National Institute for Health and Care Excellence

Medical Technologies Evaluation Programme

MT257 ENDURALIFE-powered CRT-D devices for treating heart failure

Consultation comments table

MTAC date: 16 December 2016

There were 58 consultation comments from 9 consultees (2 NHS professionals, 1 professional society, 1 professional group, 1 EAC, 3 manufacturers (including the sponsor), and the Department of Health). The comments are reproduced in full, arranged in the following groups according to the **main issue** raised in the relevant comment (**some comments contain multiple issues**):

- multiple technologies;
- recommendations based on evidence on devices no longer in use;
- factors other than battery capacity affect battery longevity;
- cost modelling; and
- matters of fact or clarity.

The draft responses to the 58 comments are based mainly on the EAC and expert advice.

Table 1

Multiple technologies

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
1	3. Professional society	1.1	We believe that modifications to the conclusions such as those suggested below *(in italics)* would be more realistic:- The case for adopting CRT-D devices *with extended longevity such as those powered by ENDURALIFE technology* is supported by the evidence. Extended battery life is of clinical benefit and associated with fewer replacement procedures.	Thank you for your comment. NICE medical technologies guidance evaluates a single medical technology based on the sponsor's claimed advantages of introducing the notified technology compared with current management of the condition. Medical technologies guidance is published with an explanatory note which states that the specific recommendations on individual technologies are not intended to limit use of other relevant technologies which may offer similar advantages.
6	3. Professional society	1.2	We believe that modifications to the conclusions such as those suggested below *(in italics)* would be more realistic:- ENDURALIFE–powered CRTDs *and others with extended longevity* should be considered as a treatment option in people who are offered CRT-D devices in line with NICE TA314	Thank you for your comment. Please see response to comment 1.
39	3. Professional society	6.3	We believe that modifications to the conclusions such as those suggested below *(in italics)* would be more realistic:- The committee concluded that, on the basis of cost modelling analysis, the use of *extended longevity CRT-Ds such as those powered by ENDURALIFE batteries* is likely to be cost saving in patients with heart failure as a result of a reduction in the need for replacement procedures	Thank you for your comment. Please see response to comment 1.

Recommendations based on evidence on devices no longer in use

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response

2	8. Manufacturer	1.1
		Page 2
			PROVISIONAL RECOMMENDATIONS:NICE STATEMENT 1.1:
			The case for adopting ENDURALIFE powered cardiac resynchronisation therapy- defibrillator (CRTD) devices for treating heart failure is supported by the evidence
			
			The evidence base has significant weaknesses, which are highlighted both by the EAC and in concerns raised by comments from the Expert Advisors and so the case for adoption in the NHS today with devices available currently is not supported by the evidence.
			
			NICE statement 1.1 is based on evidence for outdated devices and a model produced by Boston Scientific which is recognised to have significant weaknesses by both the EAC and Boston Scientific. Expert Advisors comments highlight that battery longevity data used in the model for newer devices from Boston Scientific are hypothetical, not real world experience and not based on published evidence.
			
			• From the External Assessment Report Page 90 section 5 Conclusion
			  ○ "The EAC is concerned about the applicability of the evidence to inform decisions on device selection now as the available devices are different which was a weakness highlighted by the company"
			• From the External Assessment Report Page 91 section 5 Conclusions
			  ○ "Remaining uncertainties are the longevity of devices currently on the market, patient life expectancy, and the accuracy and
				Thank you for your comment.
				
				The committee makes recommendations after considering all of the relevant evidence including expert advice.
				
				EAC considered the use of bench test data to compare current models but testing methods vary from company to company such that predictions are not comparable (and possibly unreliable). Section 3.9 discusses the use of PPRs as a source for estimating the comparative lifespan of CRT-D devices.
				
				The committee considered this comment carefully and decide to change section 3.18 to further clarify its considerations on the generalisability of evidence on earlier generation devices. The committee also concluded that all the relevant evidence has been taken into account.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			comparability of manufacturer predicted device longevity from bench tests” • Consultation Document; Page 14, 3.16 EAC Critique of the Clinical Evidence o “However some of the CRT-Ds studied in the longevity studies, particularly for comparator devices, may no longer be marketed” • Correspondence with EAC: Page 11 Paragraph 3 o “Device survival rates estimated from the KM curve in Landolina 2015 at 0.2 year intervals are for old generation devices from Medtronic and Boston Scientific” • Overview of the Assessment Report Page 18 and 19 o “the main weakness of the published data is that they appear to relate to devices no longer on the market due to the incremental development of new models” • Overview of the Assessment Report, Page Issues for consideration by the committee Page 40 section 7 o “The EAC feel some of the clinical evidence may be based on devices no longer on the market due to the rapid turnover of new models of the technology. For example some of the models listed in the Landolina et al. (2015) study as ‘recent generation’ have been withdrawn. As device longevity is related to other factors as well as battery technology, past performance is not necessarily indicative of future results” • Correspondence with the Expert Advisors. Question 8.3 “How good is this evidence for each of these additional benefits? o Dr Ernest Lau: “The clinical evidence for ENDURA-powered CRTDs lasting longer	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			than other contemporary CRTDs (largely powered by Li/SVO batteries) is strong (multi-centre independent registries). How ENDURA-powered CRTDs compare to the newer generation of CRTDs powered by large capacity Li/SVO-CFx batteries is unknown. Longevity claims by different manufacturers for their own models are very difficult to compare because of different assumptions used in their projections." ○ Dr Chris Plummer: "The technology is promising but robust data are required to substantiate the claims of doubled device longevity - it is not enough to show a doubled battery capacity. Evidence of battery longevity in other manufacturers' current devices is also required to evaluate the relative advantages" • Correspondence with the Expert Advisors: page 26 ○ Dr Chris Plummer: "To get accurate battery longevity data requires long follow-up – much longer than the 3-4 years often available. Boston's data on the performance of their batteries in real life using remote monitoring is persuasive but is essentially an extrapolation until we have "date of device change for battery depletion data" on a large consecutive cohort" • The EAC highlighted in the Assessment Report on page 91 section 6, Implications for research ○ "There is a lack of evidence for devices that are powered by Enduralife technology and that are currently on the market and for current competitor devices • Assessment Report page 89 section 4.6	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			○ "As device longevity is related to other factors as well as other technology, past performance is not indicative of future results Conclusion therefore is there is no published evidence for Enduralife Powered devices currently available and the evidence for CRT-D devices from other manufacturers is not applicable to devices on the market today, so the guidance is not able to inform decisions for device choice available in the NHS today	
8	8. Manufacturer	1.3 Page 2	**NICE STATEMENT 1.3** **Cost Modelling shows that the price and lifespan of the CRTD have the greatest effect on overall treatment costs** The EAC highlighted several weaknesses in the published economic evidence, the economic model used by Boston Scientific (and subsequently used in the base case analysis by the EAC), and the clinical data used to inform the model on which all cost savings are based. Combine these weaknesses with the data being based on devices which are no longer available in the NHS and the cost savings reported are unlikely to be realised. The guidance is not relevant to inform decisions based on devices available currently in the NHS. The economic analysis was adapted from a study funded by Boston scientific which the EAC considered may be subject to bias. From the Consultation Document; ○ Page 19, and page 20 5.7 and 5.8 EAC's critique of the Cost Evidence ○ "Gadler et al was funded by Boston Scientific , so may be subject to bias"	Thank you for your comment. Please see the responses to comments 2 and 3.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			○ "The company presented an economic model adapted from Gadler et al 2016" The EAC also highlight how the economic model relates to devices no longer on the market for use in the NHS today ○ Consultation Document; Page 19, 5.47 EAC's Critique of the Cost Evidence ○ "The EAC identified the main weakness of the published economic evidence is it relates to devices no longer on the market due to the rapid turnover of new models of the technology" A key assumption used in the company's model is flawed (also used in the EAC base case model). From Page 70 in the Assessment Report "Key assumptions in the model" ○ "data from published literature from device implanted between 2008 and 2010 can be applied to the latest generation devices currently available from the same manufacturers" This assumption is false. Medtronic introduced revolutionary new battery chemistry and capacitor technology in 2012 which is used in all Medtronic Devices since 2012 and so this assumption used in the model for older generation Medtronic devices cannot be applied to devices introduced since 2012. This information is supported by the Expert Advisors • Correspondence with the Expert Advisors: page 8 ○ Dr Ernest Lau: "Apart from changing the battery chemistry, most manufacturers have also increased the total capacity to a level comparable (or even exceeding) the ENDURALIFE battery (around 1.9 Ampere-	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			hours) used by Boston Scientific in its CRTDs". As the clinical data used in the economic model was based on Landolina which reports on devices no longer available on the market, the Guidance is outdated before it is published o Overview of the Assessment Report page 40 Issues for consideration by the committee o "The EAC feel some of the clinical evidence may be based on devices no longer on the market due to the rapid turnover of new models of the technology. For example some of the models listed in the Landolina et al. (2015) study as 'recent generation' have been withdrawn. As device longevity is related to other factors as well as battery technology, past performance is not necessarily indicative of future results" o Boston Scientific acknowledges the weakness of their model is based on devices which are no longer available and is confirmed by the EAC in the Assessment Report on page 79 paragraph 2 "The Company has correctly identified the main limitation of the model, being the difference in device models in the published literature, compared to those available now"	

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10	3. Professional society	1.3	We believe that modifications to the conclusions such as those suggested below *(in italics)* would be more realistic:- Cost modelling shows that the price and lifespan of the CRT-D have the greatest effect on overall treatment costs. Based on an average selling price of £12,404 across different devices, ENDURALIFE-powered CRT-Ds *would have saved* an estimated £2,120 to £5,627 per patient over 15 years*, as compared with other contemporary CRT-D models during the period studied,* through a reduction in the need for replacement procedures. *This could have saved the NHS in England £6 million over 5 years.*	Thank you for your comment. **The committee considered this comment carefully but decided not to change the guidance.**
35	3. Professional society	6.1	We believe that modifications to the conclusions such as those suggested below *(in italics)* would be more realistic:- the committee concluded that there is good evidence to support the clinical benefit of extended battery life and the associated reduction in cardiac resynchronization therapy-defibrillator (CRT-D) replacement procedures. *The ENDURALIFE-powered CRT-Ds studied have been shown to have a greater battery capacity and longer battery life compared with other contemporary CRT-Ds.*	Thank you for your comment. **The committee considered this comment carefully but decided not to change the guidance.**
36	8. Manufacturer	6.1 Page 25	The conclusions of the committee are not correct as this evidence is outdated and not current. There is no published evidence for newer Enduralife Powered devices currently on the market. • The EAC highlighted in the Assessment Report on page 91 section 6, Implications for research ○ "There is a lack of evidence for devices that are powered by Enduralife technology and that are currently on the market and for current competitor devices • Correspondence with the Expert Advisors: page 26	Thank you for your comment. Please refer to the response to comment 2.

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			○ Dr Chris Plummer: “To get accurate battery longevity data requires long follow-up – much longer than the 3-4 years often available. Boston’s data on the performance of their batteries in real life using remote monitoring is persuasive but is essentially an extrapolation until we have “date of device change for battery depletion data” on a large consecutive cohort”	
37	8. Manufacturer	6.2 Page 25	The conclusions of the committee are incorrect. There is no evidence to compare Enduralife powered devices with newer current devices from other manufacturers. Additionally there is no published evidence on the longevity of newer Enduralife devices as highlighted by the EAC and expert advisors: • The EAC highlighted in the Assessment Report on page 91 section 6, Implications for research ○ “There is a lack of evidence for devices that are powered by Enduralife technology and that are currently on the market and for current competitor devices • Overview of the Assessment Report, Page Issues for consideration by the committee Page 40 section 7 ○ “The EAC feel some of the clinical evidence may be based on devices no longer on the market due to the rapid turnover of new models of the technology. For example some of the models listed in the Landolina et al. (2015) study as ‘recent generation’ have been withdrawn. As device longevity is related to other factors as well as battery	Thank you for your comment. Please see the response to comment 2.

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			technology, past performance is not necessarily indicative of future results" • Correspondence with the Expert Advisors: page 26 ○ Dr Chris Plummer: "To get accurate battery longevity data requires long follow-up – much longer than the 3-4 years often available. Boston's data on the performance of their batteries in real life using remote monitoring is persuasive but is essentially an extrapolation until we have "date of device change for battery depletion data" on a large consecutive cohort"	
38	3. Professional society	6.2	We believe that modifications to the conclusions such as those suggested below *(in italics)* would be more realistic:- (*we do not believe this unsubstantiated assertion is justified, indeed manufacturers' own warranty and longevity predictions indicate that it is not the case (see Appendix))* **APPENDIX: MANUFACTURERS' OFFICIAL ESTIMATES OF LONGEVITY OF ICDS AND CRT-D DEVICES (2016)** The following document was prepared for the NHSE Clinical Reference Group in Spring 2015,by Prof Nick Linker (BHRS President and CRG Member). Dr Linker checked in November 2016 with the three manufacturers listed that the figures quoted still pertain to their current models. <u>BATTERY LONGEVITY OF ICDs AND CRT-D DEVICES</u> I contacted all 3 major device manufacturers (Boston Scientific, Medtronic and St Jude Medical) and asked them to give me their current data for battery longevity for VR ICDs, DR ICDs and CRT-Ds. I also asked them for warranty information and also for data they quote for the	Thank you for your comment. Please see the response to comments 2 and 3. MTEP methods evaluate manufacturer claims against published evidence to generate recommendations on medical device usage. This process also independently assesses economic evidence and a company economic model to ascertain potential cost savings to the NHS. Please find a link here to the MTEP process and methods guide. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-medical-technologies-evaluation-programme/process-timeline **MTEP note:** The appendix in comment 38 relates to the conclusion outlined in section 6.2 of the guidance and the general theme that the recommendations are based on evidence on devices no longer in use (see comment 42.2). Following clarification with the consultee, the data provided in the appendix are projected battery longevities based on real life remote follow up. Clinicians can see predicted longevity for the device in use, based on the experience to date with that patient. This

<table>
<tr><th>Com. no.</th><th>Consultee number and organisation</th><th>Sec. no.</th><th>Comments</th><th>Response</th></tr>
<tr><td></td><td></td><td></td><td>longevity of their competitor’s devices! It makes for interesting (and confusing) reading:

<table>
<tr><td></td><td>Battery Longevity (yrs)</td><td>Warranty (yrs)</td></tr>
<tr><td>VR ICDs</td><td></td><td></td></tr>
<tr><td>Boston Scientific</td><td>11.6 (9.6)</td><td>10</td></tr>
<tr><td>Medtronic</td><td>11.6 (9.2)</td><td>10</td></tr>
<tr><td>St Jude Medical</td><td>11.5 (7)</td><td>10</td></tr>
</table>

<table>
<tr><td>DR ICDs</td><td></td><td></td></tr>
<tr><td>Boston Scientific</td><td>11.1 (8.4)</td><td>8</td></tr>
<tr><td>Medtronic</td><td>10.9 (8)</td><td>8</td></tr>
<tr><td>St Jude Medical</td><td>10.2 (7)</td><td>8</td></tr>
</table>

<table>
<tr><td>CRT-D</td><td></td><td></td></tr>
<tr><td>Boston Scientific</td><td>7.9 (7.7)</td><td>6</td></tr>
<tr><td>Medtronic</td><td>8 (5.5)</td><td>6</td></tr>
<tr><td>St Jude Medical</td><td>7.7 (5)</td><td>6</td></tr>
</table>

The figures next to the manufacturers are their quoted device longevity and warranty. In brackets is the average longevity as quoted by the other manufacturers.

So, in essence if you ask each manufacturer individually what their device longevity is they all tell you their longevity is better than the other 2 manufacturers. Furthermore, their figures actually show little difference between the manufacturers, with identical warranties. I think it is particularly noteworthy that all manufacturers quote the same warranty which I think must reflect their real life expectation of battery life.

The problem is these are all projected figures. They are based on a number of assumptions in terms of device</td><td>allows prediction of ERI for that particular patient which includes current battery state, and patient usage. This is a prediction, and depends on the quality of test procedures and the algorithm used.

The scope of this evaluation defined the intervention as CRT-D devices with ENDURALIFE battery technology. ICD devices were within the scope.

The committee considered this comment carefully and decided to change sections 3.18 and section 3.20 to further clarify its considerations on predicted longevity data.</td></tr>
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Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			settings, therapies delivered etc. and these are different between the manufacturers making comparison difficult. Programming all the devices to the same parameters does not resolve this as the recommendations from the manufacturers as to how to setup their devices are different so they are not comparable in this respect in real life. My conclusion is that there is no advantage in terms of cost savings to NHSE in terms of differentiating between these manufacturers on battery longevity. This is supported, as ****** states, by Boston Scientific's own assertion that this would not be cost saving in Section 6 but rather cost neutral. This is likely to be because the device is more expensive. It is also worth bearing in mind that a research study is currently underway looking at real life battery longevity using the National CRM database, supported by BHRS which will give an independent view on this.	
40	1. NHS Professional	General	It is admirable that this new technology is available. The study however compares with other companies old devices. There have been advances in other company's batteries too that have comparable predicted longevity.	Thank you for your comment. Please see the response to comment 2.
41	2. NHS Professional	General	I have reviews the guidance and would like to raise some significant concerns. I am the clinical lead for a large implanting tertiary centre in the West Midlands. We currently implant a significant volume of CRTS from 3 companies (Boston Scientific, Medtronic and St Jude) and therefore well placed to comment on these proposals. Battery life is obviously an vital component of a CRT and very important in patient care. I fully agree that early depletion needs to be avoided to reduce the risk to the patient and improve health care cost utilisation. I would	Thank you for your comment. Please also refer to the responses to comment 2 and 3. **The committee considered this comment carefully and decided to change sections 4.5 and 6.3 to further clarify its considerations on the choice of device by specialist centres.**

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			counsel that the current consultation is inaccurate in the assumptions it has made in reaching their conclusions. Firstly they have admitted that the data on non-Boston Scientific manufactures is old (2008-2011) but that they have assumed that there will be little change in the new models. Both St Jude and Medtronic have changed their battery technology in this timeframe, and there is no data in the submission for current generation devices. It is also important to note that CRT has gone through a vast change in that timeframe. Quadipolar leads have been introduced and now make up the vast majority of implants. These leads tend to use less energy (due to lower thresholds and higher impedances compared to unipolar and bipolar leads which were the standard in 2008) and therefore will reduce battery drain. There are also now significant programing algorithms in Medtronic devices which reduce the amount of pacing on the right ventricular lead and hence reduce battery drain. This is not available on Boston devices and therefore whilst the battery size is bigger it would lead to more drain and hence overall similar life. Overall data on Medtronic CRT (over 295 devices on active follow up) shows that the average battery life for a CRT D is 8.7 years and also that appropriate programming and good thresholds allow us to achieve 12% better battery life with a Medtronic device compared to the rest of the UK and Europe. This highlight that batter life is a complex interaction between battery sixe, lead thresholds, appropriate programming, and algorithms. To focus on just battery size is simplistic and prone to significant overestimations of potential gains. I would also consul against NICE approving any one manufacture. Over the past 40 years of implanting devices	

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			we know that one of the most common themes is that all manufactures will suffer recalls and advisory on their devices, for this reason most high volume centres will hedge their risk across 3 companies. This makes any device alert or recall manageable in the NHS and avoids overwhelming a service with all their patients needing reviews at once. Lastly there are significant differences in the overall offering from different companies; currently clinicians are able to use these differences to tailor the right device for patients. Artificially supporting one company takes away this tailoring and will potentially reduce patient care. I'm not sure that this is best served by NICE assessment, a much better method would be for NHS England and The British Heart Rhythm Society mandating that all CRT sold in the UK came with a cast iron warranty of 6 yrs. That way we can tailor the correct device for the patient but ensure that the manufactures continue to focus on battery life improvement and save the NHS money in case of early depletion.	
42.2	3. Professional society		1. <u>Applicability of the analysis to current models</u> The studies included in the assessment included models implanted almost exclusively up to 2010 (e.g. the "recent generation" models in Landolina 2015 were implanted in 2007-2010). It is clear that during the period 2005-10 the "Enduralife" battery technology in Boston Scientific CRT-D devices endowed them with a significant longevity advantage over the competition and this set a new bar for longevity in the industry. However, as stated by the EAC, *"the main weakness of the evidence is that it appears to relate to devices no longer on the market due to the rapid turnover of new models of the*	Thank you for your comment. Please see responses to comments 2 and 3.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			technology". Likewise, *"It is likely that different manufacturers have all undertaken CRTD development focussed on numerous CRTD components such that devices marketed today may have better longevity than their predecessors studied in the included longevity studies".* Competing manufacturers have indeed recognised and responded to the longevity challenge by incorporating a number of innovations to reduce current drain. Furthermore almost all the current CRT-D models of competing manufacturers incorporate new (hybrid LiCFx/SVO) battery chemistry designed to match the capacity of Enduralife models. For many models, longevity estimates based on observed real life current drain (remote follow up of tens of thousands of patients) are now of the same order as those of Boston Scientific models. It is also noteworthy that the warranties and predicted longevities for their current CRT-D devices from Boston Scientific, St Jude Medical and Medtronic are identical at 6 years and 7.7-8 years. (see Appendix). The picture is analogous to that of other major recent advances in CRT-D technology, such as remote follow up (reducing the number of hospital visits and permitting early detection of patient deterioration or device faults), MRI conditionality (permitting patients to have any part of the body scanned) and quadripolar LV leads (greatly reducing the need for re-intervention and associated complications). Each of these advances was introduced by one manufacturer but became standard across the industry within 1-3 years. A critically timed appraisal during this period may have favoured one manufacturer at a time when others had matched or bettered its technology by the time the appraisal appeared.	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			In the face of the above considerations and the advice of the EAC, in the consultation document the Committee concludes (Section 6.1) *"the recent advances in CRT-D technology are unlikely to negate the benefits of ENDURALIFE-powered battery performance on device lifespan compared with other devices."* This assertion is unsubstantiated and we strongly contest it.	
43.2	5. Manufacturer		**Are the provisional recommendations sound, and a suitable basis for guidance to the NHS?** **1.** Recommendation 1.1 is not sound. Comparisons with devices that are no longer marketed render the analyses unreliable and not a suitable basis for guidance to the NHS. We are extremely concerned that these recommendations are based on data from implantations that took place between 2008 and 2010 and do not therefore reflect the impact of newer CRT-D technology such as changes in battery chemistry and quadripolar CRT-D. The comparisons on which the guidance is based are 6 to 8 years old and are rendered out of date by technology that has been introduced since these implantations took place. The comment in recommendation 1.1 that "*ENDURALIFE-powered CRT-Ds have a greater battery capacity and a longer battery life than non-ENDURALIFE powered CRT-Ds*" is based on data that does not include the current battery technology used by other manufacturers and therefore, not sound. **2.** Recommendation 1.3 is not sound. The cost analyses are based on comparisons of ENDURALIFE-powered CRT-D with CRT-D devices that do not feature current technology available to the NHS, or indeed, may no longer be on the market. For example, quadripolar CRT-D has been shown to reduce hospitalisation, reduce the need for	Please see the responses to comments 2 and 3. Please see the response to comment 42.3.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			generator replacement and improve mortality, yet these devices were not available when most of the implantations described in the cited literature took place. This in turn means that the cost analyses do not include comparison of ENDURALIFE-powered CRT-D with these newer technologies. The cost comparisons are therefore not sound or a suitable basis for guidance to the NHS.	

Factors other than battery capacity affect battery longevity

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3	8. Manufacturer	1.1 Page 2	**NICE STATEMENT 1.1:** **ENDURALIFE powered CRTD's have a greater battery capacity and a longer battery life than non-ENDURALIFE CRTD**. Battery capacity is a complex area of engineering and it is not clear if NICE sought advice from appropriate engineering experts with expertise in this area, but only from clinical experts. While the EAC have acknowledged that device longevity is affected by multiple factors the committee have failed to understand the impact that the efficiency of circuitry and innovative developments in battery capacitor technology beyond size can influence device longevity. From the EAC Technical Report; page 2, paragraph 2 "The battery, its capacity and chemistry are only a part of the factors that give the device longevity. The CRT-D contains complex electronics and has many functions. A combination of the amount of stored energy, how it is stored, and how it is efficiently delivered will determine the potential lifetime of the device. The patient's demands on	Thank you for your comment. **EAC response:** Additional factors such as lead technology are separate devices in their own right with CE marks and cannot be considered in a single technology assessment process. The submitted paper (Crossley et al) was assessed by the EAC. It is a large (n=1201 enrolled), prospective evaluation of the Medtronic Attain Performa quadripolar leads, implanted with Medtronic Quad family CRT-D devices. The implant period was Jan 2013-Jan 2014. The EAC concluded that the study did not provide relevant evidence on comparative battery longevity. **EAC response:** The EAC consider that this statement accurately describes the many factors that will influence CRT-D device longevity. Only empirical follow-up reveals CRT-D device longevity in clinical use. Section 3.20 of the guidance summarises the committee considerations of other factors affecting battery longevity.

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			the device will affect the longevity of any device that is actually implanted" Engineering Experts recognise that device longevity is affected by several factors: 1. Battery Capacity 2. Circuit Efficiencies 3. Device Use Conditions (current drain) Devices with inefficient use of circuitry require a larger battery capacity than devices with highly efficient circuitry. Devices with inefficient circuitry use a higher amount of background current to maintain housekeeping activities of the device. Therefore a large battery capacity is not necessarily an indication of improved device longevity versus a device with a smaller battery capacity but highly efficient circuitry. Medtronic devices on the market today have circuitry which operates more efficiently than older generation devices that were available in the time period from 2008 – 2010 and since 2010 to improve device longevity, Medtronic introduced: 1. MECC Model M945899, Hyabrid CFx lithium/silver vanadium oxide cell battery with Tantalum Capacitors (2012), 2. Innovated with new features and algorithms which are shown to increase the predicted longevity of Medtronic devices. These include a. Circuit efficiency b. Quadripolar Leads c. VectorExpress system, d. New telemetry module to reduce battery drain associated with data transmissions for remote monitoring. e. Adaptive CRT	**The committee considered this comment carefully and decided to change section 3.20 to further clarify its considerations on other factors affecting battery longevity.**

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			AdaptivCRT, in addition to improving patient response to therapy, can also increase longevity by reducing the amount of Right Ventricular pacing that is required. Quadripolar leads and vector express system increase longevity by providing additional options for low thresholds and outputs on the Left Ventricular lead. Longevity data for Medtronic CRT-D devices on the market today is presented at the end of this document in Tables 2-6. Projected survival curves have been produced to facilitate comparison to the EAC analysis and sensitivity analyses using the EAC economic model. All CRT-D devices use High Voltage Capacitors to deliver therapeutic shocks. Historically, these required capacitor reformation (charging) at regular intervals to maintain performance and prevent long charge times. Each charge or reformation will typically reduce device longevity by around 1 month and some Devices (not Medtronic new technology) require three to five capacitor remformations per year. Current Medtronic devices have introduced innovative new Tantalum capacitors which do not deform over time, and therefore do not require this regular capacitor reformation. This in turn reduces unnecessary drain on the available battery capacity. Additionally energy requirements are highly related to the quality of the electrical contact between the lead and the heart tissue. Unlike other manufacturers left heart leads, Medtronic Attain Performa quadripolar leads have steroid on each of the 4 electrodes, resulting in lower energy thresholds being needed to achieve successful CRT therapy. We would like to point out the data published from our prospective clinical trial in support of US market authorization of our Medtronic Attain Performa quadripolar	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			leads (Crossley GH, Biffi M, Johnson B et al. Performance of a novel left ventricular lead with short bipolar spacing for cardiac resynchronization therapy: primary results of the Attain Performa quadripolar left ventricular lead study. Heart Rhythm 2015;12:751-8). The minimum average pacing thresholds required to achieve CRT in this study of 1,124 patients were 1.1V±0.8 6 months post-implant. These are substantially lower than the scenarios outlined in device manuals. Our devices add a safety margin on top of that minimum threshold to guarantee CRT delivery as the patient's heart changes. In addition to reported time to battery depletion, we looked at current programming parameters in the UK: Claria Quad systems are on average programmed at 1.94V (lower is better for device longevity) and the impedance of the circuit is on average 661.91Ω (higher is better for device longevity). Please see Figures 4-5 at the end of this document for further information. Our manuals report estimates for 2.0-2.5V and 500-600Ω respectively, highlighting the conservative nature of Medtronic manuals. These developments have had significant impact on choice of device therapy, as in the last twelve months over 80% of all CRT devices and leads sold by Medtronic utilise Medtronic Attain Performa **quadripolar** technology. This is a significant advancement since 2008-2010. These changes in technology (Tantalum Capacitors, highly efficient circuitry, Medtronic Attain Performa Quadripolar Leads, combined with Medtronic specific programmable algorithms), explain the aforementioned updated results of the economic analysis outlined Medtronic's comment number 4. One Expert Advisor acknowledged the improvements in battery capacity by manufacturers in addition to Boston Scientific	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response

			• Correspondence with the Expert Advisors: page 8
			  ○ Dr Ernest Lau: “Apart from changing the battery chemistry, most manufacturers have also increased the total capacity to a level comparable (or even exceeding) the ENDURALIFE battery (around 1.9 Ampere-hours) used by Boston Scientific in its CRTDs”.
			• One Expert Advisor commented on the lack of evidence on the size of battery capacity relating to longevity
			  ○ Dr Chris Plummer: “The technology is promising but robust data are required to substantiate the claims of doubled device longevity - it is not enough to show a doubled battery capacity. Evidence of battery longevity in other manufacturers' current devices is also required to evaluate the relative advantages”
			While the conclusions of the committee on battery life for older devices from 2008 to 2010 are correct, this is not the case for devices available today as there is no published evidence for Enduralife Powered devices currently in use in the NHS. This is highlighted by both the EAC and expert advisors
			• Correspondence with the Expert Advisors. Question 8.3 “How good is this evidence for each of these additional benefits?
			  ○ Dr Chris Plummer: “The technology is promising but robust data are required to substantiate the claims of doubled device longevity - it is not enough to show a doubled battery capacity. Evidence of battery	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			longevity in other manufacturers' current devices is also required to evaluate the relative advantages” • The EAC highlighted in the Assessment Report on page 91 section 6, Implications for research o “There is a lack of evidence for devices that are powered by Enduralife technology and that are currently on the market and for current competitor devices • Assessment Report page 89 section 4.6 o “As device longevity is related to other factors as well as other technology, past performance is not indicative of future results • Correspondence with the Expert Advisors: page 26 o Dr Chris Plummer: “To get accurate battery longevity data requires long follow-up – much longer than the 3-4 years often available. Boston’s data on the performance of their batteries in real life using remote monitoring is persuasive but is essentially an extrapolation until we have “date of device change for battery depletion data” on a large consecutive cohort”	
27	8. Manufacturer	3.19 Page 15	**From section 3.19 page 15 ‘One of the central factors in lifespan is related to the charge a battery is capable of carrying; this has changed little across all manufacturers in the recent past. Compared with others Boston Scientific ENDURALIFE batteries have one of the largest charge ratings’** • The above comments came from clinical expert advisors.	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response

			• However other Clinical Expert Advisors also commented on battery capacity with differing opinions from the above quote:
			
			• Correspondence with the Expert Advisors: page 8
			  ○ Dr Ernest Lau: "Apart from changing the battery chemistry, most manufacturers have also increased the total capacity to a level comparable (or even exceeding) the ENDURALIFE battery (around 1.9 Ampere-hours) used by Boston Scientific in its CRTDs".
			
			• One Expert Advisor commented on the lack of evidence on the size of battery capacity relating to longevity
			  ○ Dr Chris Plummer: "The technology is promising but robust data are required to substantiate the claims of doubled device longevity - it is not enough to show a doubled battery capacity. Evidence of battery longevity in other manufacturers' current devices is also required to evaluate the relative advantages"
			
			In reference to the sentence "One of the central factors in lifespan is related to the charge a battery is capable of carrying; this has changed little across all manufacturers in the recent past" (page 15 point 3.19) this is an incorrect statement. Medtronic has made significant changes since 2012 of which this particular commentator appears not to be aware. Battery capacity is a complex area of engineering and it is not clear if NICE sought advice from appropriate engineering experts with expertise in this area, but only from clinical experts. While the EAC have acknowledged that device longevity is affected by multiple factors the
				Please see the responses to comments 2 and 3.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			committee have failed to understand the impact that the efficiency of circuitry and innovative developments in battery capacitor technology beyond size, can impact on device longevity. From the EAC Technical Report; page 2, paragraph 2 "The battery, its capacity and chemistry are only a part of the factors that give the device longevity. The CRT-D contains complex electronics and has many functions. A combination of the amount of stored energy, how it is stored, and how it is efficiently delivered will determine the potential lifetime of the device. The patient's demands on the device will affect the longevity of any device that is actually implanted. Engineering Experts recognise that device longevity is affected by several factors: • Battery Capacity • Circuit Efficiencies • Device Use Conditions (current drain) Devices with inefficient use of circuitry require a larger battery capacity than devices with highly efficient circuitry. Devices with inefficient circuitry use a higher amount of background current to maintain housekeeping activities of the device. Therefore a large battery capacity is not necessarily an indication of improved device longevity versus a device with a smaller battery capacity but highly efficient circuitry. Medtronic devices on the market today have circuitry which operates more efficiently than older generation devices that were available in the time period from 2008 – 2010 and since 2010, to improve device longevity, Medtronic introduced:	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			3. MECC Model M945899, Hyabrid CFx lithium/silver vanadium oxide cell battery with Tantalum Capacitors (2012), 4. Innovated with new features and algorithms which are shown to increase the predicted longevity of Medtronic devices. These include a. Circuit efficiency b. Quadripolar Leads c. VectorExpress system, d. New telemetry module to reduce battery drain associated with data transmissions for remote monitoring. e. Adaptive CRT AdaptivCRT, in addition to improving patient response to therapy, can also increase longevity by reducing the amount of Right Ventricular pacing that is required. Quadripolar leads and vector express system increase longevity by providing additional options for low thresholds and outputs on the Left Ventricular lead. All CRT-D devices use High Voltage Capacitors to deliver therapeutic shocks. Historically, these required capacitor reformation (charging) at regular intervals to maintain performance and prevent long charge times. Each charge or reformation will typically reduce device longevity by around 1 month and some Devices (not Medtronic new technology) require three to five capacitor remformations per year. Current Medtronic devices have introduced innovative new Tantalum capacitors which do not deform over time, and therefore do not require this regular capacitor reformation. This in turn reduces unnecessary drain on the available battery capacity. Additionally energy requirements are highly related to the quality of the electrical contact between the lead and the	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			heart tissue. Unlike other manufacturers left heart leads, Medtronic Attain Performa quadripolar leads have steroid on each of the 4 electrodes, resulting in lower energy thresholds being needed to achieve successful CRT therapy. We would like to point out the data published from our prospective clinical trial in support of US market authorization of our Medtronic Attain Performa quadripolar leads (Crossley GH, Biffi M, Johnson B et al. Performance of a novel left ventricular lead with short bipolar spacing for cardiac resynchronization therapy: primary results of the Attain Performa quadripolar left ventricular lead study. Heart Rhythm 2015;12:751-8). The minimum average pacing thresholds required to achieve CRT in this study of 1,124 patients were 1.1V±0.8 6 months post-implant. These are substantially lower than the scenarios outlined in device manuals. Our devices add a safety margin on top of that minimum threshold to guarantee CRT delivery as the patient's heart changes. In addition to reported time to battery depletion, we looked at current programming parameters in the UK: Claria Quad systems are on average programmed at 1.94V (lower is better for device longevity) and the impedance of the circuit is on average 661.91Ω (higher is better for device longevity). Our manuals report estimates for 2.0-2.5V and 500-600Ω respectively, highlighting the conservative nature of Medtronic manuals. These developments have had significant impact on choice of device therapy as in the last twelve months over 80% of all CRT devices and leads sold by Medtronic utilise Medtronic Attain Performa quadripolar technology. This is a significant advancement since 2008-2010. These changes in technology (Tantalum Capacitors, highly efficient circuitry, Medtronic Attain Performa Quadripolar Leads, combined with Medtronic specific programmable algorithms	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			, explain the aforementioned updated results of the economic analysis outlined Medtronic's comment number 4. Importantly, because of technological advancements and changes in lead design, Medtronic devices are able to achieve capture at significantly lower voltages than other devices. Specifically, data reported in Crossley et al. 2015 reported that Viva Quad can achieve adequate capture at an average of 1.2V immediately after implantation and 1.1V 6 months after implantation. This explains how Medtronic devices can outperform devices with increased battery capacity – via reduced energy needs. It also speaks to the fact that no single programming profile can be applied across all manufacturers. One Expert Advisor acknowledged the improvements in battery capacity by manufacturers in addition to Boston Scientific • Correspondence with the Expert Advisors: page 8 o Dr Ernest Lau: "Apart from changing the battery chemistry, most manufacturers have also increased the total capacity to a level comparable (or even exceeding) the ENDURALIFE battery (around 1.9 Ampere-hours) used by Boston Scientific in its CRTDs". • One Expert Advisor commented on the lack of evidence on the size of battery capacity relating to longevity o Dr Chris Plummer: "The technology is promising but robust data are required to substantiate the claims of doubled device longevity - it is not enough to show a doubled battery capacity. Evidence of battery	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			longevity in other manufacturers' current devices is also required to evaluate the relative advantages"	
42.1	3. Professional society		2. <u>Determinants of device longevity</u> The evaluation focuses on the sponsor's proprietary "Enduralife" battery design. As recognised by the EAC, *"battery capacity is an important factor … but … it cannot be considered in isolation"*. Even with identical settings and clinical demand (pacing for bradycardia, shocks), other technical factors can be leveraged to affect longevity. These include circuit constructions to minimize the "housekeeping" current use, telemetry, the frequency of capacitor reform and algorithms to minimize unnecessary pacing. In addition to developing new batteries with improved capacity, competing manufacturers have also incrementally improved these factors to significantly improve device longevity. We feel it is inappropriate to highlight one kind of battery technology when the issue is overall device longevity.	Thank you for your comment. Please refer to the responses to comments 2 and 3.
46	8. Manufacturer	General	Medtronic would like to thank NICE for the opportunity to comment on this draft guidance. We are happy for any information contained within our response to be in the public domain. We acknowledge that the committee in arriving at their decisions utilise multiple sources of evidence. We believe, however, the Committee expressed an unsubstantiated opinion in section 6.2 in concluding that "although some of the published evidence relates to devices not currently in use, the recent advances in CRT-D technology are unlikely to negate the benefits of ENDURALIFE-powered battery performance on device lifespan compared with other devices". There are multiple factors which have led to this	Thank you for your comment. Please see responses to comments 2 and 3. **The Committee carefully considered the value of predicted longevity data compared to clinical evidence. The committee concluded published empirical data were likely to be a better measure of future performance than predicted longevity data.**

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			incorrect statement, in our opinion. Firstly, the nature of the decision is underpinned by complex aspects about device electronics and battery chemistry, and we are concerned that these subjects have not been duly investigated. This is important with regard to advances in Medtronic devices since 2010 substantially improving projected longevity of CRT-D devices. A second concern is there was not a single reference within the EAC report or the Consultation documents related to information submitted by Medtronic on July 1st 2016, beyond a blanked out reference to Medtronic Warranty, and no evidence to suggest our information was reviewed. Our submission provided important information about improvements in device longevity with Medtronic CRT-D devices currently marketed in UK, in comparison to the older devices used in studies relied upon by EAC and NICE (which included devices no longer marketed in UK). We note the submission from Boston Scientific included a sensitivity analysis on improvements in longevity in recent devices, however, this greatly under-represented the improvements that have occurred. The EAC was provided by Medtronic with detailed information on technical improvements and improved longevities of our recent devices, and we believe that in the very least these information should have been used to inform further sensitivity analyses. This particular concern about the apparent disregard for the information submitted by Medtronic reinforces our view that the MTG process is not the appropriate pathway for this assessment, which by definition is a comparison of one manufacturer's devices compared to other devices on the market and therefore it required a multiple technology evaluation pathway. This was a concern that Medtronic raised in our response to the draft scope for this appraisal. Lastly, the recommendations in the draft guidance differ from the evaluation of the evidence by the External Assessment Centre and Expert Advisors as recorded in the consultation document.	The EAC technical report collated technical data on CRT-Ds. Manufacturers of CRT-Ds were contacted in June 2016 to help inform this report. Information provided by manufacturers was greatly received, however some of the information provided was out of scope. The assessment report focused on published empirical studies of CRT-D longevity. The EAC considered all submitted data that were within the scope of the evaluation.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			The draft recommendations therefore undermine the credibility of the NICE process and provide draft recommendations that are invalid in the context of current clinical practice. Additionally there is no published evidence for newer Enduralife –powered devices available today Medtronic acknowledge the influence of battery technology in relation to device longevity, this is demonstrated in the product development we undertake and the resultant technologies we have released in the market since 2012. However it is concerning how much emphasis is being placed on longevity when there is clear commentary from many sources within the consultation documents stating that, battery longevity cannot be evaluated in isolation above all else. Other settings such as clinical programming or automatic algorithms (established or recent innovations) have equal or potentially a greater influence on patient outcomes and costs. The goal is to deliver efficacious therapy which impacts on mortality and quality of life rather than extended battery life per se Medtronic provided feedback on the draft scope to highlight these concerns as follows: 1. "If the scope of this guidance is intended to look at clinical outcomes in device patients, then only looking at battery technology is unnecessarily narrow. Features that affect outcomes such as complications, ER visits, admissions, bed days, quality of life, and device-related adverse events are not included in this guidance. Medtronic acknowledges that device longevity can affect these outcomes, but is not the ONLY feature that affects outcomes or provide savings" 2. "As NICE recognizes there has been a step change in battery technology by other manufacturers over recent years the technology under review should be focused on battery chemistry which relates to Enduralife rather than	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			the Enduralife brand. As a consequence of the focus being on the battery chemistry we feel a multiple technology approach is more appropriate to inform the NHS on the correct use of resource." 3. "Acknowledging that the MTG takes a single technology approach we question whether any guidance produced could be considered valid. We are happy to participate in a multiple approach if NICE deems this appropriate" 4. "Medtronic agrees in your assessment that longevity is an important factor in providing better outcomes to device patients, but is not the only factor, and it is our hope that the committee will include in this discussion other features that improve clinical outcomes. " 5. "This includes therapies and features that increase clinical response to CRT (such as Medtronic's exclusive AdaptivCRT algorithm, decrease painful unnecessary shocks (such as Medtronic's exclusive SmartShock technology), and clinically oriented device diagnostics (such as Medtronic's exclusive OptiVol fluid status monitor), among other features." 6. "Battery longevity in isolation provides limited patient benefits for the condition for the treatment of patients with Heart Failure. Features that promote effective delivery of treatment by their nature can consume battery so we encourage that the discussion should be broader than the battery chemistry alone accepting that trade-offs may occur." Given the recommendations highlighting savings for the NHS, we are concerned that the MTEP methods prevent full explorations of the scenarios from all the manufacturers i.e The absence of a multiple technology approach within	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			the MTEP process, or one in which all manufacturers could present their most contemporary data for full review by the assessment group and for the committee scrutiny. Therefore we do not believe the recommendations in the draft, related to savings would ever be realised, given the use of historical data, notwithstanding these legitimate and evidenced concern's the dynamic nature of innovation within the device sector makes the validity of such claims likely to be outdated on publication. We note that some Expert Advisors stated they were unable to take up Warranty Claims for device malfunctions as systems were not in place within their NHS Trusts to enable this reimbursement. All suppliers are organised to assess and recompense all legitimate warranty claims irrespective of NHS trust process. Where national registries are available and are suitably resourced and funded we would encourage public disclosure of all data contained in the registry that improves patient outcomes and resource allocation in line with other geographies	

Cost modelling

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
9	8. Manufacturer	1.3 Page 2	**"Based on an average selling price of £12,404 across different devices, ENDURALIFE-powered CRT-Ds will save an estimated £2,120 to £5,627 per patient over 15 years as compared with other CRT-D devices through a reduction in the need for replacement procedures. This could save the NHS in England £6 million over 5 years."**	Thank you for your comment. One of the agreed condition under which consultees can request a copy of the executable model is that it only be re-run for the purpose of testing of its reliability and informing consultee's understanding of the Medical Technology Consultation Document (MTCD). Any results derived by

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			Following our request, Medtronic has received a copy of the model used for this guidance on 16th November 2016 which gave a short amount of time to audit the model and collect data to populate it appropriately. We have populated the model with two separate sets of updated device generator survival data per annum. The first was generated from a sample of 2,063 Viva XT Quad™, 179 Claria™ Quad, and 100 Claria™ Quad with AdaptivCRT™ turned on active CRT-D devices implanted in the UK. These devices represent the current Medtronic commercial offering in the UK. Please see Figure 3 and Table 6 for further information on the projected longevities for these devices *(provided in the supplementary email sent by Medtronic as part of this consultation)* The second set was generated from a sample of 51,885 active Viva XT™ devices, 25,005 active Viva XT™ devices with AdaptivCRT™ turned on and 9,897 active Viva Quad™ devices with AdaptivCRT™ turned on across the United States. This dataset represents a substantial amount of patients receiving generators that were also available in the UK in the preceding years and after the Consulta devices the EAC model used were obsoleted. Please see Figure 1 and 2, Tables 4 and 5 for further information on the projected longevities for these devices *(provided in the supplementary email sent by Medtronic as part of this consultation)* All data were obtained by auditing the remote management system (Medtronic CareLink Network Service, NICE MIB 64), a system similar to the Latitude system operated by Boston Scientific that has been used for publications referenced in this guidance. When the provided economic model from the EAC is populated with the generator survival projections of current UK Medtronic CRT-D commercialised models, the model	editing the model with new parameters are not admissible as comments.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			results reverse and demonstrate savings with Medtronic devices over Enduralife. Over 15 years, Medtronic savings compared to Enduralife, are £1,192.50, £1,702.13 and £1,940.71 depending on device used. The newest Medtronic models achieve most savings. In addition, when the provided economic model from the EAC is populated with the generator survival projections of Medtronic CRT-D models currently commercialised in the United States, the model we received reverses with Viva XT and Viva Quad with AdaptivCRT™ turned on, generating a saving of £164.74 and £934.11 respectively over Boston Scientific Enduralife devices. For Viva XT only (no AdaptivCRT™ turned on, or Viva Quad) savings with Enduralife over 15 years fall to £3,115.64 per patient (instead of the calculated £5,627) The difference in savings between the US and the UK can be attributed to a technology lag in the US. Viva Quad devices were not available in the US until March 2014 and the Claria CRTD is yet to be launched in the US Medtronic have submitted the model populated with this data and further details on the generator survival in a supplementary email as part of our submission, as the on line comments form is only able to accept text (agreed by NICE). Medtronic also repeats the note that most devices currently sold in the UK are Claria Quad with AdaptivCRT™ turned on. The above sensitivity analysis using the EAC economic model is predicated on the projected longevities of UK Medtronic CRT-D devices from live implanted devices that are registered on the remote patient management Carelink system. Supporting evidence for the validity of these projections is presented at the end of this document in Figure 1 and Table 4 (validity of Consulta projections), in	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			Figure 2 and Table 5 (validity of Viva projections) *(provided in the supplementary email sent by Medtronic as part of this consultation)* Furthermore, in Figures 4 and 5, *(provided in the supplementary email sent by Medtronic as part of this consultation)* we present data on current device programming from live implanted devices in the UK which explain and prove how part of the improvements in longevity have been obtained, through lower mean pacing amplitude voltages and higher mean pacing impedance thresholds.	
31	9. Manufacturer	5.11 – 5.25 Page 21-25	We are disappointed that the additional work by the EAC (pages 21 to 24) appears to have omitted non-cost related outcomes. As per the final scope issued by NICE, non-cost related outcomes such as number of admissions/replacement procedures per patient are key result to reflect the impact on patients and provider capacity of performing procedures. For example, in our sponsor submission, we found that using Medtronic and St Jude Medical CRT-Ds would result in more than 5 times and 4 times as many replacement procedures respectively when compared with using ENDURALIFE-powered CRT-Ds. For example, the list price analysis described in section 5.17 and the cost threshold analysis described in section 5.25 performed by the EAC do not present these additional non-cost results which could unintentionally imply that reducing device cost will mean the results are comparable (as indicated in the threshold analysis) where in reality the non-cost impact will remain regardless of the price difference between devices. We feel this could be viewed as misleading and would request that this point is clarified in the final guidance document.	Thank you for your comment. **EAC response:** The EAC did not manipulate the replacement probability data within the company's model as it was considered they were based on the empirical data. The EAC emphasised the probability of replacement could depend on the time horizon and that the time horizon should relate to patient life expectancy. These factors were not varied in the company's model so the EAC sought patient survival data from NICOR. The additional threshold analysis carried out by the EAC was at the request of the Committee. **The committee believe that the summaries of the clinical effectiveness and resource savings are reasonable interpretations of the submitted evidence.**

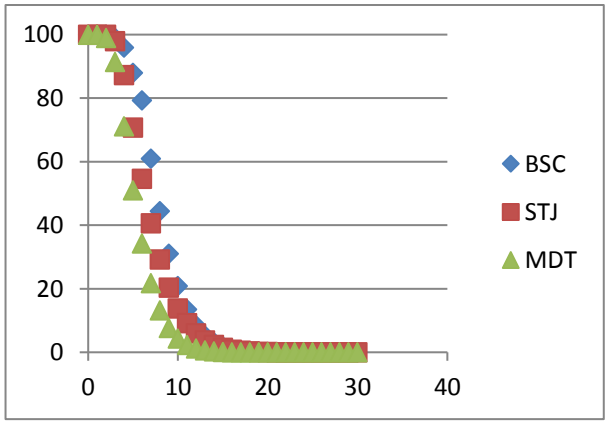
<table>
<tr><th>Com. no.</th><th>Consultee number and organisation</th><th>Sec. no.</th><th>Comments</th><th>Response</th></tr>
<tr><td>32</td><td>9. Manufacturer</td><td>5.14
Page 22</td><td>We note that the EAC have used an incorrect HRG when applying reference costs to the economic modelling (assessment report, page 72). As we have already highlighted to the EAC, replacement CRT-D procedures are reflected under HRG EY02 in the 2014/15 reference costs (relating to OPCS code K594; as confirmed by NHS Digital's Grouper application) and are not related to HRGs EY10 or EY09. The correct cost for replacement CRT-D procedures in the 2014/15 reference costs is £13,198.27 vs the figure of £2,864.01 used by the EAC. Unfortunately it appears that this has not been corrected and means the input costs for replacement CRT-D procedures using reference costs are incorrect and therefore the results in section 5.14 are also incorrect. We are concerned that this error means that the economic benefits of longer lasting devices is significantly underestimated in the guidance document and request that this is corrected as a priority before publication of the final guidance.</td><td>Thank you for your comment.

The analysis behind the figures presented in the consultation document (section 1.3, page 2) used the company's base case model inputs with changes limited to the following:

<table><tr><td>Patient survival</td><td>NICOR data, all patients aged 50-84 fitted with Weibull and extrapolated to 15 years</td></tr><tr><td>Device survival</td><td>Extrapolation using comparator survival profile</td></tr><tr><td>Device price</td><td>average selling price as per company base case</td></tr></table>This means the analysis above uses the PbR tariff for CRT-D replacement procedures used by the company in their original model. The hospital costs for replacement of CRT-D in the analysis leading to the results presented in section 1.3 of the consultation document are as per the company's base case model which was £4,700, for the replacement procedure.</td></tr>
<tr><td>33</td><td>9. Manufacturer</td><td>5.2
Page 23</td><td>We welcome NICE's engagement with NICOR in order to further improve the cost modelling for this guidance.</td><td>Thank you for your comment.</td></tr>
<tr><td>34</td><td>9. Manufacturer</td><td>5.22
Page 23</td><td>We would welcome further information as to exactly how the EAC extrapolated 6-year CRT-D survival data out to 15 years for both ENDURALIFE-powered CRT-Ds and non-ENDURALIFE powered CRT-Ds. We feel this is not entirely clear from the current description.</td><td>Thank you for your comment.

This analysis was performed at the request of the committee.

EAC response: The EAC found that the Company's model format did not permit simple manipulation to enable a longer time horizon to be modelled. Due to this the EAC revised the relevant functions of the Company's model for</td></tr>
</table>

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
				the purpose of extrapolation beyond the original six year time horizon. The EAC extrapolated the CRT-D longevity data reported by Landolina et al. 2015 to predict CRT-D longevity up to 30 years (i.e. the same degree of extrapolation employed by Yao et al. 2007) using a survival profile for comparator devices. This takes an average distribution based on Medtronic and St Jude Medical CRT-D longevities reported in Landolina et al. 2015, and then applies the average distribution to the Enduralife-powered CRT-Ds from the point at which the Enduralife-powered CRT-Ds begin to reach ERI, at five years following implantation. Figure: Average comparator distribution extrapolation to 30 years of CRT-D longevity data (Landolina et al. 2015): % of CRT-Ds that have not reached ERI (y axis) over time (years, x axis), by device manufacturer  The EAC considered that there is high uncertainty around the extrapolation of the CRT-D longevity data and concluded that a fifteen year time horizon represents the

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
				optimal compromise between representing the life expectancy of patients and retaining some confidence in the extrapolated CRT-D longevity values.
42.3	3. Professional society		3. Time horizon considerations As acknowledged in the report, the time horizon is critical in examining treatment cost. The 6 year time horizon used in the initial analysis happens to significantly favour Boston Scientific models included over contemporary comparators, as most of the former would not have required replacement, while most of the latter would. Horizons of 4 or 8 years would have given very different results. As noted by the EAC *"the choice of a 6 year time horizon potentially exaggerates the cost saving of a slightly longer lasting device."* NICOR data submitted in confidence indicates that CRT-D patient survival >6 years is common. Unfortunately, the rapid changes in device technology mean that extension of the cost model beyond 8 years (when most implants will have replaced by models 2-3 generations more advanced), cannot be realistic, making such an analysis problematic.	Thank you for your comment. Please also see the response to comment 2 and 3. **The committee considered this comment carefully and decided not to change sections 5.20 to 5.25 or 5.26 to 5.28 of the guidance.** These summarise the additional work done by the EAC to address the uncertainty of a 6 year time horizon; sections 5.26 to 5.28 summarise the committee's considerations on the cost modelling.
42.4	3. Professional society		4. Acquisition costs The EAC recognized that *"the purchase price of the device is a key driver of the cost model"*. Unfortunately, the advent of national procurement during the current financial year is likely to disrupt the market to such an extent that the purchase price comparisons in the appraisal are likely to become obsolete. We can only suggest that purchase price differences be excluded from modelling (i.e. a uniform cost of say, £10,000 be assumed). This would still permit the effect of device longevity on cost to be examined.	**The committee considered this comment carefully and decided not to change sections 5.26 to 5.28 of the guidance.**

Matters of fact or clarity

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
4	9. Manufacturer	1.1 Page 2	We are pleased that the committee have acknowledged the greater battery capacity of ENDURALIFE-powered CRT-Ds and the contribution that this can make to device longevity. We would suggest that the guidance is amended to clarify this further by referencing '**usable** battery capacity'. Usable capacity is the capacity available for the system to use during its lifetime and is defined as the capacity from Beginning of Service (BOS) to Elective Replacement Indicator (ERI)/Recommended Replacement Time (RRT). There is a small amount of battery capacity used prior to BOS during the manufacturing and storage process. Similarly, there needs to be some capacity left in the device once it is indicated for replacement (ERI/RRT) before it stops functioning (e.g., while clinicians schedule the replacement procedure; all manufacturers state a three month period between ERI/RRT and the end of the device service life). The capacity that different CRT-Ds require for pre-implantation and to sustain the device for the final 3 months vary. For this reason, comparing the actual usable capacity of the devices while they are in service may also be helpful here.	Thank you for your comment. The EAC stated that usable capacity is a valid parameter, information on which is available for all CRT-Ds. It can be seen as a refinement of 'battery capacity'. Battery capacity was term used in the EAC technical report, however the capacity stated as the main figure for each manufacturer is not always the capacity measured over the same period. The EAC addressed this by stating the periods used, and adding additional information where available, so that the capacity from beginning of service to end of service was available for all devices. **Following expert advice, the committee decided to amend section 3.18 of the guidance to refer to 'usable battery capacity'.**

<table>
<tr><th>Com. no.</th><th>Consultee number and organisation</th><th>Sec. no.</th><th>Comments</th><th>Response</th></tr>
<tr><td></td><td></td><td></td><td>For information, the usable capacity for the latest generation CRT-D devices from different manufacturers is as follows:

<table><tr><td>Manufacturer</td><td>CRT-D models</td><td>Usable capacity (BOS to ERI/RRT)*</td></tr><tr><td>Boston Scientific</td><td>Autogen/Inogen/Dynagen/Origen</td><td>1.8Ah</td></tr><tr><td>Medtronic</td><td>Claria/Amplia/Compia</td><td>1.0Ah</td></tr><tr><td>St Jude Medical</td><td>Unify Assura/Quadra Assura/Quadra Assura MPP</td><td>Not available</td></tr><tr><td>Sorin</td><td>Platinum/Platinum SonR</td><td>1.53Ah</td></tr><tr><td rowspan="3">Biotronik</td><td>Inventra 7</td><td>1.59Ah</td></tr><tr><td>Itrevia 7/Iperia 7</td><td>1.6Ah</td></tr><tr><td>Itrevia 5/Iperia 5</td><td>1.39Ah</td></tr></table>
* Device technical manuals</td><td></td></tr>
<tr><td>7</td><td>9. Manufacturer</td><td>1.2
Page 2</td><td>While we appreciate that NICE have a standard format for phrasing their recommendations, we believe the current wording could be misconstrued by readers. At a recent meeting with ****** ******* from NICE’s adoption and impact team, we were advised that a positive Medical Technology guidance can be referred to as ‘NICE recommends’ in press releases. We would like to question whether it would be possible to include this approved wording within section 1 also, to clarity that this draft recommendation is positive.</td><td>Thank you for your comment.

The guidance wording follows a standard format. The content of media releases is routinely discussed between the company and the NICE communications team.</td></tr>
<tr><td>11</td><td>9. Manufacturer</td><td>2.1
Page 3</td><td>We would like to note that lithium manganese dioxide battery chemistry is not only “claimed” to be less susceptible to the variations in voltage and resistance associated with early battery depletion but has been demonstrated as such: Root (2008)** found Li/MnO2 batteries exhibited predictable voltage behaviour and low internal resistance throughout their operational lifetime. We propose this statement is changed to read “… lithium manganese dioxide (Li/MnO2) battery chemistry, which has</td><td>Thank you for your comment.

EAC response: there are potentially many factors that could influence variations in voltage and resistance, not only the battery chemistry.

The EAC assessed the study by Root et al. (2008) which is a summary of battery development. It is a well laid out, clearly written peer reviewed article, however it does not present any original research. There is a graph presented showing the capacitor charge times versus time from</td></tr>
</table>

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			been shown to result in predictable voltage behaviour thereby reducing the risk of early battery replacement." **Root. J. of Cardiovasc. Trans. Res. (2008) 1:254-257.	implant for three different battery types. The graph shows Li/SVO batteries to have a less uniform capacitor charge time over their life than either Li/MnO_2 or Li/CF_x-SVO batteries (which are represented by the same line). There is no information presented on the batteries tested, test protocol, or how the information was obtained. The EAC conclude that this article does not provide relevant evidence on comparative battery longevity.
12	9. Manufacturer	2.1 Page 3	We would like to highlight that the EAC reported in their 'ENDURALIFE Technical Report' (addendum to assessment report; page 2) that "Comparison of device volumes based on data available in the device manuals showed that ENDURALIFE-powered CRT-D devices have a smaller volume compared to currently available non-ENDURALIFE powered CRT-D devices." The smaller size relative to other CRT-D devices is not a claim, as is indicated in the consultation document. We would request this is corrected in the final guidance document to clarify this.	Thank you for your comment. The technical report also states "The comparison does not give information on the clinical significance of the smaller size." **It is acknowledged that this is not a claimed benefit and the guidance has been amended.**
13	9. Manufacturer	2.3 Page 3	We would like to note that the statement "ENDURALIFE-powered CRT-Ds cost £12,404" is factually incorrect. We did not state this anywhere in our company submission. The mean cost of £12,404 for a complete CRT-D system and £11,858 for a replacement implantable pulse generator only (excluding leads) was assigned in our de novo economic model for both ENDURALIFE-powered CRT-Ds and comparator CRT-Ds in the de novo economic model to reflect an average industry price. We feel the current wording may be misleading and would request it be rephrased to ensure clarity.	Thank you for your comment. **The Committee decided to change section 2.3.**

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
14	9. Manufacturer	2.7 Page 5	We welcome the reference to NICE's medtech innovation briefing on the LATITUDE NXT remote monitoring system. For transparency, we feel it may be helpful to mention here that the LATITUDE NXT system is compatible with Boston Scientific's devices only.	Thank you for your comment.
15	9. Manufacturer	3.2 Page 6	We would like to highlight that the "20 studies (17 observational studies and 3 systematic reviews)" that were submitted highlight patient preference of size versus longevity of CRT-Ds as well as complications associated with replacements. The patient preference element has been omitted in the description here.	Thank you for your comment. This has been amended.
16	9. Manufacturer	3.2 Page 6	We would like to note that the 6 observational studies mentioned are described in 7 published studies. We feel it may be helpful to reference Alam 2014 in addition to the other 6 publications for clarity.	Thank you for your comment.
17	9. Manufacturer	3.3 Page 7	We kindly request the mention of the ENDURALIFE brand is corrected to ensure it is appropriately referred to as follows: "…51 had a non-ENDURALIFE **powered** Boston Scientific device…"	Thank you for your comment. This has been amended.
18	9. Manufacturer	3.7 Page 9	We note that there is a small error in the p value reported in the final sentence of section 3.7, which should read "airwise comparisons showed a significant difference between Boston Scientific and St Jude Medical (p=0.0018) and between Boston Scientific and Medtronic (p<0.0001)."	Thank you for your comment. The error has been amended.
19	9. Manufacturer	3.8 Page 10	We note that there is a small error in the description of the Williams 2014 abstract in section 3.8, which should read either "A total of 90 patients with CRT-Ds were implanted" or "A total of 91 CRT-Ds were implanted".	Thank you for your comment. This sentence has been amended.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
20	8. Manufacturer	3.9 Page 10	**"However, it judged that data in the PPRs could not be used to compare the lifespan of ENDURALIFE-powered devices with that of other devices."** Medtronic is aware of limitations of PPRs and the lack of comparability between the PPRs between manufacturers. We would like to note, in defence of our PPR estimates, that the data in the Consulta CRT-D PPR closely match (if not identical) with the data independently provided by Landolina et al. 2015 and used in this assessment. We believe this validates Medtronic PPRs' ability to accurately report normal battery depletions – please see Figure 1 and Table 4 which demonstrates this point *(provided in the supplementary email sent by Medtronic as part of this consultation)*	Thank you for your comment. **The committee considered this comment carefully and decided not to change the guidance.**
21	9. Manufacturer	3.9 Page 10	We would like to note that product performance reports (PPRs) are based both on data derived from devices that have been replaced and returned to the manufacturer and manufacturer tracking (e.g., for devices removed but not returned to the manufacturer). As we discussed with the EAC, in addition to returned devices, we may label a device as being out-of-service if we receive record from a BSC employee (sales representative), a healthcare provider, a patient, or a family member, as well as if it is returned to us.	Thank you for your comment. This has been amended.
22	9. Manufacturer	3.11 Page 11	We note that there are two small errors in the results reported from Polyzos 2015 in section 3.11, which should read "The pooled OR for the risk of infection associated with generator change (20 studies; 33,322 patients) was 1.74 (95% CI 1.22 to 2.49). Device replacement/revision was associated with a pooled OR of 1.98 (95% CI 1.46 to 2.70) for infection."	Thank you for your comment. This has been amended.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
23	9. Manufacturer	3.15 Page 14	We welcome the inclusion of the Kirkfeldt study as an additional source of evidence that we did not identify in our original submission. We believe it may be helpful in the summary to include additional information on the infection rates for new implants and generator replacements (0.6% and 1.5% respectively) as this is referenced by the EAC analysis later in the document in section 5.11.	Thank you for your comment. **The committee chose to include in section 3.15 additional information on the infection rates for new implants and generator replacements.**
24	8. Manufacturer	3.17 Page 14	**From section 3.17 page 14 "the EAC noted that the PPR's submitted by the company demonstrated that for the majority of CRTD's, it is normal battery depletion that leads to CTRD replacement, and not device malfunction"** While normal battery depletion is the most common reason for device replacement, the impact of device malfunction should not be underestimated and is the second most common reason for device replacement. Importantly the increased cost associated with device malfunction can negate any potential savings and we note the EAC has not taken into account the device malfunctions in the economic model. We suggest the committee re-visit the Assessment Report on pages 58 to 61 referencing device malfunctions in particular the advisory highlighted by the EAC in the Assessment report on page 59 to 60 where Enduralife devices have been subject to 5,086 device related advisories including adverse events for premature battery depletion due to a problem with a low voltage capacitor issue affecting 1,885 patients in the UK with a prevalence of 2%.	Thank you for your comment. **EAC response:** The EAC is not aware of any evidence for large differences in device malfunctions between manufacturers or any trend. The EAC checked its intended statement on adverse events with clinical experts who supported the statement. The 2% prevalence referred to on p59-60 of the Assessment Report is taken from MDA/2014/039 and means 2% of the original advisory population which was a subset of Boston Scientific COGNIS™ CRT-Ds and TELIGEN™ ICDs. The EAC judge that these data in isolation are insufficient to conclude that there is a significant and lasting difference in malfunction rates between CRT-D suppliers. Section 4.5 of the guidance highlights expert's opinion that, despite battery life being an important patient benefit, it is standard practice for a single centre to use CRT-Ds from more than one manufacturer. The rationale is to spread the risk of undue pressure on clinical services in the face of possible future device-related technical failure necessitating recall and replacement. **The committee decided not to change the guidance.**
25	9. Manufacturer	3.18 Page 15	We believe it may be helpful to add a reference here to the discussion by the committee and experts relating to the comparative lack of published literature from some manufacturers (e.g., LivaNova/Sorin, Biotronik) and newer	Thank you for your comment. **The Committee revised section 3.18 to further clarify its considerations.**

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			generation devices from all other major manufacturers. Since newer generation devices was a concern raised by the committee to the EAC (as per question 2, page 2, ENDURALIFE Technical Report addendum to assessment report) we feel that it may be helpful to explicitly state the committee's views on this area and would propose to add the following statement to the end of section 3.18: "However, clinical experts advised that the company's claims relating to battery life and the ENDURALIFE [battery] technology have been borne out in the published literature and their own clinical practice, **unlike non-ENDURALIFE powered CRT-D devices which do not yet have such evidence**."	
26	9. Manufacturer	3.18 Page 15	We would like to note that the ENDURALIFE brand refers to the battery technology and would propose the reference here is changed to read "the ENDURALIFE battery technology"	Thank you for your comment. This has been amended.
28	9. Manufacturer	3.19 Page 15	As per our previous comment, we suggest that comments on the battery capacity refer to usable battery capacity so as to reflect actual real-world performance. We would also like to highlight that the ENDURALIFE brand refers to the battery technology, not only the battery. We propose that the final sentence of this paragraph is changed to read: "Compared with others, Boston Scientific's ENDURALIFE-powered CRT-Ds have the largest usable capacity (charge rating)."	Thank you for your comment. Please see the response to comment 4. The sentence will be amended to refer to ENDURALIFE battery technology appropriately.
29	9. Manufacturer	4.4 Page 17	We would like to note that telemonitoring and remote monitoring features affect battery drain differently depending on manufacturer, since the way this feature is powered can vary. We would propose this is clarified in the document as follows "telemonitoring and remote monitoring affect battery drain across all manufacturers devices, but this drain is different depending on the manufacturer."	Thank you for your comment. The EAC feel the statement in the consultation document is accurate as it is but if the statement is to be amended, "and this drain may differ depending on the manufacturer". **The committee decided to change section 4.4 to separately describe telemonitoring and remote monitoring.**

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
30	9. Manufacturer	5.11 Page 21	We would like to highlight that the infection rate figure of 0.6% from Kirkfeldt 2014 refers to the infection rate for new implants only. We would recommend this bullet point is clarified to make clear the EAC analysis changed this infection rate input for new implants only.	Thank you for your comment. The sentence will be amended.

Other

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
5	9. Manufacturer	1.1 – 1.3 Page 2	We agree with the recommendations made in the draft consultation document and are pleased that both the clinical and economic benefits that CRT-D devices with longer longevity can offer to patients and the healthcare system have been recognised.	Thank you for your comment.
42	3. Professional society	General	This document was prepared on behalf of BHRS Council and has been read and approved by its Consultant Cardiologist and Physiologist members. ***Introduction*** We support the view of the Medical Technologies Advisory (MTA) Committee that device longevity is an important consideration in selecting devices for delivering cardiac resynchronization defibrillator (CRT-D) technology because of cost considerations and the complications associated with device replacement. However, it is not the sole factor in determining device choice and other technical advances (see 4 below) may be equally important for some patients. We fully accept the findings of the evaluation, that the CRT-D devices with “Enduralife” battery chemistry that were examined showed significantly better longevity than *contemporary* competitors. However, we have serious	Thank you for your comment.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			concerns that the conclusions expressed in the consultation document have understated or simply ignored important reservations expressed by the EAC and others. We would strongly urge the Committee to consider qualifying their conclusions, which may otherwise have deleterious and unintended consequences for procurement and for patient care. Our concerns are as follows.	
42.5	3. Professional society		1. <u>Diversity of procurement as a hedge against the risk of faults</u> As currently written, the current appraisal might be seen as a wholesale endorsement by NICE of Boston Scientific CRT-D products to the exclusion of competitors. The consultation document notes that *"despite battery life being an important patient benefit, it is standard practice for a single centre to use CRT-Ds from more than one manufacturer. The rationale is to spread the risk of undue pressure on clinical services in the face of possible future device-related technical failure necessitating recall and replacement.*" Over the last two decades all three major manufacturers have had ICD/CRT-D generators and/or leads subject to major advisories and recalls, sometimes years after the models came to market. Although any clinical harm from system faults has statistically been very small in comparison to the therapeutic benefit, these advisories have incurred considerable distress for patients, a huge workload for centres and not infrequently actual clinical harm related to device revision/extraction procedures. To mitigate the risk of 100% of patients being affected by a recall/advisory, a degree of diversity in procurement of these devices is therefore a well-established principle in all larger centres in the UK, as noted in Section 4.5 of the Consultation Document, but not in the conclusions.	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			We note that the recently-created National Procurement department, which has very little clinical input, has expressed interest in this appraisal. We are concerned that the simple conclusions in the consultation document might, in the extreme case, result in 100% procurement from a single manufacturer. This would be counter to good practice clinically and would be a very risky step.	
42.6	3. Professional society		***Summary*** The improvement in CRT-D device longevity introduced by Boston Scientific has been very welcome and set a new bar which the rest of the industry has followed and to a large extent, met. While acknowledging the excellent work of the External Assessment Centre and the MTA Committee, we believe that the appraisal can only be applied with great caution to the choice of CRT-D devices currently on the market. We are concerned that the conclusions expressed in the consultation document are oversimplified and possibly even misleading in relation to current models, and should therefore be qualified. Otherwise, observations of obsolete models may inform inappropriate and potentially risky procurement decisions for years to come. This document has been read and approved by: Dr Mark Earley (Treasurer, BHRS) Consultant Cardiologist, St Bartholemew's Hospital, London Dr Dr Dhiraj Gupta (Council Member, BHRS) Liverpool Heart and Chest Hospital Prof Pier Lambiase (Research Lead, BHRS) University College, London	

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			Prof Nick Linker (President, BHRS) Consultant Cardiologist, James Cook University Hospital, Middlesborough Dr Martin Lowe (Adult Congenital Lead, BHRS) Consultant Cardiologist, St Bartholemew's Hospital, London Dr Francis Murgatroyd (CRM Audit Lead, BHRS/NICOR) Consultant Cardiologist, King's College Hospital, London Dr Kim Rajappan (Council Member, BHRS) Oxford University Hospitals Prof Richard Schilling (President-Elect, BHRS) Consultant Cardiologist, St Bartholemew's Hospital, London Dr Alistair Slade, Secretary (Secretary, BHRS) Royal Cornwall Hospitals, Truro	
43	5. Manufacturer	General	**Has all of the relevant evidence been taken into account?** 1. The referenced work by Lau et al (2015) and Williams and Stevenson (2014) are both abstracts rather than full publications. Is the Institute certain that abstracts are reliable? Is it normal practice to use abstracts rather than peer-reviewed publications? 2. The Williams and Stevenson (2014) abstract includes 90 CRT-D implantations, yet earlier in the consultation document, data reported by Landolina et al (2015) were excluded on the basis that there were fewer than 100 implants. In order to be consistent, the Williams and Stevenson data should also be rejected for this reason, as well as point 1 above.	Thank you for your comment. Medical technologies guidance uses the best available published or unpublished evidence which is systematically assessed for quality and relevance. Both the company and EAC placed greater emphasis on fully reported, published studies in peer-reviewed journals. Abstracts were included in the company's submission therefore a reference to them was made in the assessment report, stating that they are abstracts. The data from the abstracts are not used in the cost model. The EAC assessed the two Behar et al. studies (2015 and 2016). The EAC consider this UK 3 centre registry study and subsequent economic analysis to be outside of the guidance scope.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			3. Point 3.19 in the consultation document notes that "*The committee heard from clinical experts that battery depletion depends on a number of factors including the needs of the patient, lead technology, battery design and the algorithms used in the CRT-D*." We do not see an attempt to control for these factors and to ensure like-for-like comparisons or indeed, comparisons with contemporary CRT-D devices. In fact, UK data published by Behar et al (2015 and 2016) shows a reduction in hospitalisation, reduction in generator replacement and an improvement in mortality in patients who had a quadripolar lead implanted, rather than a bipolar lead. As the clinical experts have testified, lead technology is also an important factor. The evidence review has not considered the impact of these other factors – ie does the proposed ENDURALIFE benefit disappear in the context of newer CRT-D improvements - such as recent battery improvements and quadripolar lead technology?	
43.1	5. Manufacturer		**Are the summaries of clinical effectiveness and resource savings reasonable interpretations of the evidence?** 4. The Ellis (2016) paper is cited as evidence for the benefit of battery longevity. However, we note that the paper also cites mortality to be 28% for Boston Scientific devices, 21.8% for Medtronic and 16.7% for St Jude Medical devices. Two points arise from this: o Outcomes, of which mortality is the highest priority, are important to patients and the NHS. The recommendations make no reference to this apparent mortality disadvantage. What steps have been taken	Thank you for your comment. Mortality is an outcome measure in the scope. The mortality data reported by Ellis (2016) were cited in the EAC assessment report which was provided to the committee. No direct claimed benefits related to mortality were made by the sponsor.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			to consider mortality in this guidance – particularly as mortality was a key driver in TA314. o One of the claimed benefits of ENDURALIFE-powered CRT-D is that "*reduction in the number of replacement surgeries can reduce the risk of complications which is higher in replacement procedures than in de novo (initial) implant procedures. The increased risk of complications and infections can have a measurable impact on morbidity and mortality".* If the claimed relationship between battery life and mortality is reliable, then patients treated with ENDURALIFE-powered CRT-D would be expected to show a survival benefit. The Ellis data (which reports mortality) does not show a survival benefit to ENDURALIFE-powered CRT-D, hence this claim cannot be upheld. 5. Point 3.16 in the consultation document states that "*however some of the CRT-Ds studied in the longevity studies, particularly for comparator devices, may no longer be marketed*." This is supported by point 3.18: "*It was noted that some of the studies the committee had considered included CRT-Ds no longer in use.*" This is particularly concerning. If some of the comparator devices are no longer available, then the comparisons are flawed and the conclusions are in turn, not sound. Recommendations to the NHS should not be made on the basis of comparisons with devices that are no longer available. 6. Even if the Lau study is considered, it should be noted that both the Lau and Landolina studies did not compare ENDURALIFE batteries with St Jude	Please also the responses to comment 2 and 3

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			Medical's current SVO/CFX technology. MnO_2 batteries have approximately 15% lower energy density compared to SVO/CFX batteries which would therefore require a larger battery volume to accomplish the same longevity. Claims suggesting the largest battery should not be considered without noting the corresponding energy density. 7. We have seen no evidence that ENDURALIFE batteries reduce hospital admissions, or bed-days compared with non-ENDURLIFE CRT-D devices. This relationship has been implied, but not proven.	No direct evidence was presented or assessed on hospital admission avoidance or length of stay.
43.3	5. Manufacturer		**Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?** 8. No.	
44	6. Department of Health	General	Thank you for the opportunity to comment on the evaluation programme documents for the above medical technology. **I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.** Many thanks and best wishes	Thank you for your comment.
45	7. Professional group	General	The national device audit is the first in the world and holds records on virtually all cardiac implantable electronic device implants in the UK in the last four decades (recent correlation with market data supplied by EUCOMED shows agreement of >99.9% with devices sold in 2014-15). We welcome the notion of surveying real world longevity (for ICDs as well as CRTD devices): this is extremely important for all the reasons mentioned in the consultation	Thank you for your comment. **The Committee amended section 3.19 to add their support to these data on comparative battery longevity being made publically available.**

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			document. It is inevitable that studies of actual (rather than predicted) longevity will be "dated" by the time they appear as the models studies will have been superseded. However, a programme of rolling and (hopefully) timely reporting of device longevity could be of even greater value than a one-off exercise such as the current appraisal of Enduralife devices implanted around 2005-10. We would like to set up such a programme, perhaps initially reporting every 2 years but eventually "live". However, we do not currently have the resources for the substantial cleaning of historic data and the analytic task required. Unfortunately this is not a priority of HQIP that currently commissions our reports. We would welcome the opportunity to work with NICE and/or MHRA on such an ongoing project.	
47	8. Manufacturer	General	Medtronic has sent supplementary information by email containing tables and figures with a publication to support our comments.	Thank you for your comment.
48	8. Manufacturer	General	Medtronic Device Longevity Information	Thank you for your comment.

Table 2: Additional editorial comments

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
49	4. EAC	2.4 Page 4	Last but 1 bullet cites £33 million saving. We suggest a fuller explanation of what this is.	Thank you for your comment. This figure came from the company as part of their claimed benefits.
50	4. EAC	3.9 Page 10	Currently reads "However, it judged that data in the PPRs could not be used to compare the lifespan of ENDURALIFE-powered devices with that of other devices." Suggest "However, it judged that data in the PPRs could not be used to reliably compare the lifespan of ENDURALIFE-powered devices with that of other devices."	Thank you for your comment. The sentence will be amended.
51	4. EAC	3.16 Page 14	Currently reads: "The published studies demonstrate that ENDURALIFE-powered CRT-Ds implanted since 2008 have greater longevity than comparator CRT-Ds. " Suggest: "The published studies demonstrate that ENDURALIFE-powered CRT-Ds implanted in the period 2008-2010 have greater longevity than comparator CRT-Ds implanted in the same period. " Rationale: the EAC report on page 6 states "The studies show that for devices implanted during the time interval c2008-c2010, ENDURALIFE-powered CRT-Ds have better longevity than their contemporarily implanted comparator CRT-Ds."	Thank you for your comment. The sentence will be amended.
52	4. EAC	3.19 Page 15	We don't recall the term 'charge rating' used in literature, which refers to battery capacity in Ampere-hours, but if this is a quote of the experts we wouldn't argue.	Thank you for your comment. Following clarification with the clinical experts, this has been amended to ampere hours.
53	4. EAC	4.1 Page 16	Currently reads: "The company also claimed that using ENDURALIFE-powered cardiac resynchronisation therapy-defibrillator (CRT-D) devices could lead to cost savings through a reduction in associated costs such as post-operative complications and infections."	Thank you for your comment. This sentence will be amended.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			Perhaps consider: "The company also claimed that using ENDURALIFE-powered cardiac resynchronisation therapy-defibrillator (CRT-D) devices could lead to cost savings through a reduction in associated costs such as post-operative complications and infections resulting from replacement procedures". Rationale: we think risks at initial implant are about equal across different devices.	
54	4. EAC	5.1 Page 17	We think the Gadler study is now published (cited as unpublished, which it was when used by the company for this work).	Thank you for your comment. The publication status of the Gadler et al. (2016) study will be amended.
55	4. EAC	5.11 Page 21	Currently reads "5.11 The EAC re-ran the company's base case and univariate sensitivity analyses and conducted additional analyses using its preferred estimates. " Suggest: "The EAC re-ran the company's base case and univariate sensitivity analyses and conducted additional analyses using revised input values" Rationale: clearer.	Thank you for your comment. This sentence has not been amended.
56	4. EAC	5.13 Page 22	Currently reads "the effect of allowing a price difference" Suggest "the effect of introducing a price difference" Rationale: clearer.	Thank you for your comment. This section will be amended.
57	4. EAC	5.17 Page 22	Currently reads "Using data from the National....." Suggest: "Using patient survival data from the National..... Rationale: clearer	Thank you for your comment. This section will be amended.
58	4. EAC	5.20 Page 23	First reference to NICOR is in 5.17. The flow may be improved by stating that the EAC contacted NICOR in 5.17. i.e. introduce NICOR here?	Thank you for your comment. **The Committee amended section 5.17.**

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or Advisory committees."