National Institute for Health and Care Excellence

External Assessment Centre correspondence

ENDURALIFE-powered CRT-D devices for the treatment of heart failure

The purpose of this table is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the sponsors' original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the sponsor
b) need to check "real world" assumptions with NICE's expert advisers, or
c) need to ask the sponsor for additional information or data not included in the original submission, or
d) need to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is made available to MTAC. The table is presented to MTAC in the Assessment Report Overview, and is made available at public consultation.

Submission Document Section/Sub-section number	Question / Request	Response	Action / Impact / Other comments
General	Cedar requested information on currently marketed CRT-D devices in order to identify relevant comparators and their characteristics. For consistency cedar requested the same information from Boston Scientific:  Microsoft Office Word 97 - 2003 Docu	[redacted]	Cedar used some of the information as inputs (e.g. while modelling additional scenarios) to the company's economic model
General	As above	[redacted] Total documents provided to Cedar: 1. [redacted] [redacted]	As above

Submission Document Section/Sub-section number	Question / Request	Response	Action / Impact / Other comments
		3. PPT World's longest Longevity 4. Livanova Warranty terms and conditions 5. PPT Option Study	
General	As above	[redacted]On the pricing, I appreciate that list pricing is often used in NICE MT guidance (and can often be justified as the ASPs are similar if not the same as list prices for many devices). However in the CRM sector it is well known that list prices for all manufacturers are unrepresentative of ASPs hence my caution here. To give you an idea of what I mean - attached are list prices for our CRT-D devices currently commercially available in the UK. The prices are given for the different device models for box (IPG only) and system (box plus leads) for the various configurations (Latitude and LHFM refer to our remote monitoring offerings). [redacted] [redacted]The above ASPs are collated by Eucomed each quarter and are based on manufacturer sales which we and other manufacturers submit to Eucomed so they can collate. What we get back is average market data plus Boston Scientific specific data (but no data for other manufacturers broken out – other manufacturers would get market plus	As above

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		their own specific data). As you can see, these ASPs are significantly different from the list prices, hence my view that perhaps the list prices are not the best data point to rely on here. While we don't get a breakdown of ASP by manufacturer, perhaps Eucomed might share such data with you for the purposes of this evaluation? Let me know if it's helpful for me to get you a contact name of someone you can approach if you are interested in pursuing this. Please note that all of the above pricing information should be considered confidential and should not be made public. Re: your other suggestion, the centralised procurement scheme for CRM has not yet been implemented in any Trusts yet so I'm not sure if the prices they would have are up to date (indeed, I would need to check if the Boston prices would be correct or not yet). In term of the projected longevity, as we mentioned in our submission, the only up to date standard for programming parameters we are aware of are those defined by the French Health Authorities. They developed their criteria (which came into force earlier this year) in order to help set a minimum longevity for these types of devices. As you will know, unfortunately there is no equivalent available in the UK as yet. Unless you have any objections, I will aim to provide our projected longevity figures using these settings but would note that they should only be directly compared to other longevity projections calculated at the same exact settings. I will try and get you this	

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		plus the launch dates early next week if that's ok?	
General	As above	[redacted]	As above
General	As above	Response from Medtronic: Please find enclosed our response to your questions. I have enclosed two documents as PDF's for you. One is the completed table, the other is supplementary evidence on Device Longevity. [redacted]	As above
Economic model	Cedar queried Boston Scientific why the Tang (2010) paper was not used in the economic model as a source of data on complications	Response from Boston Scientific: The Tang 2010 paper was not identified in the 997 studies from our	Cedar Assessment Report

Submission Document Section/Sub-section number	Question / Request	Response	Action / Impact / Other comments
	associated with CRT-D replacement.	outcomes/adverse event literature search (see section 7.7 of our submission for information on our search strategy) therefore was not considered as part of the clinical evidence reviewed. When we began the economic modelling, we first assessed whether we could use any of the 20 relevant studies we identified in the clinical evidence submission to support the complications modelling. As we highlighted in section 9.2.4 of the submission "In order to tailor the cost analysis to reflect real-world clinical practice as closely as possible, the model was structured to include both replacement and initial implant complication rates. While we have previously identified 20 relevant studies (see section 7.7.1), few were high quality systematic reviews or meta-analyses and those that were did not report a comparison of complication rates for both initial implant and replacement procedures. Therefore, we concluded that the base-case could not be based on any of the 20 studies." Once we had come to that conclusion, we chose to look into how the NICE Technology Appraisal had considered complications as part of their economic evaluation. We believed this evaluation to have a robust methodology and one that we could look to replicate for our own economic modelling. From the detailed HTA report (Colquitt et al., 2014) we identified the three main complications that were considered relevant and the associated costs. However, the HTA report itself did not report the complication rates used in their evaluation but only that they had been sourced from the Tang 2010 paper. For that reason, we cited Tang 2010 as the source of the complication rates and the HTA report as the source of the associated costs (but both originated from the NICE evaluation). As you'll see in the submission, we did rely on the Lewis et al (2016)	worded accordingly.

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		systematic review (as identified in the clinical evidence submission) for the sensitivity analysis on complication rates.	
Economic model	Question from Cedar to Boston Scientific: The economic model uses data from Landolina (2016) as 'event-free battery survival' in the model. Did you use data based on Figure 3 in the Landolina paper? Sorin and Biotronik CRT-Ds are not included as comparators in the economic model. In the Landolina paper they were not included in Figure 3 because fewer than 100 devices had been implanted. Is your justification for not including all comparators in the model based on small numbers? I wonder, do you have UK market share data which could shed light on this from a different source?	Response from Boston Scientific: For the base case values, we took these from the Landolina 2016 paper (event-free battery survival = 1 - cumulative probabilities of replacement; cumulative probabilities of replacement are taken directly from the "Recent generation" charts in Figure 2 of the paper). Since this data was already available, we did not need to follow an estimation approach as used for the sensitivity analysis. As you correctly note, we excluded Sorin and Biotronik as they were absent from the Landolina 2016 paper results (which we viewed as the most relevant and contemporary paper on which to base our economic analysis). Had we had access to reliable data on a larger cohort of devices from these manufacturers we would have happily included them. Should you have access to further data here, we would be very interested to have them included here. Unfortunately we do not have reliable market share information for competitors, only for ourselves (this was something we looked into including but were not able to). I can tell you that Medtronic, St Jude Medical and Boston Scientific make up a significant proportion of the market, with Sorin and Biotronik much smaller players but I don't have any quantitative data to support that I'm afraid. Perhaps something you could ask the NICOR team who manage the National Audit of CRM Devices – I would assume they are	No further action.

<table>
<tr><th>Submission Document Section/Sub-section number</th><th>Question / Request</th><th>Response</th><th>Action / Impact / Other comments</th></tr>
<tr><td></td><td></td><td>able to analyse the database for information on market share by volume in the UK?</td><td></td></tr>
<tr><td>Economic model</td><td>Question from Cedar to Boston Scientific:

In the model you’ve based the cumulative patient survival for years 1 to 6 on the published economic model by Guiqing Yao et al. 2007. This paper extrapolates the survival from the prior published RCT by Cleland et al. 2005, which had mean follow-up 2.45 (range 1.5,3.7) years.

Looking at Figure 3 in the Guiqing Yao paper I can roughly approximate the cumulative patient survival for each of years 0 to 6: going by eye (& with a ruler), producing something close to your values:

<table><tr><th>Year</th><th>% survival (Boston Scientific model)</th><th>Andy (by eye)</th></tr><tr><td>0</td><td>100</td><td>100</td></tr><tr><td>1</td><td>95</td><td>95</td></tr><tr><td>2</td><td>90</td><td>90</td></tr></table></td><td>Response from Boston Scientific:

We chose to use the Guiqing Yao et al. 2007 study for patient survival as it was based on the CARE-HF RCT, a landmark study of CRT devices for heart failure. We followed a similar methodology as you did to reading the survival values from the curve. We then tested these values as part of the sensitivity analysis using alternative patient survival data from Gasparini et al (2014).</td><td>No further action.</td></tr>
</table>

Submission Document Section/Sub-section number	Question / Request	Response	Action / Impact / Other comments
	<table><tr><td>3</td><td>85</td><td>84</td></tr><tr><td>4</td><td>81</td><td>80</td></tr><tr><td>5</td><td>77</td><td>75</td></tr><tr><td>6</td><td>72</td><td>72</td></tr></table> Could you please advise whether your team did a similar thing, or whether you have performed some kind of statistical analysis?		
Economic model	Cedar asked Boston Scientific to further explain the methods used in sensitivity analysis of CRT-D device longevity to reflect recent generation CRT-D devices.	Information provided by Boston Scientific: We wanted to use the sensitivity analysis on device survival to address the question in the scope regarding newer generations of CRT-D devices (and performed a one-way sensitivity analysis using higher device survival only as devices have typically improved their longevity/device survival in their newer generation devices compared to older generations). We tried and failed to use the following two (preferred) approaches to perform this analysis: • Use real-world evidence on device/battery survival of the newest generation devices – given the lag in collecting real-world evidence, we would have to wait a minimum of 6 years to obtain comparable independent evidence on the most recent generation devices (launched in 2016) from other manufacturers	No further action.

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		• Use a like-for-like comparison of manufacturer's projected longevity – device manuals include point-estimates on projected longevity for devices but the figures are all reported using different settings. While there is a standard which defines parameters at which all manufacturers should report projected longevity at, these parameters do not cover all settings that may affect battery life and the use of these estimates would still not produce a completely like-for-like comparison for manufacturers. In its place we tried to use a more up-to-date, publicly available source which considered a more comprehensive range of programming parameters in defining a standard for longevity projections and found the French Haute Autorité de Santé had done just this. However, there was not enough information in the device manuals to be able to carry out this like-for-like comparison. Our third approach to performing this analysis was to carry out a more limited comparison based on a combination of device manual data plus device survival data from the existing Landolina 2015 publication. Due to the availability of data in device manuals and the device survival data in the Landolina 2015 publication, we were only able to carry out this analysis for the newest generation of devices from Medtronic. Below I have detailed the steps we took to do this: (1) Identify dominant device models used in Landolina 2015 cohort (2) Calculate average percentage increase in projected longevity between the older generation device models used in the Landolina 2015 cohort compared with the most recent generation device models on the market using device manuals	

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		• see tables C19 and C20 for details of the different device settings we were able to use for like-for-like comparisons across generations for Boston Scientific & Medtronic (St Jude Medical do not publish this information in their device manual so it was not possible to perform the analysis for their devices; other manufacturers were not included in the Landolina 2015 cohort and so had no data on older generation devices to use as a starting point) • this approach meant it was possible to see the manufacturer-specific increase in projected average device longevity for newer generation devices (+17% and +6% for Medtronic and Boston Scientific CRT-Ds respectively) – however, note that the individual longevity projections in years shown in table C19 are not considered comparable to those shown in table C20 due to different device settings used in the device manuals for Medtronic and Boston Scientific (3) Device survival rates estimated from the KM curve in Landolina 2015 at 0.2 year intervals for old generation devices from Medtronic and Boston Scientific (4) Percentage improvement from step (2) applied to time points (i.e., x-axis) from Landolina KM curve data from step (3); device survival data left unchanged – for example, considering Medtronic survival, we extrapolated the time from implant data by assuming that the increase in longevity from step (2) for newer generation devices would result in the same device survival being reached 17% later for all data points, not only the median as published in the device manuals, and thus the device survival data estimated in step (3) would occur at 0.23, 0.47, 0.70 years rather than 0.2, 0.4, 0.6	

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		years etc. (5) Using the existing device survival data from step (2) and the new time points from step (4), the KM curves were redrawn and in this way, shifted to the right along the time axis by 17% (6) The remapped KM curves from step (5) were used to estimate the adjusted (new generation) device survival at 1 year intervals for use within the economic model for the sensitivity analysis (see table C21 in submission for adjusted device survival values) While we replicated this analysis for ENDURALIFE-powered CRT-Ds and Medtronic CRT-D devices, we decided to keep the base case input for ENDURALIFE-powered CRT-Ds for the sensitivity analysis and use the revised survival probability for Medtronic only (see Table C19). This was a decision so as to be conservative.	
Table B9	Cedar asked Boston Scientific to clarify the methods used to calculate CRT-D device longevity in Product Performance Reports and to confirm that PPR data were not used as inputs to the economic model.	Regarding the PPR data, you are correct, we have not used data from the Product Performance Reports in our economic model. As we discussed a few weeks back, we included the PPRs in the clinical submission specifically to address a question raised by NICE in the scope around the relative importance of battery survival versus other component failure. With the majority of the outcomes NICE had asked us to look at (and the claimed benefits) focusing on the implications of extended battery longevity, NICE were concerned that this may not be reflective of overall device survival (i.e., whether the battery was the “weak link” of the device or not). This is not something that we felt was sufficiently addressed in the	No further action.

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		published literature so we considered PPRs as an unpublished (but publicly available) source of data to supplement this area of the submission. You will see from the PPRs that normal battery depletion is consistently a much more significant factor in overall device survival than device malfunction (i.e., component failure) for all manufacturers. This inter-device comparison of reasons for device failure was considered less bias than intra-manufacturer comparisons (due to the methodology used to collect the data) and hence we included it purely to address NICE's original concerns. We chose to populate the model with published clinical data based on a real-life cohort of CRT-D patients rather than PPR data based on device returns for individual manufacturers with inconsistent methodology to estimate battery longevity.  Response to Questions on PPR_24	
Page 104, PRISMA flow diagram	On page 104 of the submission there is mention of three studies excluded due to "no direct correlation between longevity and costs described (n=3)". So that we can understand this, please would you let us know which three	Boston Scientific provided pdf files of three studies: Fanourgiakis 2016 Groarke 2012	No further action

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	studies are referred to?	Sohail 2010	
Economic evidence	Cedar requested that Boston Scientific send two unpublished studies cited as evidence in the submission of clinical and economic evidence.	Boston Scientific provided two unpublished (Landolina now published) studies as academic in confidence information: [redacted] (51) Landolina 2016 [ACADEMIC IN CONF	The papers enabled Cedar to understand the data used in the submission.
Clinical evidence	The Cedar team requested clarification of their understanding of technical parameters which may impact on CRT-D longevity discussed in published studies.	Response from Boston Scientific: Technical parameters v0.1 - Clonmel Notes.	This document is not reproduced in the Assessment Report but is available to inform discussion of the report.

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<td>General (company's claimed benefit)</td>
<td>Question from cedar to Dr David Jay Wright:

Query regarding long term survival: Boston Scientific's economic model has a six year time horizon, but with rates extrapolated from an RCT with shorter follow-up: Cleland et al. 2005: mean follow-up 2.45 (range 1.5,3.7) years.

Cumulative survival probability, years 0 to 6 (Guiquing Yao 2007, extrapolated from Cleland 2005)

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<tr><td>5</td><td>77</td></tr>
<tr><td>6</td><td>72</td></tr>
</table>

Our literature search for CRT-D devices revealed the following reports of patient survival, but they are only abstracts. Are you</td>
<td>Response from Dr David Jay Wright:

Please find attached 3 publications in EUROPACE and my abstract from LHCH presented in June of this year

Our data goes a little further with follow up.

  Longevity poster cardiostim 2016.pptx
  Saba europace eut301 full.pdf
  Europace-2013-Boriani-1453-621.pdf
  Boriani_Europace2016.pdf</td>
<td>Cedar sought further data from NICOR (see below).</td>
</tr>
</table>

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	aware of any more robust data? (1) Day, J.D. 2010. Real world ICD/CRT-d patient survival: Do women fare better than men? Gender comparison in the altitude study. Heart Rhythm, Conference, (var.pagings) S121 (2) Gadler, F. 2010. Device longevity and patient survival in the Swedish National Pacemaker registry. Europace, Conference, (var.pagings) June (3) Hauser, R.G. 2011. Long-term outcomes after icd implantation in the 21st century: Survival, therapy, and complications. Heart Rhythm, Conference, (var.pagings) S297		
General (company's claimed benefit)	Cedar presented a query on complications to Dr David Jay Wright as follows: Boston Scientific's (Boston Scientific) economic case is that Enduralife-powered CRT-Ds have better device longevity resulting in less frequent need for CRT-D replacement.	Response from Dr David Jay Wright: The data varies slightly from one study to another and similarly for meta analyses The best complication data is from Kirkfeldt at al European Heart Journal (2014) 35, 1186–1194 – this looks at complications to 6 months and thus	Cedar critiqued the Kirkfeldt (2014) paper and cited its data in the

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	We have found that the available published evidence based on cohorts of patients implanted since 2008 (with typically 3-4 years' follow-up) shows that Enduralife-powered CRT-D longevity is improved compared to comparator CRT-Ds from other manufacturers. I'd be grateful to hear your experience of complication rates due to replacement procedures for patients who require explants of their CRT-D. The Boston Scientific economic model has the following complication rates following CRT-D replacement as its inputs: • Infection 2.4% • Complication requiring reintervention (e.g. lead dislodgement, haematoma) 8.5% • Device pocket problem requiring revision 0.5% 1. These are loosely based on Tang et al. 2010, a Canadian RCT comparing de novo ICD versus de novo CRT-D in people with	picks up more late infections Essentially new CRT D implants have a complication/reoperation rate of 8-10% with an infection rate of 0.6-1% CRTD box changes have a similar complication/reoperation rate but a higher infection rate 2-2.5% Also there are more reoperations due to pain and haematoma after a CRTD box change and both these predispose to an infection further down the line This is supported by a huge review of the US data (JACC;58:10:1001-6) which apportioned the increase in infections to the introduction of CRT and an aging population having more box changes Out internal audit is in line with this and is currently at review with the European Heart Journal. We have looked at complications to one year as many infections are not evident immediately and initially present as pain or pre-erosion – there is much gaming in the real world to avoid reporting infections. They require a complex and expensive extraction procedure and then re-implantation of a new system on the other side. as a ball park figure an extraction for infection costs £10-12 000 and a further CRTD implant and device costs approximately £20 000.	Assessment Report.

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	heart failure (complications within 30 days of replacement). Do you think they are sensible? 2. The model assumes that replacement CRT-D procedures carry equal rates to de novo CRT-D – Is this your experience? 3. Boston Scientific also submits a number of studies reporting complications due to replacement procedures. We have summarised this evidence in the attached word document. At a glance 8.5% would appear a higher than typical rate of reintervention. Again, does your experience shed further light?		
General (company's claimed benefit)	Cedar sought from Clinical Experts a source of data on overall survival in patients who undergo implantation with a CRT-D device (and was directed to NICOR). The claimed benefit is that better CRT-D longevity results in fewer replacement procedures needed. We would like to understand this in terms of anticipated patient overall survival. Could you please recommend a source of patient overall survival in the CRT-D treated population? It would be useful to	Response 1 from Dr David Jay Wright: There are 2 possible sources of long term data on this, sadly there is little published data on longer term follow up although I think the COMPANION study has now tackled this – I will check and get a reference to you shortly. In the meantime the two National (and thus most relevant to the UK population) data sets are the NICOR device survey and the HES data. The former is managed by Morag Cunningham (morag.cunningham@ucl.ac.uk) and the latter by Prof Paco Leyva at the Queen Elizabeth Hospital in Birmingham, I don't have his e-mail but he is	[redacted] made available to Lead team Meeting (16.08.16)

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	refer to a credible figure. For an example, if two different CRT-Ds have average 5 year and 6 year longevities respectively, there would be only 1 replacement procedure anticipated in either case if anticipated patient survival is 8 years. The company's economic model has a 6 year time horizon.	easily contacted via the hospital switchboard. I hope this is helpful and will chase the COMPANION reference.	
General (company's claimed benefit)	As above	Response 2 from Dr David Jay Wright: I have looked at the published data on long term follow up after CRTD implantation. It is very disappointing and is mostly from registries looking at remote follow up. As such all the publications relate to one manufacturer per study only and are thus potentially biased. I suggest you try Morag and Paco – please feel free to let them know I have directed you to them as I have worked closely with both of them.	As above
General (company's claimed	As above	Response from [redacted] (NICOR): [redacted]	As above

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benefit)		[redacted]	
Economic model	Request from Cedar to NICOR to make additional use of NICOR data [redacted]	Response from [redacted](NICOR): [redacted]	Data planned for presentation at MTAC meeting (Part 2a)
Economic	Request from Cedar to NICOR for additional	NICOR responded with the data as requested.	Data planned for

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model	NICOR demographic data:  		presentation at MTAC meeting (Part 2a)
Economic model			Analysis worded accordingly

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	[redacted]	[redacted]	
Economic model	Cedar requests that Health Economic colleagues (SCHE) check of methods used for additional analyses requested at MTAC	Response from SCHE: [redacted]	Analysis worded

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	meeting: [redacted]	[redacted]	accordingly
Adverse events	Question from Cedar about adverse events put to clinical experts: In the attached we have summarised what we know of adverse events relating to CRT-Ds. This is broader than the specific case where patients undergo CRT-D replacement and face risk of complications (this is covered by submitted evidence from BSC). Do you agree with our draft conclusion statement below? Is there anything that you would suggest we add or change?	Response from Dr Chris Plummer: I think your "adverse events" document is a good summary of the data. Your conclusion is also fair although I wouldn't necessarily criticise the company for not including the 2 alerts in this submission – they are well-reported elsewhere and explain the cause of some of the adverse events rather than indicating additional ones. My only caveat, as I said in my first e-mail today, is that the manufacturers' device registries are very highly regulated and collect very specific events which do not include all adverse events associated with device implantation and replacement.	Assessment Report worded accordingly.

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	"**EAC conclusion on adverse events** The company identified over 8000 adverse events relating to ENDURALIFE-powered CRT-D devices, whereas the EAC identified c3000 (the nature of the US FDA MAUDE database does not permit greater accuracy since it will identify a maximum of 500 records per search term). The company is likely to be highly vigilant for adverse events for all of the implantable devices that it markets, and has likely identified more adverse events than the EAC by its own active surveillance and close communication with regulatory bodies and clinical sites. Nevertheless the EAC quickly identified two relevant Medical Device Alerts via the MHRA database (both issued by Boston Scientific and summarised above) that were not described in detail in the company's submission. The EAC has not attempted to further categorise the large number of adverse events identified. The EAC considers that CRT-Ds are technologically advanced, active implantable, Class III medical devices with indications in patients at risk of serious morbid incident or		

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	mortality. Published evidence indicates that CRT-Ds improve patient survival, though due to their complex design and function, plus implantation in large numbers of patients globally, adverse events are to be expected across all manufacturers. High vigilance for adverse events is likely to be a feature of the entire relevant industry and the EAC is not aware of specific trends by which adverse events related to CRT-Ds from any particular manufacturer are more likely than from other manufacturers.		
Adverse events	As above	Response from Dr David Jay Wright: I agree with the conclusion statement as it stands.	No further action
Economic model	Question from Cedar about warranty claims put to clinical experts: The economic model considers warranties for CRT-D devices, specifically the % of warranties claimed by the manufacturer. In your experience what circumstances lead to this? We'd expect this to be some kind of malfunction or premature battery depletion. Could you state your typical % of CRT-D	Response from Dr Chris Plummer: There isn't a single figure I can quote you for the % or warranty claims but you are right that the vast majority are for premature battery depletion. This varies between manufacturer, it varies over time (some batteries are definitely better than others) and it varies according to the exact wording of the warranty. The most accurate source of data on warranty claims would come from the manufacturers who will have data on every one. If you would like data from our centre, I would be happy to see what we have if you let me know whether this is for Boston devices or all manufacturers and over what	No further action

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	implants that lead to a warranty claim?	time period.	
Economic model	As above	Response from Dr David Jay Wright: The warranties are usually pretty impressive as CRTD devices are robust – in reality they are very rarely claimed by clinical teams as there is no process in most hospitals – I know this sounds ridiculous but it is sadly true.	As above
Economic model	Question from Cedar about complications (due to CRT-D replacement) put to Dr Chris Plummer: Boston Scientific's (BSC) economic case is that Enduralife-powered CRT-Ds have better device longevity resulting in less frequent need for CRT-D replacement. We have found that the available published evidence based on cohorts of patients implanted since 2008 (with typically 3-4 years' follow-up) shows that Enduralife-powered CRT-D longevity is improved compared to comparator CRT-Ds from other manufacturers. I'd be grateful to hear your experience of complication rates due to replacement procedures for patients who require explants of	Response from Dr Chris Plummer: My first point is that this assessment focuses on CRT-D devices when the Enduralife battery technology is in multiple other Boston devices. It is very difficult to give you complication rates for CRT-Ds as published rates are subject to publication bias, registry rates are subject to ascertainment bias and individual centre rates are a very small sample. All device companies collect device performance data but this has very strict (narrow) inclusion criteria and will not include all complications. 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. Complications data are also affected by new technologies – for example, the use of quadrapolar leads has dramatically reduced re-intervention for lead displacement. Complications also differ between de novo implants and box-changes – lead displacement is more common at implant and infection more common at box-change, so it	No further action (use made of Kirkfeldt study discussed above).

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	their CRT-D. The BSC economic model has the following complication rates following CRT-D replacement as its inputs: • Infection 2.4% • Complication requiring reintervention (e.g. lead dislodgement, haematoma) 8.5% • Device pocket problem requiring revision 0.5% These are loosely based on Tang et al. 2010, a Canadian RCT comparing de novo ICD versus de novo CRT-D in people with heart failure (complications within 30 days of replacement). Do you think they are sensible? The model assumes that replacement CRT-D procedures carry equal rates to de novo CRT-D – Is this your experience? BSC also submits a number of studies reporting complications due to replacement procedures. We have summarised this	is important to be clear what is being compared. For device replacements (box-changes): Infection 2.4% - this is similar to frequently quoted rates around 2% Complication requiring re-intervention (e.g. lead dislodgement, haematoma) 8.5% - this is much higher than would be expected at box-change. Haematoma requiring re-intervention should be <0.5% and lead displacement should be <1% Device pocket problem requiring revision 0.5% - this is lower than conventionally quoted and is inconsistent with the infection point as infection is a sub-set of pocket problems requiring re-intervention. I would be very happy to review the literature you have identified to derive some meaningful complication rates but we need to ensure that the definitions are consistent.	

Submission Document Section/Sub-section number	Question / Request	Response	Action / Impact / Other comments
	evidence in the attached word document. At a glance 8.5% would appear a higher than typical rate of reintervention. Again, does your experience shed further light?		
Economic model	Question from Cedar to NHS Supply Chain re: Centralised procurement of CRT-D devices Dear NHS Supply Chain I am working on NICE guidance in development for implantable Cardiac Resynchronisation Therapy – Defibrillators (CRT-Ds) supplied by Boston Scientific and powered by the ENDRALIFE battery technology: https://www.nice.org.uk/guidance/indevelopment/gid-mtg10004 I understand that procurement of CRT-Ds in the NHS in England is managed by a centralised supply chain as of April 2016: https://www.supplychain.nhs.uk/news/company/centralisation-of-the-supply-chain-for-high-	Response from NHS Supply Chain: Thanks for reaching out to NHS Supply Chain and giving us an overview of Cedar's role and the work around CRT-Ds and the NICE guidance. First of all I'd like to introduce myself, I am the category buyer on the NHS England national supply chain initiative for excluded devices focusing on ICD and ICD with CRT devices. The first phase of the centralised procurement process is very much about gaining adequate market share/information to help inform NHS England and the clinical bodies with decision making in the later phases. One of the aspects we very keen to understand is the whole life cost of these devices for the NHS, especially with regard to battery-life. I think it would be useful for us to arrange a meeting to discuss the project at length.	Ongoing 20.09.2016

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	cost-tariff-excluded-devices/ Is it possible to identify the price paid for specific CRT-Ds in order to inform the NICE guidance? If prices are to be considered as commercial in confidence, then NICE has a procedure to ensure that the prices remain confidential and are not made public. I'd be very grateful for your response.		
Economic model	Follow-up by Cedar to response above (NHS Supply Chain): Thank you for your response. At the moment Cedar's involvement is limited to the requirements of the NICE process, and the ENDURALIFE guidance topic has reached a key stage – that of the NICE MTAC committee meeting 2 (this Friday). We'd expect the committee to make draft recommendations which would be put out to public consultation (along with supporting evidence) between 26 October 2016 - 23 November 2016 with another review by the NICE committee on 16 December 2016.		Ongoing 20.09.2016

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	The committee makes the recommendations but it may be of interest to NICE and to its committee if centralised procurement prices for CRT-Ds were to be defined during the timescale described above. This would depend on your timescale for defining the prices. I have copied colleagues at NICE so that we're all in contact. Would it be acceptable to see how the committee meeting goes, and then decide whether a meeting would be useful? I should add that the committee meetings have strict confidentiality procedures, but we could discuss a specific issue if NICE requested that we pursue it. https://www.nice.org.uk/guidance/indevelopment/gid-mtg10004		
Economic model	Request from NICE to NICOR seeking a data sharing agreement: [redacted]	Response from NICOR: [redacted]	For consideration by NICE

Submission Document Section/Sub-section number	Question / Request	Response	Action / Impact / Other comments
	[redacted]	[redacted]	