NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence

Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

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

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from Cedar to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12:00pm Wednesday 20th July 2016, using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

Submitted for company fact check on 15 July 2016.

NICE National Institute for Health and Care Excellence

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Lack of alignment with NICE scope in results presented	Inclusion of additional non-cost outcomes to reflect impact on patients and providers (e.g., number of procedures), particularly where cost threshold analysis is performed	The EAC report appears to have omitted non-cost related outcomes in its presentation of results, particularly in section 4, Economic Evidence. For example, the economic model submitted by the manufacturer incorporates number of admissions per patient as a key result to reflect the impact on patients and provider capacity of performing procedures. The cost threshold analysis performed does not present these additional results which could unintentionally imply to the MTAC that reducing device cost will mean the results are comparable where in reality the non-cost impact will remain.	The threshold analysis attempts to tackle the sole issue of high uncertainty around the device costs from one manufacturer to another. We do not intend that the threshold analysis be considered in isolation from other important considerations.

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Use of list prices (section 4.5)	Ask clinical advisers for current pricing by manufacturer or approach manufacturers to ask for Eucomed Q1 2016 ASP data for their company	List prices are not relevant to the NHS today as they are significantly different from actual selling prices. There are many other options available to the EAC or NICE to find	This issue will be explored with NICE.

		appropriate prices. One way would be to ask one of the EAC expert advisers for their current pricing. It is important to note that using the list prices renders the analysis irrelevant.	

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Lack of justification for statements regarding applicability of past performance/clinical evidence to newest generation devices (pages 8, 87, 89)	Revision of text to include clear justification for statements and reference to the technical report where consideration is given to the implications of technological improvements to device longevity	Statements currently lack reasonable justification to provide the MTAC with evidence-based rationale behind these opinions. Development of CRT-D devices is, by nature, iterative and builds on previous generation devices. As a result, for Boston Scientific, we are confident that our past performance in device longevity is maintained (and improved upon) in our newest generation devices.	We have aimed to present the evidence in the context of what we observe is happening in the industry. Some comparator devices implanted c2008-2010 are no longer present on company websites. Clinical studies suggest to us that devices are continually improved. In providing list prices, companies have also provided details of their own claimed innovations. We make reference to the technical assessment which will identify all parameters which may have a bearing on CRT-D longevity. Our aim is to assist the committee in making an informed decision.

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Lack of clarity on and justification for statements regarding likelihood of device survival curves to retain their shape (page 77)	Revision of text to: "It is *unclear* if the CRT-D device survival, ~~of one manufacturer relative to another~~ *of newer generation versus older generation devices from the same manufacturer, can be extrapolated in this way*, i.e. that the survival curves shown above [5] would retain ~~their~~ *a similar* shape"	The EAC have not provided justification or evidence for their statements. Furthermore, the current statement on "…CRT-D device survival, of one manufacturer relative to another…" incorrectly implies that the analysis sought to keep the relative difference between manufacturers the same in the sensitivity analysis. Instead, the analysis sought to extrapolate evidence from older to newer generation devices for each manufacturer separately. The result is a version of the original "old generation" survival curve which is stretched along the time axis and hence not exactly the same shape.	We have made the change as requested.

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Boston Scientific is incorrectly spelt "Boston Sicentific" in a large section of the report and the word "Scientific" is incorrectly written in lower case in many places also	Replace with correct spelling "**Boston Scientific**" where appropriate	Correct spelling and capitalisation	Thank you. Corrections made

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Incorrect references to ENDURALIFE Battery Technology throughout	Replace with correct references to ENDURALIFE as either "**ENDURALIFE-powered CRT-D devices**" or "**ENDURALIFE battery technology**" where appropriate	Correct references to trademark – the name "ENDURALIFE" should never be used as a standalone reference but always with a reference to either "ENDURALIFE-powered CRT-D devices" or "ENDURALIFE battery technology". The "ENDURALIFE" brand does not refer only to the battery but the entire battery technology.	Thank you. Corrections made.

Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Confusion around references to six clinical studies described in seven publications (pages 6,13)	Revision of text on page 6 to read: "The Company provided evidence on the longevity of ENDURALIFE-powered CRT-Ds compared to comparator CRT-Ds in the form of *seven* retrospective analyses *of six* case series, *five* of which are published in full" Revision of text on page 13 to read: "The six submitted *case series exploring* longevity report the following outcome measures"	The references to the seven clinical publications referenced in the manufacturer submission, drawn from six case series are confusing and should be corrected to ensure consistency across the report	We wish to state that the Alam study is one study reported at two different follow-up points. Page 6 amended to read: "The Company has provided evidence on the longevity of ENDURALIFE-powered CRT-Ds compared to comparator CRT-Ds in the form of six case series studies (referred to by first author: Alam, Ellis, Landolina, Lau, von Gunten, Williams) [1-7], four of which are published in full (Alam, Ellis, Landolina,

			von Gunten) [1-4;6] and two of which are available as abstracts [5;7]. One of the case series studies is reported in two papers, the second with longer follow-up [1;2]. All analyses are retrospective.” Minor amendment made to Section 3.2 accordingly.

Issue 8

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The base case economic model uses year by year device survival figures are from Landolina 2016, not 2015 should be marked as academic in confidence (page 86)	Revision to text and marking of relevant section as academic in confidence as follows: “The model uses ~~a~~ year by year survival data to represent device longevity based on data from Landolina 2016.”	The economic model submitted uses Landolina 2016 as the base case for device survival rates. This study is as yet unpublished and as such should be marked academic in confidence.	Checked throughout. Summary now reflects the relationship between these two papers as follows: In the Landolina 2015 study [4] the number of CRT-Ds still in service at five years following implantation were 88% for Boston Scientific, 75% for St Jude Medical and 52% for Medtronic. In the company’s economic model CRT-D longevity data were used as inputs based on a subsequent, accepted-for-publication economic analysis by the same group of authors and based broadly on the same patient series (Landolina 2016, unpublished).

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Comments referring to the inclusion of the Landolina study "used for the Company's economic model" should be marked as academic in confidence (pages 6, 75, 86)	Marking of relevant sections as academic in confidence	The economic model submitted uses Landolina 2016 as the base case for device survival rates. This study is as yet unpublished and as such should be marked academic in confidence where the base case analysis/main model is referenced. The Landolina 2015 publication is used only in the sensitivity analysis.	Thank you. Checked throughout.

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Details of CAPTIVATE, ENABLE MRI and RallyX4 studies (page 11)	Removal of three paragraphs detailing CAPTIVATE, ENABLE MRI and RallyX4 studies.	The EAC have acknowledged that "none of [these studies] are directly relevant to the decision problem" and they do not reflect an exhaustive list of ongoing studies into CRT-Ds.	We have moved this content to the appendices. They do not contribute to the report but it shows that we searched for and identified material in the correct general area.

Issue 11

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
References to ENDURALIFE	Removal of references to ENDURALIFE Battery	This section is not specific to a	Thank you. Corrected.

Battery Technology in EAC description of a CRT-D device (page 12)	Technology in this section and replacement with generic CRT-D terms – e.g., "…small demand for power on *the* battery".	single manufacturer and as such should not contain references to Boston Scientific's trademarked ENDURALIFE Battery Technology	

Issue 12

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Device models missing from regulatory approval section (page 13)	Revision of text to read: "For the INCEPTA, ENERGEN, *PUNCTUA NE* and PUNCTUA CRT-Ds the Design-Examination Certificate no. is CE566332 and for the AUTOGEN, DYNAGEN, *ORIGEN* and INOGEN CRT-Ds the Design-Examination Certificate no. is CE602838."	The regulatory approval information is incomplete and is missing details on the PUNCTUA NE and ORIGEN models	Thank you. Corrected.

Issue 13

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Incorrect reference to battery capacity (page 14)	Revision of the text to read: "PPR data suggest that the biggest driver of device longevity is *normal* battery *depletion*, rather than device malfunction."	The PPR data indicates that the biggest driver of device longevity is normal battery depletion – the PPR data does not refer to battery capacity	Thank you. Corrected.

Issue 14

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Missing information in relation to von Gunten study (pages 16, 63)	Amendment to summary to include reference to the 100% ENDURALIFE-powered sub-group analysis available in the von Gunten study.	The summary of von Gunten refers only to the overall 39% of Boston Scientific CRT-Ds that are ENDURALIFE-powered and has omitted to mention that there is sub-group analysis within the study's supplementary materials which reflects 100% ENDURALIFE-powered devices (i.e., all COGNIS devices).	Thank you test revised throughout the report to reflect: "A supplement to this paper reports longevity for 76 ENDURALIFE-powered COGNIS CRT-Ds: in the study period there was 1 replacement representing 97.5% longevity at 4 years following implantation."

Issue 15

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Incorrect statement regarding complications studies (page 17)	Revision of text to refer to the use of the Lewis 2016 study as a source for the sensitivity analysis for rate of complications (sensitivity analysis #4)	The EAC report states that none of the 19 complications studies identified were used as inputs for the economic model – this is incorrect.	Thank you: statement revised: "Only one of these studies was used by the company to provide inputs to the economic model (Lewis, 2016)"

Issue 16

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Table 1, page 22, EAC comments	Revision of text to read:	In the Landolina study, there are	Thank you: statement revised. However

column. "the analysis of recent generation devices (marketed 2007 onwards) appears to include only 29 Livian CRT-Ds, suggesting that 291/320 = 91% of recent generation BSC CRT-Ds were ENDURALIFE-powered."	"the analysis of recent generation devices (marketed 2007 onwards) appears to include only *COGNIS devices i.e., 100% ENDURALIFE-powered CRT-Ds*"	291 devices in the recent generation category, i.e., the same number as COGNIS devices. The 29 Livian devices are not included in the recent generation analysis.	the wording in the paper is vague: recent generation stated as 'for the most part after 2007'. Livian launch date = 2007.

Issue 17

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Table 1, page 24, Patient population column. "N (BSC CRT-D devices) = 102/257 = 40%"	Revision of text to read: "N (BSC CRT-D devices) = 102/259 = *39*%"	In the von Gunten study, there were 259 Boston Scientific CRT-Ds included	Thank you. Corrected.

Issue 18

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Table 1, page 25, "Williams 2014 Lebanon"	Revision of text to read: "Williams 2014 USA"	The Williams study was carried out in the US, in Lebanon Pennsylvania	Thank you. Corrected.

Issue 19

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 27 – Population paragraph "The studies of longevity are retrospective analyses of case series originating From the USA, Europe, UK and Lebanon"	Revision of text to read: "The studies of longevity are retrospective analyses of case series originating From the USA, Europe and UK"	The Williams study was conducted in the US and not in Lebanon	Thank you. Corrected.

Issue 20

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 28 – "In some instances the company appears to have utilised their own data on the proportion of Boston Sicentific devices that were powered by ENDURALIFE."	Revision of text to read: "The Company has requested and received personal communication from authors to ascertain proportion of Boston Scientific devices that were powered by ENDURALIFE Battery Technology"	The data is not from Boston Scientific but from authors' communications to the company	Thank you. Corrected.

Issue 21

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Missing information in relation to von Gunten study (page 28)	Revision of text to read: "in von Gunten only 39% of Boston Scientific CRT-Ds are ENDURALIFE-powered*, however there is a 100% ENDURALIFE-powered sub-*	The summary of von Gunten refers only to the overall 39% of Boston Scientific CRT-Ds that are ENDURALIFE-powered and has	Thank you. Corrected at several places in the report.

	group analysis available within the study's supplementary materials"	omitted to mention that there is sub-group analysis within the study's supplementary materials which reflects 100% ENDURALIFE-powered devices (i.e., all COGNIS devices).	

Issue 22

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Numbers referring to Boston Scientific CRT-D devices included in the Alam studies is incorrect (page 28)	Revision of text to read: "122/*188* = *64.9%*"	In the Alam studies, there were 188 Boston Scientific CRT-Ds included	Thank you. Corrected.

Issue 23

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Table 2, % Boston Scientific CRT-Ds studied that are ENDURALIFE-powered CRT-Ds column (page 29)	Amendment of text to include reference to sub-group analyses in Landolina and von Gunten studies with 100% ENDURALIFE-powered CRT-Ds	The current summary of proportion of Boston Scientific devices in the Landolina and von Gunten studies omits to reference available sub-group analyses which can be identified as 100% ENDURALIFE-powered CRT-Ds	Table revised. The Landolina paper was vague re: definition of recent generation devices: "for the most part marketed after 2007".

Issue 24

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 29 The Company uses, in the economic model, the Landolina data for the latest generation of CRT-Ds in the study period, so it is likely that a high proportion of these would be COGNIS i.e. ENDURALIFE-powered.	Revision of text to read: "The Company uses, in the economic model, the Landolina data for the recent-generation of CRT-Ds in the study period, *as 100% of the recent-generation devices are* COGNIS i.e. ENDURALIFE-powered."	The recent generation sub-group analysis in the Landolina study is exclusively COGNIS devices, i.e., 100% ENDURALIFE-powered CRT-Ds	The Company uses, in the economic model, the Landolina data for the latest generation of CRT-Ds in the study period (Landolina 2016, unpublished). These are the subgroup of ENDURALIFE-powered COGNIS CRT-Ds (note: both Landolina papers are derived from the same series of patients. It is unclear why in the first paper {Landolina, 2015 11 /id} there are 291 COGNIS devices and in the second paper (Landolina 2016, unpublished) there are 376 COGNIS devices). The EAC accepts that the Landolina data represent ENDURALIFE-powered CRT-Ds.

Issue 25

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Missing information in relation to von Gunten sub-group analysis (page 34)	Amendment of text to include reference to sub-group analysis by device model in the von Gunten study, including a group containing 100% ENDURALIFE-powered CRT-Ds	The current summary of proportion of Boston Scientific devices in the von Gunten study omits to reference available brand specific sub-group analysis	Thank you. We have added: "In the sub group of 76 ENDURALIFE-powered COGNIS CRT-Ds there was 1 replacement representing 97.5% longevity at 4 years following implantation."

Issue 26

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Table 6 Results of Landolina 2015, EAC comments "Of 608 patients in the Boston scientific group 291 had the Cognis CRT-D i.e. 42% were powered by ENDURALIFE batteries."	Revision of text to read: "Of 608 patients in the Boston *S*cientific group 291 had the Cognis CRT-D i.e. 4*8*% were powered by ENDURALIFE *battery technology*.	The calculation is incorrect and the reference to "ENDURALIFE batteries" in incorrect – ENDURALIFE is not the name of the batteries only but the battery technology, including non-battery aspects such as circuitry	Thank you. Corrected.

Issue 27

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Mis-spelling of "van Gunten" (page 63)	Correction of spelling to "von Gunten"	Mis-spelling	Thank you. Corrected.

Issue 28

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Reference to EAC data presented on predicted battery longevity (page 63)	Removal of statement: "For this reason the EAC presents data on predicted battery longevity for currently available CRT-Ds across manufacturers."	The EAC did not present this data – as per the statement on pages 85-86, "the EAC hoped to develop some scenarios based upon the projected battery lifespan as estimated by the manufacturers or from PPR reports for currently	Accepted. We have reworded the statement to read: "For this reason the EAC collected and examined data on predicted battery longevity for currently available CRT-Ds across manufacturers. However the EAC

		available models of the technology and comparators. However the EAC concluded this was not a valid approach…"	considers these data to have high uncertainty because they are derived from bench testing under conditions which differ across manufacturers. Therefore no further analyses were performed by the EAC using projected longevity data."

Issue 29

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Reference to importance of battery capacity to longevity projections (page 63)	Removal of the word "only"	The statement that battery capacity is "only" one factor which may determine device longevity could be misconstrued as implying a lack of significance but contains no appropriate evidence or justification	This isn't a factual inaccuracy but a question of how to word our conclusion. Now reworded as: "The EAC considers that battery capacity is an important factor which may potentially determine CRT-D device longevity, but also that it does not act in isolation and that other CRT-D factors are also important (see Technical Assessment). It is likely that different manufacturers have each undertaken constant CRT-D development focussed on numerous CRT-D components such that devices marketed today may have better longevity than their predecessors studied in the included published longevity studies."

Issue 30

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement that "The observational data is likely to be biased" (page 66)	Inclusion of justification as to why the observational data is considered biased	The statement is currently not supported by evidence or justification	It's widely accepted that observational data are not as robust as prospective, experimental data. However the nature of the longevity evidence across the industry is that observational studies dominate, so we need not criticise this too much. Statement revised to reflect the limitations of abstracted reports as follows: "Studies presented as abstracts lack sufficient descriptions of their methodology to enable thorough critique."

Issue 31

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 66 "The unpublished Landolina 2016 manuscript describes an economic analysis based on a subset of the data from Landolina 2015 with a 6 year time horizon and a hospital perspective"	Revision of text to read: "The unpublished Landolina 2016 manuscript describes an economic analysis based on a subset of the data from Landolina 2015 with a 6 year time horizon *and 2 perspectives: a healthcare system and a hospital perspective*"	The article presents results both from the perspective of the hospitals and the healthcare system	We have amended the statement to read: "two perspectives: a hospital perspective and the Italian healthcare system perspective".

Issue 32

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 67 [redacted]"	Revision of text to read: [redacted]"	The article presents results both from the perspective of the hospitals and the healthcare system	Proposed revision presents the 40% and the 19% the wrong way around. We have amended the statement to: "[redacted]."

Issue 33

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Lack of capitalisation of "enduralife" (page 68	Capitalisation of word to "ENDURALIFE"	References to ENDURALIFE Battery Technology should ensure the term is capitalised	Thank you. Correction made.

Issue 34

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 70 "An estimated percentage	Revision of text to read: "An estimated percentage improvement in	The percentage improvement analysis was not applied to Boston Scientific CRT-Ds in the sensitivity	Thank you. Correction made.

improvement in projected battery survival was applied to Boston Scientific and Medtronic technologies to account for the expected improvement in the newer generation devices compared with those in the published literature"	projected battery survival was applied to ~~Boston Scientific and~~ Medtronic technologies to account for the expected improvement in the newer generation devices compared with those in the published literature."	analysis, only Medtronic (one-way sensitivity analysis)	

Issue 35

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement that "the EAC felt NHS reference costs to be a more appropriate data source" (page 72)	Removal of reference costs or inclusion of justification as to why reference costs were felt to be more appropriate	This statement contains no justification; the use of reference costs would provide a provider perspective which conflicts with the payor perspective that the model has been designed to take	We can accept that use of NHS reference costs does not perfect the model but we feel their use is definitely worth exploring. The assessment report already provides a justification as follows: "The company has taken procedure costs from the payment by results (PbR) tariff and chose not to use NHS reference costs from 2014-15. The tariff is the price paid to the organisation for a procedure which may include adjustments to support particular policy goals, whereas NHS reference costs reflect the actual cost of the procedure averaged across the NHS. Therefore the EAC considers that NHS reference costs warrant exploration as a data source for the model." The MTEP methods guide states: "Costs resulting from or associated with the use of the technology should be estimated using prices relevant to the NHS and personal social services"

			https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-medical-technologies/Medical-technologies-evaluation-programme-methods-guide.pdf We add the following as further description: **Tariff – payment by results** Payment by Results (PbR) system in the UK. It uses Healthcare Resource Groups (HRGs) - clinically similar treatments and diagnoses which require similar levels of resources - to set national tariffs for the payment of hospitals. Each HRG attracts a different tariff, or a fixed price, based on the national average cost for the HRG and all hospitals are then paid according to this national tariff. If the actual cost of treating a particular patient in an HRG is more than the national tariff, the hospital will make a loss on that patient. If the actual cost of treating the patient is less than the national tariff, the hospital will make a surplus.) (University of York 2010) **NHS reference costs** Reference costs are the average unit cost to the NHS of providing secondary healthcare to NHS patients. Reference costs are used to set prices for NHS-funded services in England. https://www.gov.uk/government/collections/nhs-reference-costs

Issue 36

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Reference cost HRGs for replacement CRT-D procedures	Correction of reference cost data from EY10 to EY02 to reflect correct HRGs for replacement CRT-Ds and removal of references to HRG EY09	Replacement CRT-D procedures are reflected under HRG EY02 in the 2014/15 reference costs (relating to OPCS code K594) and are not related to HRGs EY10 or EY09	Neither set of costs are perfect. We don't feel that our use of NHS reference costs offer a definitive answer, but we felt that their use was worth exploring. We maintain that they don't have some of the complications that the PbR tariffs have (e.g. incentives) The type of cost data selected does not have a significant impact on the model results.

Issue 37

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Lack of clarification as how reference costs are used in economic modelling (page 73)	Clarification as to how inflation has been applied to reference costs and whether the underlying model analytics have been adjusted to remove double counting of device costs when reference costs are used as the input	There is no clarification as to whether the EAC have adjusted the economic model to account for potential double counting of device costs (excluded device costs which are added in addition to the tariffs in the base case model vs reference costs which include these device costs). There is also no clarification	We have not inflated the 2014/15 prices to reflect 2016 prices. This is a limitation but its impact on the outcome of the model is minor compared to the problem of selecting the most appropriate price for CRT-Ds. Regarding risk of double counting the NHS reference cost "EY01B: Implantation of cardioverter defibrillator

		as to whether the 2014/15 reference costs have been adjusted to account for inflation to reflect 2016 prices.	with cardiac resynchronisation therapy“ (£14,984) is close to the average selling price used by the company in the model: £12,404 and falls far short of most list prices, therefore double counting is unlikely. This issue would apply equally to PbR tariffs. In summary we feel that NHS reference cost versus PbR tariff and also inflating costs from 2014/15 to 2016/17 would have little impact on the model.

Issue 38

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement on page 73: “The sensitivity analysis did not test the structural assumptions in the model, such as the cost of the technology being the same as the cost of comparators.”	Please remove this statement	The submission includes a sensitivity analysis looking at CRT-D price differences for each manufacturer one at a time (+/- 20% for Medtronic and +/- 20% for St Jude Medical)	We have removed the statement.

Issue 39

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Base case data in table 21 (page	Data in base case column should be marked as	This data is from an unpublished	Thank you. Correction made.

76)	academic in confidence	manuscript (Landolina 2016)	

Issue 40

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement on page 77: "The sensitivity analysis was applied only to Medtronic and Boston Scientific CRT-Ds in the model because St Jude Medical documents do not state projected longevity."	Revision of text to read: "The sensitivity analysis was applied only to Medtronic ~~and Boston Scientific~~ CRT-Ds in the model because St Jude Medical documents do not state projected longevity."	This approach was not applied to Boston Scientific CRT-Ds in the economic model	Thank you. Correction made.

Issue 41

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement on page 78: "Two abstracts (Priest 2015, Duxbury 2014) demonstrated cost saving for longer lasting batteries using data from Boston Scientific's latitude patient management system when compared with unspecified 'industry standard' batteries taken from 'a recent NICE review'."	Revision of text to read: "Two abstracts (Priest 2015, Duxbury 2014) demonstrated cost saving for longer lasting batteries using data from Boston Scientific's Latitude patient management system when compared with a market average taken from the recent NICE TA 314, based on the NICOR registry which includes all implants in the UK for a 10 year period. "	We are disappointed that CEDAR qualifies the NICOR battery life data included in TA 314 as an 'unspecified industry standard' and the TA 314 Final Appraisal Determination as a 'recent NICE review'	This is not factual inaccuracy. We cited the two abstracts. Priest et al. refer to a 'recent NICE review'. Duxbury et al. refers to 'industrial standard' batteries. We have made the requested change as it is more informative.

Issue 42

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Reference to Duxbury 2016 (page 78)	Revision of text to read: "Duxbury 201*4*"	Reference is incorrect	Thank you. Corrected.

Issue 43

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement on page 79: "The company did not investigate the effect of a price difference between the technology and the comparators, even though purchase cost is a key driver of the model."	Revision of text to read: "The company investigated the effect of a price difference between the technology and the comparators in a sensitivity analysis."	The submission includes a sensitivity analysis looking at CRT-D price differences for each manufacturer at a time (+/- 20% for Medtronic and +/- 20% for St Jude Medical)	Thank you. We have revised the statement as follows: "The company investigated the effect of a price difference between the technology and the comparators by applying +/- 20% to the average selling price (based on all manufacturers in NICE TA314) for Medtronic CRT-Ds and for St Jude Medical CRT-Ds. The effects of these analyses on the model are small compared to the effects of using highest and lowest device list prices: purchase cost is a key driver of the model."

Issue 44

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement on page 81: "The company has stated that list prices do not reflect actual selling prices."	Revision of text to read: "The company has *provided evidence to demonstrate* that list prices do not reflect actual selling prices."	We submitted evidence to support this point and would appreciate if this was referenced	Thank you. we have revised the statement as follows: "The company has provided evidence that list prices do not reflect actual selling prices. This evidence is average selling prices collated by Eucomed based on quarterly sales data: each manufacturer receives both a generalised market average selling price plus their own specific average selling price. The EAC accepts that differences between list price and actual selling price exist. However the assumption in the model that all of the device prices are the same (based on the generalised average selling price) is also unrealistic."

Issue 45

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Statement on page 81: "However the assumption in the model that all of the device prices are the same is also unrealistic and the company did not explore the effect of a price difference	Revision of text to read: "The assumption in the model that all of the device prices are the same was tested in a sensitivity analysis as it is a key driver of the model."	The submission includes a sensitivity analysis looking at CRT-D price differences for each manufacturer at a time (+/- 20% for Medtronic and +/- 20% for St Jude Medical)	Thank you. we have revised the statement as follows: "However the assumption in the model that all of the device prices are the same (based on the generalised average selling price) is also unrealistic. The

between different manufacturers in the sensitivity analysis even though device cost was identified as a key driver of the model."			company explored varying the generic average selling price by +/- 20% for Medtronic CRT-Ds and for St Jude Medical CRT-Ds. Because device cost was identified as a key driver of the model, the EAC undertook threshold analysis as follows."

Issue 46

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
References to warranties applied in EAC analysis omit to mention eligibility (page 82)	Revision of text to read: "In sensitivity analysis the option for 100% of refunds to be *eligible and* claimed within the warranty period is explored.	Warranties depend both on the proportion claimed as well as the proportion which will be eligible for payment – this eligibility factor should also be mentioned for clarity	Thank you. revised as requested. We have also added one comment from an expert two paragraphs down: "A clinical expert stated to the EAC that CRT-D warranties are comprehensive because CRT-D devices are robust, and that in reality warranties are very rarely claimed by clinical teams as process to do so in most hospitals are lacking."

Issue 47

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Clarification of complication rates used by the manufacturer (page 84)	Revision of text to read: "The company's rates of different kinds of complications used in the model were taken from a randomised study comparing de novo	We would welcome clarification that the rates used in the economic model were chosen to reflect those used by NICE in TA314	Thank you. revised as requested.

	ICD versus de novo CRT-D in people with heart failure, *and were the same rates as used by NICE in their Technology Appraisal 314.*"		