National Institute for Health and Clinical Excellence

Single Technology Appraisal (STA)
Ivabradine for the treatment of chronic heart failure

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Servier	Yes, it is appropriate for NICE to appraise ivabradine for the treatment of CHF in order to establish its place in therapy in England & Wales, particularly given that it was not considered in NICE Clinical Guideline 108 for chronic heart failure (2010).	Comments noted. Following the scoping workshop an appraisal of ivabradine was considered appropriate.
	British Association for Nursing in Cardiovascular Care (BANCC)	It is appropriate to refer to NICE for appraisal in the light of clinical trial results	Comments noted. Following the scoping workshop an appraisal of ivabradine was considered appropriate.
	Central and Eastern Cheshire PCT / CSAS/ NHS Devon PCT	Topic seems appropriate	Comments noted. Following the scoping workshop an appraisal of ivabradine was considered appropriate.
	Pfizer	No comment	Comment noted.

Section	Consultees	Comments	Action
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	Since the 2010 NICE HF update was published there have been two new studies of interest in HF which it would be appropriate to be referred to NICE for appraisal: 1) SHIFT which pertains to Ivabridine and is now under consideration. This is a drug with a novel mode of action with potential interest in HF. 2) EMPHASIS-HF. The effect of Epleronone on all cause mortality, alongside a reduction in readmissions for patients with mildly symptomatic HF suggests this agent should also be referred to NICE for appraisal.	Comments noted.
Wording	Servier	Yes, wording is appropriate.	Comments noted.
	British Association for Nursing in Cardiovascular Care (BANCC)	Please see comments on scope population.	Comments noted. Scoping workshop attendees considered that the wording of the remit incorporated the population specified in the scope.
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Wording appropriate.	Comments noted.

Section	Consultees	Comments	Action
	Pfizer	The wording of the remit should be amended in line with suggested changes to the population. Please see comments on the population.	Comments noted. Scoping workshop attendees considered that the wording of the remit incorporated the population specified in the scope.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	This could be improved and should include reference to "……..for the treatment of patients in sinus rhythm with symptomatic (NYHAii/iii) chronic heart failure due to left ventricular systolic dysfunction.	Comments noted. Scoping workshop attendees considered that the wording of the remit incorporated the population specified in the scope.
Timing Issues	Servier	It is appropriate that the appraisal is started in advance of market authorisation being obtained in order to assist regional NHS organisations including GP commissioners in their decision making.	Comments noted. NICE aims to provide guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted.

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	British Association for Nursing in Cardiovascular Care (BANCC)	Recent evidence trial shows that heart rate is a strong predictor of cardiovascular mortality and morbidity in the general population, and in patients with hypertension, ischaemic heart disease and heart failure (Bohm, et al, 2010) SHIFT Lancet 376:886-94 Meta analysis of betablocker in heart failure trials showed the mortality benefit related to the magnitude of the heart rate reduction and not to the dose of the betablocker (McAllister et al, 2009) Annals of Internal Medicine (2009);150:784-794	Comments noted.
	NHS Devon PCT	If the drug should receive a licence extension it is quite important that patient criteria are selected in a timely manner otherwise this will need to be determined by local decision making from trial information.	Comments noted.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	The rapidity with which this drug is being appraised is surprising. It appears to have a role for carefully treated and selected patients. There is a real risk that too early adoption of this technology might mitigate against the improved use of beta-blockers (addessed by 2010 NICE HJF guidance and the 2011 Quality standards). Of note Ivabridine has a lesser effect where patients are well treated (>50% target dose) with beta-blockers. Urgency of this appraisal to the NHS - low.	Comments noted. NICE aims to provide guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted.

Section	Consultees	Comments	Action
Additional comments on the draft remit	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	The draft remit refers to an appraisal "of the clinical (use) and cost effectiveness of Ivabridine within its licensed indication for the treatment of chronic heart failure". Since Ivabridine does not yet have a license (though one is expected) this remit is curious.	Comments noted. The scope is prepared before the licence for the technology has been granted and the topic will not be appraised until the marketing authorisation has been approved.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Servier	paragraph 1: - "Heart failure may be due to LVSD…" may be more accurately replaced with, "Heart failure may be associated with LVSD…" as LVSD is a feature of some heart failure syndromes rather than a causal factor per se. paragraph 5: - In addition to improving the life expectancy and quality of life of patients, another primary goal of managing heart failure is to avoid hospitalisations (NICE CG 108 for CHF). paragraph 6: - cites NICE CG108 and lists agents "…for second-line use in people who remain symptomatic despite first-line treatment". A more precise wording is suggested, "…for second-line use in particular patient groups who remain symptomatic despite first-line treatment". Consideration should also be given to acknowledging the importance of heart rate in the management of heart failure and how this is best achieved. Elevated heart rate is a risk factor in heart failure and is linked to outcomes (e.g. mortality, hospitalisations and quality of life) (1–16).	Comments noted. The background section has been updated.

Section	Consultees	Comments	Action
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	NICE costing data suggest annual incidence is 63,000 in England (CG108 Chronic heart failure: costing template), while British Heart Foundation Coronary Heart Disease Statistics (2010) suggest annual incidence of 27,000 in the UK. These figures differ from the 68,000 annual incidence quoted for the UK in the draft scope. National Horizon Scanning Centre report on Ivabradine for Chonic Heart Failure (April 2010) suggests 8,650 registered deaths due to heart failure in England and Wales for 2008, which is lower than the 24,000 deaths quoted for the UK in the draft scope. A clarification of prevalence and hospitalisations would be useful to assess the financial impact on the PCT.	Comments noted. The background section has been amended and the incidence figures have been aligned with those in the costing template. The number of deaths has been deleted. The hospitalisations have not been included since that level of detail is not normally included in a scope.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	For completeness it might include reference to emphasis on beta-blocker usage including up-titration in both the 2010 NICE guidance and the 2011 HF Quality Standards.	Comments noted. The scope has not been amend since this level of detail is not included in the scope
The technology/ intervention	Servier	Yes	Comment noted.
	British Association for Nursing in Cardiovascular Care (BANCC)	No comments to add.	Comment noted.

Section	Consultees	Comments	Action
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Information appears accurate.	Comments noted.
	Pfizer	The description of the populations in which ivabradine has been studies should include the specification that patients not only had to have symptomatic chronic heart failure, and left ventricular systolic dysfunction, but also inadequately controlled heart rate, as per the patient population in SHIFT.	Comments noted. Scoping workshop attendees agreed that it was appropriate to amend the population to specify symptomatic chronic heart failure in line with the SHIFT trial population. The workshop attendees did not consider that baseline heart rate was clinically relevant for defining the expected population as the relevance of heart rate is still an issue of debate.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	There is only only study in heart failure of Ivabridine so reference to trials is a little disengenious. It should specify that the trial was in symptomatic patients in sinus rhythm.	Comments noted. This section has been updated.

Section	Consultees	Comments	Action
Population	Servier	Yes, the population is reasonably defined. It may be more precisely defined as, "Adults with chronic heart failure and left ventricular systolic dysfunction of ischaemic or non-ischaemic origin". (Again, this helps to distinguish between causal and associated factors) The submission will examine whether cost effectiveness is demonstrated in all patients across the full range of baseline heart rates in SHIfT. However baseline heart rate was observed to modify the treatment effect such that the benefit appears to be weaker in the subgroup with baseline heart rate of less than the median (1). Although lacking statistical power to reach significance, the point estimate in the lower heart rate group is suggestive of a modest benefit of treatment (HR = 0.93). The SHIfT sister paper (Böhm et al) identifies heart rate quintiles that may be informative in considering this treatment effect modifier (2).	Comments noted. This level of detail is not usually included in the scope. Based on clinical practice, attendees did not consider baseline heart rate to be an appropriate factor to define a subpopulation, as there is not a clear consensus of its role in the management of chronic heart failure.

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	British Association for Nursing in Cardiovascular Care (BANCC)	Population needs to be more specific: adults with chronic heart failure due to left ventriculatr systolic dysfunction who are symptomatic, already established on optimal or maximum tolerated dose of ACE inhibitor and betablocker (unless contraindicated) in sinus rhythm, with a resting heart rate of 70 or more beats per minute.	Scoping workshop attendees agreed that it was appropriate to amend the population to specify symptomatic chronic heart failure in line with the SHIFT trial population, in sinus rhythm and, as this is an add-on treatment, to specify that the population will be on optimal standard treatment for chronic heart failure. Ivabradine will be appraised in line with its expected marketing authorisation. At this stage it is not known how or if heart rate will be defined in the UK marketing authorisation. Based on clinical practice, attendees did not consider baseline heart rate to be an appropriate factor to define a subpopulation, as there is not a clear consensus of its role in the management of chronic heart failure.

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	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Population appears appropriate. There may be subgroups which could be addressed at the analysis stage.	Comments noted.
	Pfizer	The population should be more specifically defined as "adults with chronic heart failure due to left ventricular systolic dysfunction with inadequately controlled heart rate." The study population was limited to those with inadequate HR control, which inextricably links all results to heart rate. To define the population solely on the basis of left ventricular systolic dysfunction inadequately characterises the population in which ivabradine will likely be used.	Comments noted. Ivabradine will be appraised in line with its expected marketing authorisation. At this stage it is not known how or if heart rate will be defined in the UK marketing authorisation. Based on clinical practice, attendees did not consider baseline heart rate to be an appropriate factor to define a subpopulation, as there is not a clear consensus of its role in the management of chronic heart failure.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	The population studied was patients with symptomatic (NYHAii and iii) treated chronic HF due to LVSD, in sinus rhythm. The pre-specified sub-population which should be considered against all the outcomes are the patients who were prescribed 50% or more of their target beta-bloker dosage.	Comments noted. This was not considered to be an appropriate subgroup.

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Comparators	Servier	Yes, this is an appropriate comparator. Again, to clarify further and echo the Background information, "Standard pharmacological treatment without ivabradine" would be more precise. This represents a range of therapies titrated to maximum tolerated dosages. Recommendations may vary according to patient profile, for example the evidence for the hydralazine/nitrate combination centres on black populations (1-4). We expect to supply data e.g. from the National Heart Failure Audit to demonstrate that background therapies in SHIfT may be regarded as a good surrogate for 'best achievable care', which exceeds average levels of treatment observed in UK clinical practice.	Comments noted. The attendees at the scoping workshop discussed whether to define standard treatment and decided that, as this is an add-on treatment that can be added on to various treatments in the treatment pathway, a more specific definition was not appropriate. The current treatment pathway is clearly defined in the NICE Clinical Guideline for chronic heart failure No. 108. Attendees also agreed that there was no current alternative to ivabradine so no other comparators were required.

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	British Association for Nursing in Cardiovascular Care (BANCC)	Perhaps need to clarify what do we mean by "Standard treatment" e.g. .do we mean those patients who are already established on optimal dose of Ace inhibitor and betablocker, including those whom betablocker is contraindicated. Ivabradine is currently the only If channel blocker available in the market and therefore there's no other technology to compare it with as like for like	Comments noted. The attendees at the scoping workshop discussed whether to define standard treatment and decided that, as this is an add-on treatment that can be added on to various treatments in the treatment pathway, a more specific definition was not appropriate. The current treatment pathway is clearly defined in the NICE Clinical Guideline for chronic heart failure No. 108. Attendees also agreed that there was no current alternative to ivabradine so no other comparators were required.

Section	Consultees	Comments	Action
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Could define standard treatment.	Comments noted. The attendees at the scoping workshop discussed whether to define standard treatment and decided that, as this is an add-on treatment that can be added on to various treatments in the treatment pathway, a more specific definition was not appropriate. The current treatment pathway is clearly defined in the NICE Clinical Guideline for chronic heart failure No. 108.
	Pfizer	Although the treatment algorithm in the current NICE guidance on CHF makes no mention of treatment choice with respect to heart rate control, ivabradine will likely be used in patients with LVSD whose HR is inadequately controlled with standard therapy. The current standard therapy to control heart rate in patients with CHF is beta-blockers. For those whose HR is not controlled with a maximum up-titrated dose of beta-blockers, or for those intolerant to beta-blockers, digoxin may be the most appropriate comparator, as it - like ivabradine - effects the sino-atrial node. Ivabradine will not be considered as an alternative treatment choice to angiotensin-converting enzyme inhibitors, aldosterone antagonists or angiotensin receptor blockers.	Comments noted. See response above. The scoping workshop attendees did not consider digoxin to be an appropriate comparator. It is not used as an add-on in the same way that ivabradine is expected to be used in the treatment of chronic heart failure for the specified population.

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	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	Since this is a novel agent (in terms of mechanism of action) and its use is as an adjunct to existing therapies there is no comparator.	Comments noted. In terms of a NICE appraisal, the comparator is current NHS standard treatment.
Outcomes	Servier	Yes. Whilst cardiovascular and all-caused mortality are the favoured mortality outcome measures, it should also be noted that in the context of the SHIfT study heart failure mortality is important.	Comments noted. Attendees at the scoping workshop did not consider it relevant to add heart failure mortality to the scope.
	British Association for Nursing in Cardiovascular Care (BANCC)	Yes	Comments noted.
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Consider the addition of myocardial infarction and coronary revascularisation.	Comments noted. Scoping workshop attendees did not consider these outcomes to be relevant to the measure of clinical and cost effectiveness of treatments for chronic heart failure.

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	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	We would recommend all cause hospitalisations is also included. From the patients perspective (and economic argument) being at home rather than in hospital is the area of interest, rather than the cause of the readmission.	Comments noted. All cause hospitalisations has been added as an outcome.
Economic analysis	Servier	A lifetime horizon is most appropriate in the base case and shorter time horizons will be explored in sensitivity analyis.	Comments noted.
	Central and Eastern Cheshire PCT	A reduction in hospitalisation costs should be assessed as well.	Comments noted.
	CSAS	Agree.	Comments noted.
	NHS Devon PCT	Agree.	Comments noted.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	The urgency with which this is being appraised is not clear from the economic perspective	Comments noted

Section	Consultees	Comments	Action
Equality and Diversity	British Association for Nursing in Cardiovascular Care (BANCC)	In the SHIFT trial, the proportion of elderly patients (over 65 years old) were low and therefore assumption of benefit to these group cannot be generalised.	Comments noted. Scoping workshop attendees noted the issues in term of recruitment to clinical trials but did not consider it necessary to revise the scope.
	NHS Devon PCT	Recommendation that further trials are initiated covering a greater variety of ethnic groups. SHIFT was undetaken in a mainly white male population	Comments noted. Scoping workshop attendees noted the issues in term of recruitment to clinical trials but did not consider it necessary to revise the scope.
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	The study was conducted largely without the UK and this is reflected in recruitment from a very young population (for HF), a predominance of males, and a lack of ethnic diversity - nearly all (89%) were white. The appraisal might usefully consider modes of elimination of Ivabridine and if these change with age, and the issue of polypharmacy (particularly around drugs modifying p450 3A4 cytochrome) when considering the use of this drug in older HF patients. Variations in handling in female patients would also be relevant. Recent NICE gidance suggests second line treatment should be considered in discussion with or referral to the HF specialist (which is defined). This would be particularly important for this third or (even fourth line) agent to ensure its use is driven by clinical indication rather than commercial pressure.	Comments noted.
Innovation	Servier	INNOVATION Professor Sir Ian Kennedy's 2009 report for NICE highlighted three areas with regard to innovation (1). Servier believes that each of these applies to	Comments noted.

Section	Consultees	Comments	Action
		ivabradine in heart failure and this criterion for innovation has therefore been met. 1. Is new: Ivabradine is currently being considered by the EMEA for license as a new treatment for the management of heart failure. Its mechanism of action is unique and there are no other related agents currently in clinical development for heart failure. 2. Constitutes an improvement on existing therapies: The SHIfT trial showed that the addition of ivabradine to standard best practice treatment further improved outcomes compared to best practice treatment plus placebo, for the composite primary endpoint of cardiovascular death and hospitalisation for heart failure, and also death from heart failure and hospitalisation for heart failure (2). These findings are consistent with the objectives of heart failure treatment outlined in NICE CG108 (3). If the therapy for heart failure has been optimised there is currently no additional non-surgical option other than ivabradine to achieve further benefit in these patients. 3. Offers something more: a step-change in terms of outcomes for patients [note the Kennedy report highlights that a 'step-change' relates to meeting a need recognised as important by the NHS, and furthermore that the NICE Citizen's Council (May 2009) ranked quality of life as the most highly valued innovation (1)]: The NHS has identified heart failure as being important (3,4). The Quality and Outcomes Framework 2011/12 states, "Heart failure represents the only major cardiovascular disease with increasing prevalence and is responsible for dramatic impairment of quality of life, carries a poor prognosis for patients, and is very costly for the NHS to treat (second only to stroke)." (4) In line with this, improving quality of life is one of the objectives for heart failure treatment as	

Section	Consultees	Comments	Action
		defined in NICE CG108 (3). Published evidence has shown no improvement in the quality of life of patients with any current treatments (e.g. beta-blockers, ACEi, ARB, aldosterone antagonists etc), either through generic or condition-specific measures (3,5-7). The PRO-SHIfT study (a pre-defined quality of life sub-study) showed, using the Kansas City Cardiomyopathy Questionnaire, that the addition of ivabradine to standard best practice significantly improved health related quality of life (8). In terms of both clinical outcomes and quality of life improvements, the SHIfT study clearly demonstrates that the use of ivabradine in patients with heart failure will result in improvements to patient care. HEALTH RELATED BENEFITS NOT CAPTURED IN THE QALY The Kennedy report indicates a number of benefits potentially not captured by the QALY measure (1): From a personal perspective, disease-specific quality of life improvements and reduced heart failure hospitalisations may impact positively on patients' dignity and independence, and lead to a reduction in the social visibility of the disease and its care. From a societal perspective, heart failure may be considered an end of life issue as it carries a very poor survival prognosis (one-year mortality rates 30-40% (3,9)) which is at least comparable with the survival rate for many cancers such as breast (10) and prostate (11).	

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	British Association for Nursing in Cardiovascular Care (BANCC)	Yes In clinical practice, some patients cannot simply tolerate higher doses of betablocker to get heart rates down, so if rates can be lowered by another drug, that can impact outcome.	Comments noted.
	NHS Devon PCT	Ivabradine is the first in a new class of drug for heart failure which highlights its suitability for its health related benefits to be assessed.	Comments noted.
Other considerations	British Association for Nursing in Cardiovascular Care (BANCC)	The use of devices was low in SHIFT trial (1% had CRT, 3-4% had ICD), interactions between ivabradine and devices is unknown and needs to be studied. As ivabradine is currently unlicensed for patient with chronic heart failure, it is likely that primary care will stipulate that ivabradine is initiated and titrated by specialist heart failure teams. The selection of appropriate patients(symptomatic heart failure due to left systolic dysfunction,with ejection fraction ≤ 35% ,in sinus rhythm with resting heart rate ≥70bpm, on optimal dose of ace inhibitor and betablocker) will be essential to ensure benefits of ivabradine are realised in clinical ptactice. Whether "hospitalisation within the last 12 months" needs to considered (also in the inclusion criteria in SHIFT trial) remains an area of debate.	Comments noted. The scoping workshop attendees did not consider these to be appropriate subgroups. Guidance on who should prescribe ivabradine is not defined within the scoping process. If appropriate, this is considered by the Appraisal Committee when formulating its recommendations in line with the marketing authorisation.
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Could consider subgroup analysis based on NYHA classes, left ventricular ejection fraction or heart rate.	Comments noted. The scoping workshop attendees did not consider these to be appropriate subgroups.

Section	Consultees	Comments	Action
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	Would early adoption of this agent undermine the 2011 Quality Standard 7, and so put patients with LVSD and an EF < 35% at increased risk through a continued sub-optimal use of beta-blockers ?	Comments noted.
Questions for consultation	Servier	At what point in the pathway of care is ivabradine expected to be used? - For specialist initiation in both secondary and primary care	Guidance on who should prescribe ivabradine is not defined within the scoping process. If appropriate, this is considered by the Appraisal Committee when formulating its recommendations in line with the marketing authorisation.

Section	Consultees	Comments	Action
	Central and Eastern Cheshire PCT / CSAS / NHS Devon PCT	Existing trials appear to suggest that benefit may be greater in people with higher initial heart rate.	Ivabradine will be appraised in line with its expected marketing authorisation. At this stage it is not known how or if heart rate will be defined in the UK marketing authorisation. Based on clinical practice, attendees did not consider baseline heart rate to be an appropriate factor to define a subpopulation, as there is not a clear consensus of its role in the management of chronic heart failure.
	Pfizer	See comments on population and comparators.	See responses to comments on population and comparators
	The British Society for Heart Failure, The British Cardiovascular Society, The Royal College of Physicians	The agent is innovative and may be of particular interest in patients truly ineligible for beta-blokers though this was not the group primarily under study. It is of note that patients well treated with beta-blockers (>50% target dose) derived less benefit from the intervention. Since beta-blockers confer a reduction in all cause mortality (and all cause readmission) it is important that Ivabridine does not become a default easier prescribing option.	Comments noted

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Healthcare Improvement Scotland (formerly NHS Quality Improvement Scotland)
Public Health Wales Trust
British Cardiovascular Intervention Society
Department of Health
sanofi
Royal College of Nursing

Comment 2: the provisional matrix

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	**Proposal made by:**		**Action taken:** **Removed/Added/Not included/Noted**	**Justification:**
1.	Add Grown Up Congenital Heart Patients Association	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Grown Up Congenital Heart Patients Association has been included in the matrix of consultees and commentators under Patient /Carer Groups.
2.	Add HEART UK	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. HEART UK has been included in the matrix of consultees and commentators under Patient / Carer Groups.

3.	Add Network of Sikh Organisation	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Network of Sikh Organisation has been included in the matrix of consultees and commentators under Patient / Carer Groups.
4.	Add British Association of Emergency Medicine	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. British Association of Emergency Medicine has been included in the matrix of consultees and commentators under Professional Groups.
5.	Add British Atherosclerosis Society	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. British Atherosclerosis Society has been included in the matrix of consultees and commentators under Professional Groups.

6.	Add British Nuclear Cardiology Society	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. British Nuclear Cardiology Society has been included in the matrix of consultees and commentators under Professional Groups.
7.	Add Heart Rhythm UK	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Heart Rhythm UK has been included in the matrix of consultees and commentators under Professional Groups.
8.	Add Royal Pharmaceutical Society	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Royal Pharmaceutical Society has been included in the matrix of consultees and commentators under Professional Groups.

9.	Add Cardiac and Cardiology Research Dept., Barts	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Cardiac and Cardiology Research Dept, Barts has been included in the matrix of consultees and commentators under Research Groups.
10.	Add Cardiovascular Research Initiative, University of Oxford	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Cardiovascular Research Initiative, University of Oxford has been included in the matrix of consultees and commentators under Research Groups.
11.	Add CORDA	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. CORDA has been included in the matrix of consultees and commentators under Research Groups.

12.	Add European Council for Cardiovascular Research	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. European Council for Cardiovascular Research has been included in the matrix of consultees and commentators under Research Groups.
13.	Remove Chinese Healthy Living Centre	NICE Secretariat		Removed	This organisation has requested only to be contacted specifically about Chinese-related topics. This topic is not of specific interest to the Chinese community and therefore the organisation has been removed from Patient / carer Groups on the matrix.
14.	Add Blood Pressure Association	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Blood Pressure Association Research has been included in the matrix of consultees and commentators under Patient / carer Groups.

15.	Add Cardiac Risk in the Young (CRY)	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. European Council for Cardiovascular Research has been included in the matrix of consultees and commentators under Patient / carer Groups.