: NICE (2005) CG30 Long-acting reversible contraception: full guideline. Available at: https://www.nice.org.uk/guidance/cg30/resources/cg30-longacting-reversible-contraception-full-guideline2 [Accessed 24 June 2014]	Thank you. We do not agree that 'high dropout rates' is an inaccurate description here. The comment was in relation to the effect of dropout on the quality of the evidence, not in comparison with other methods of long-acting reversible contraception. High dropout rates, as were seen in most of the studies in the evidence review, could have a serious impact on the

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							estimates of the reported outcomes, and so this warrants comment in the quality section of the linking evidence to recommendations table. This is the case irrespective of whether dropout rates are comparable to other forms of contraception or not.
SH	Merck Sharp & Dohme Ltd (MSD)	11	Addendum	2.1.5		Table 1, section "Quality of evidence": The section currently states that "The topic-specific Committee members were particularly interested to know whether barium, which is included in the device Nexplanon but not Implanon, was associated with an increase in implant site reactions, but the data to determine this was not available." We would like to comment that barium sulfate is an insoluble salt and barium sulfate particles do not leach out of the implant. Even when the implant is cut with a razor lengthwise, the release of barium ions is considered insignificant. It has been shown by Back Scatter Electron (BSE) detector photographs that the barium sulfate particles are mainly encapsulated in the EVA28 material of the implant (Ref 6) Also after the release of etonogestrel from the implant the barium sulfate is still present in the EVA28 material of the core. Barium sulfate does not migrate into the skin layer, as Barium sulfate particles do not leach out of the implant (Ref 6). Ref 6: Graaff, Wouter De; Harm, Veenstra. 2005. X-Ray visible drug delivery device. European Patent EP 1729819 A1 20061213 (EN), filed 14 Mar 2005 and issued 29 Sep 2005.	Thank you for the information. The aim of the linking evidence to recommendations is to document the discussions of the committee when making recommendations and this concern was raised by topic-specific members. It remains true that comparative data for implant site reaction for Implanon and Nexplanon was not found in the evidence review, and so we have not changed the comment in the 'linking evidence to recommendations table' on this point.

These organisations were approached but did not respond:

Association for Perioperative Practice
Association of Anaesthetists of Great Britain and Ireland
Association of British Healthcare Industries
Association of Surgeons of Great Britain and Ireland
Barnsley Hospital NHS Foundation Trust
Barton Surgery
Bayer HealthCare
Belfast Health and Social Care Trust
British Association for Sexual Health and HIV
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Psychological Society
British Red Cross
Brook Centres
Cambridge University Hospitals NHS Foundation Trust
Care Quality Commission
Cochrane Fertility Regulation Group
Co-operative Pharmacy Association
Cumbria Partnership NHS Trust
CWHHE Collaborative CCGs
Department for Communities and Local Government
Department of Health
Department of Health, Social Services and Public Safety - Northern Ireland
Directorate of Sexual and Reproductive Health - Gwent Healthcare NHS Trust

DNU Health Protection Agency
Down's Syndrome Association
Eastern and Coastal Kent Primary Care Trust
Equalities National Council
Ethical Medicines Industry Group
Faculty of Public Health
Faculty of Sexual and Reproductive Healthcare
Family Planning Association
Fibroid Network Charity
GP update / Red Whale
Health & Social Care Information Centre
Health and Care Professions Council
Healthcare Improvement Scotland
Healthcare Infection Society
Healthcare Quality Improvement Partnership
Healthwatch East Sussex
Hertfordshire Partnership NHS Trust
Janssen
Johnson & Johnson
Kingston University and St Georges, University of London
Lancashire Care NHS Foundation Trust
Leeds Teaching Hospitals NHS Trust
Local Government Association
Medical Foundation for AIDS and Sexual Health
Medicines and Healthcare products Regulatory Agency
Microsulis Medical Limited
Mid Staffordshire NHS Foundation Trust

Ministry of Defence (MOD)

NANCSH

National Clinical Guideline Centre

National Collaborating Centre for Cancer

National Collaborating Centre for Mental Health

National Collaborating Centre for Women's and Children's Health

National Deaf Children's Society

National Institute for Health Research Health Technology Assessment Programme

National Institute for Health Research

National Osteoporosis Society

National Patient Safety Agency

National Public Health Service for Wales

NHS Clinical Knowledge Summaries

NHS Connecting for Health

NHS Fife

NHS Hardwick CCG

NHS Health at Work

NHS Herefordshire

NHS Improvement

NHS Luton CCG

NHS North Somerset CCG

NHS Plus

NHS Sheffield CCG

NHS Southern Derbyshire CCG

NHS Suffolk

NHS Sussex

NHS West Leicestershire CCG

Niger Delta University
NORTH EAST LONDON FOUNDATION TRUST
North of England Commissioning Support
North Tees and Hartlepool NHS Foundation Trust
North West London Hospitals NHS Trust
Northern Health and Social Care Trust
Nottingham City Council
Nottinghamshire Acute Trust
Nursing and Midwifery Council
Oxfordshire Clinical Commissioning Group
Oxleas NHS Foundation Trust
Pelvic Pain Support Network
PERIGON Healthcare Ltd
Pfizer
PHE Alcohol and Drugs, Health & Wellbeing Directorate
PrescQIPP NHS Programme
Public Health Agency for Northern Ireland
Public Health England
Public Health Wales NHS Trust
Queen Mary's Hospital NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition

Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Cornwall Hospitals NHS Trust
Royal Pharmaceutical Society
Royal Society of Medicine
Royal West Sussex NHS Trust
Schering Health Care Ltd
Scottish Intercollegiate Guidelines Network
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence
Society and College of Radiographers
Society for Endocrinology
Society of Consultants and Lead Clinicians in Reproductive Health
Solent NHS Trust
South Eastern Health and Social Care Trust
South London & Maudsley NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
Southern Health & Social Care Trust
SSL International plc
Staffordshire and Stoke on Trent Partnership NHS Trust
Tameside Hospital NHS Foundation Trust
The Association of the British Pharmaceutical Industry
The Princess Alexandra Hospital NHS Trust
The Rotherham NHS Foundation Trust

UK Specialised Services Public Health Network
University College London Hospital NHS Foundation Trust
University College London Hospitals NHS Foundation Trust
Welsh Government
Welsh Scientific Advisory Committee
Western Health and Social Care Trust
Western Sussex Hospitals NHS Trust
York Hospitals NHS Foundation Trust