Appendix D

National Institute for Health and Clinical Excellence

Single Technology Appraisal (STA)

Aflibercept solution for the treatment of wet age-related macular degeneration

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	**Royal National Institute of Blind People**	Yes. Aflibercept for first-line treatment of wet age-related macular degeneration offers patients a new treatment option with a less onerous dosage regimen. Aflibercept can be administered at a dose of 2mg every eight weeks; whereas currently available anti-VEGF therapies need to be administered monthly to achieve the best possible efficacy. This new therapy will be less burdensome for patients, their carers and health professionals.	Comments noted.
	Bayer plc	The draft remit is appropriate.	Comment noted.
	NHS North Somerset	This topic is appropriate.	Comment noted.
	The Royal College of Ophthalmologists	yes	Comment noted.

Section	Consultees	Comments	Action
	CSAS	This topic is appropriate.	Comment noted.
Wording	**Royal National Institute of Blind People**	The wording is appropriate	Comment noted. No action required.
	Bayer plc	The wording is appropriate.	Comment noted. No action required.
	NHS North Somerset	The wording is accurate.	Comment noted. No action required.
	The Royal College of Ophthalmologists	yes	Comment noted. No action required.
	CSAS	The wording is accurate.	Comment noted. No action required.
Timing Issues	**Royal National Institute of Blind People**	The timing is appropriate	Comment noted. No action required.
	Bayer plc	The timing is appropriate.	Comment noted. No action required.
	NHS North Somerset	if there is potential cost savings to the NHS then should be priority	Comment noted. No action required.

Section	Consultees	Comments	Action
	The Royal College of Ophthalmologists	as soon as possible	Comment noted. No action required.
Additional comments on the draft remit			

Comment 2: the draft scope

Section	Consultees	Comments	Action

Section	Consultees	Comments	Action
Background information	**Royal National Institute of Blind People**	This section is accurate, however, in terms of completeness, we would like the following information to be added: (1) In paragraph one: please include the fact that AMD usually affects both eyes. (2) In paragraph two: please include the risk factor of exposure to UV light. Suggested wording is outlined below: Some studies suggest that exposure to high levels of sunlight (particularly UV light contained in sunlight) may increase the risk of developing AMD. (3) In the final paragraph: we would like reference made to the importance of patients receiving rapid treatment. Example wording is as follows: Wet AMD can develop very quickly, making serious changes to central vision in a short period of time. Treatment needs to be given rapidly before new blood vessels cause excess damage to the macula, leading to scarring and permanent sight loss. (4) Also in the final paragraph, we would like the following passage clarified: "The Royal College of Ophthalmologists has issued guidance on the management of wet age-related macular degeneration including the use of intravitreal ranibizumab and bevacizumab". Please ensure readers are told that the guidance recommends ranibizumab but not bevacizumab for use in patients with wet AMD.	Comment noted. The background information section has been amended accordingly. The management paragraph in the scope references the guidance or guidelines that are available for this condition. This paragraph has been amended to allow the reader to view the Royal College of Opthalmologists guidance on ranibizumab and bevacizumab.

Section	Consultees	Comments	Action
		The Royal College released a statement in December 2010 stating that: "the use of an unlicensed drug (bevacizumab) cannot be recommended by the College when a licensed alternative is available". See: http://www.rcophth.ac.uk/news.asp?section=24&itemid=281&search=	
	Bayer plc	No comment	Comment noted. No action required.
	NHS North Somerset	This is accurate.	Comment noted. No action required.
	The Royal College of Ophthalmologists	correct	Comment noted. No action required.
	CSAS	This is accurate.	Comment noted. No action required.
The technology/ intervention	**Royal National Institute of Blind People**	Yes	Comment noted. No action required.
	Novartis Pharmaceuticals	Novartis suggests the following revised wording: "Aflibercept solution for injection (Eylea, Bayer Schering and Regeneron) is a soluble VEGF receptor fusion protein which binds to all forms of VEGF-A, VEGF-B and placental growth factor (PIGF)". Please see attached 'role of placenta growth factor' for supporting documentation.	Comment noted. The scope has been amended accordingly.
	Bayer plc	Please do not use the brand name Eylea at this stage. Aflibercept solution for injection is not yet approved for use in Europe. Aflibercept solution for injection is the name currently being used.	Comment noted. The brand name Eylea has been removed from the scope.

Section	Consultees	Comments	Action
	NHS North Somerset	It could specify here that the intervention is being assessed for first-line use.	Comment noted. The scope now specifies that the intervention is being assessed for first-line use.
	The Royal College of Ophthalmologists	yes	Comment noted. No action required.
	CSAS	It could specify here that the intervention is being assessed for first-line use.	Comment noted. The scope now specifies that the intervention is being assessed for first-line use.
Population	**Royal National Institute of Blind People**	The population is defined appropriately	Comment noted. No action required.
	Bayer plc	The population is appropriate.	Comment noted. No action required.
	The Royal College of Ophthalmologists	yes	Comment noted. No action required.

Section	Consultees	Comments	Action
Comparators	**Royal National Institute of Blind People**	(1) Ranibizumab We are satisfied that ranibizumab is an appropriate comparator. Clinical experts tell us that it is considered routine and best practice in the NHS for first-line treatment of wet AMD. We would like to highlight that the Royal College of Opthalmologists recommends ranibizimab for the treatment of wet AMD. NICE guidance (TA 155) also recommends ranibizumab as a possible treatment for people with wet AMD, although patients must meet certain criteria for this recommendation to apply. (2) Bevacizumab Bevacizumab is currently not licensed for use in wet AMD. Patient organisations and clinical professionals agree that there is still insufficient data to draw firm conclusions on the comparative safety of this drug in the treatment of the condition. Therefore, this therapy should not be considered routine and best practice in the NHS, and should not be used as a comparator. There is also no existing NICE guidance on the use of bevacizumab for wet AMD.	Comment noted. Comparators should include technologies which constitute routine practice in the NHS even if they are unlicensed. During the scoping workshop it was confirmed by consultees that bevacizumab is currently being used in the NHS to treat wet age-related macular degeneration. It was decided that bevacizumab should remain as a comparator in the scope.

Section	Consultees	Comments	Action
		(3) Best supportive care Clinicians have informed us that ranibizumab is the routine treatment given to patients with wet AMD and not supportive care. (4) Photodynamic therapy NICE has issued guidance on the use of photodynamic therapy for wet AMD (TA 68) which states that: Photodynamic therapy (PDT) is recommended for the treatment of wet AMD for individuals who have a confirmed diagnosis of classic with no occult subfoveal choroidal neovascularisation (CNV) (that is, whose lesions are composed of classic CNV with no evidence of an occult component) and best-corrected visual acuity 6/60 or better. Therefore, PDT could be used as a comparator for this subgroup.	Best supportive care has now been removed as a comparator in the scope. Photodynamic therapy has now been added as a comparator in the scope.

Section	Consultees	Comments	Action
	Royal College of Nursing	Standard Comparators - it is acceptable to use Ranibizumab as a comparator as it too has been trialled but as yet Avastin still remains unlicensed and therefore may not be as strong in terms of evidence.	Comment noted. Comparators should include technologies which constitute routine practice in the NHS even if they are unlicensed. During the scoping workshop it was confirmed by consultees that bevacizumab is currently being used in the NHS to treat wet age-related macular degeneration. Therefore, it was decided that bevacizumab should remain as a comparator in the scope.

Section	Consultees	Comments	Action
	Novartis Pharmaceuticals	Intravitreal bevacizumab is not an appropriate comparator for inclusion in this appraisal. Bevacizumab is a cancer drug which is unlicensed for the treatment of ocular conditions. Furthermore, there is a lack of robust clinical effectiveness and safety data for bevacizumab.	Comment noted. Comparators should include technologies which constitute routine practice in the NHS even if they are unlicensed. During the scoping workshop it was confirmed by consultees that bevacizumab is currently being used in the NHS to treat wet age-related macular degeneration. It was also noted that published clinical trial evidence is available that directly compares bevacizumab and ranibizumab for people with wet age-related macular degeneration. Therefore, it was decided that bevacizumab should remain as a comparator in the scope.

Section	Consultees	Comments	Action
	Bayer plc	The updated NICE guide to the methods of technology appraisal (June 2008) defines relevant comparator technologies with specific consideration given to routine and best practice in the NHS (including existing NICE guidance), including technologies that do not have a marketing authorisation for the indication defined in the scope but that are used routinely for the indication in the NHS. Ranibizumab is currently considered routine and best practice in the NHS (including existing NICE guidance) for the first-line treatment of wet age-related macular degeneration (wAMD). Ranibizumab is recommended by the Royal College of Ophthalmologists for the management of wAMD and is recommended by NICE (TA155) for the treatment of wAMD in people with baseline visual acuity between 6/12 and 6/96 who meet criteria that ensure the presence of wAMD. Photodynamic therapy (PDT)/verteporfin is also recommended by NICE (TA68) for the treatment of people with wAMD who have classic with no occult subfoveal choroidal neovascularisation with a visual acuity off 6/60 or better and is therefore an appropriate comparator for that subgroup alone (see comments on subgroups in 'other considerations'). Bevacizumab and best supportive care cannot be appropriately considered routine and best practice in the NHS (including existing NICE guidance) for the first-line treatment of wAMD for the following reasons: • The Royal College of Ophthalmologists recommends bevacizumab as part of research rather than routine and best practice in the NHS. In a recent statement issued on 4th May 2011, the College clarified that	Comment noted. Best supportive care has now been removed as a comparator in the scope. Photodynamic therapy has now been added as a comparator to the scope. Comment noted. Comparators should include technologies which constitute routine practice in the NHS even if they are unlicensed. During the scoping workshop it was confirmed by consultees that bevacizumab is currently being used in the NHS to treat wet age-related macular degeneration. Therefore, it was decided that bevacizumab should remain as a comparator in the scope.

Section	Consultees	Comments	Action
		"the College is fully aware of the current NHS funding issues but remains committed to maintaining professional standards and patient safety. It would be inappropriate for the College to compromise on safety and urges caution in the interpretation of the CATT Study. Until the safety concerns are properly addressed, ranibizumab remains the recommended treatment for wet AMD. The College however continues to support use of bevacizumab as part of research. Where informed consent has been taken to use a drug outside of its licensed product indication, the responsibility for its use lies with the clinician". • A NICE workshop in December 2011 on the potential appraisal of bevacizumab for eye conditions (where clinical experts, industry and academia were represented) indicated that bevacizumab is used second-line for wAMD: *"Ophthalmologists at the workshop gave the reasons why bevacizumab might be considered as a treatment option. Although not licensed as a treatment for eye conditions, it is administered in some hospitals in the UK as an intravitreal injection to treat eye conditions where there are no other licensed treatments, or in a minority of wet AMD cases where improvements in vision have not been achieved with ranibizumab. It is also given to patients whose wet AMD does not meet the criteria in TA155, to recover some vision before further deterioration occurs*." • There is no existing NICE guidance on bevacizumab for wAMD. Despite the workshop in December 2010, in a recent parliamentary questions, [70741], Mr Simon Burns stated there are no immediate plans to refer this topic to NICE for appraisal, but will keep this position under review.	

Section	Consultees	Comments	Action
		Moreover, the manufacturer has indicated that it does not intend to apply for a license for bevacizumab in wAMD. In the absence of NICE guidance, some local PCTs have recently issued recommendations on the use of bevacizumab for wAMD. However, these recommendations are based primarily on difference in acquisition cost (i.e. budget impact) rather than a comprehensive cost utility analysis using NICE methods. • In the absence of any referral of bevacizumab to NICE for appraisal, the inclusion of bevacizumab as a comparator in the draft scope for aflibercept solution for injection is likely to be considered by stakeholders as a substitute for a NICE appraisal of bevacizumab. However, this contradicts the report from the NICE workshop that indicates provisions for safety are necessary for any appraisal of bevacizumab: "*There is support for an appraisal of intravitreal bevacizumab for eye conditions. Stakeholders agreed that an appraisal would need to be conditional on, or incorporate the assessment of, the safety and quality of intravitreal bevacizumab by a regulatory body or through the involvement of regulatory expertise. It was suggested that options for commissioning the relevant skills and expertise for this purpose be explored. Arrangements for safety monitoring / pharmacovigilance will need to be explored*". Ongoing RCTs (CATT and IVAN) are insufficiently powered to assess bevacizumab safety and are unlikely to be available in time for inclusion in an aflibercept submission.	

Section	Consultees	Comments	Action
		• Bevacizumab has previously been included as a comparator in NICE scopes for the appraisal of ranibizumab for diabetic macular oedema and macular oedema secondary to RVO. However, these are different indications for which there was previously an absence of licensed alternative therapeutic options. In the case of wAMD, ranibizumab is licensed and recommended by NICE in TA155. The cost effectiveness of aflibercept solution for injection compared with bevacizumab cannot be evaluated using NICE methods for technology appraisal given the variable and highly uncertain cost for intravitreal bevacizumab and the absence of routine or best practice guidelines. • The NICE methods state that the list price of a technology should be used in the base-case of any technology appraisal (section 5.5.2) and that if the acquisition price paid differs from the public list price, prices are required to be transparent, consistently available across the NHS and the period for which the specified price is available is guaranteed (see section 5.5.2). • The price paid for the intravitreal bevacizumab used in the treatment of wAMD is not transparent, consistent across the NHS, and defined for a specific period of time, as deemed necessary by NICE methods. Intravitreal bevacizumab is currently manufactured by independent centres from the concentrate for intravenous infusion that is licensed in the UK for the treatment of metastatic colorectal cancer and listed in the BNF at a list net price of £242.66 for a 4-ml (100mg) vial. These centres charge variable prices and have limited capacity to supply the NHS. In future, other centres may start to manufacturer bevacizumab at different prices.	

Section	Consultees	Comments	Action
		• The Southampton Assessment Group report also indicated that *"…there are no dose escalating/ranging studies of intravitreal bevacizumab and the optimum dose and dose-frequency are unknown…Safety concerns have also been raised as bevacizumab was not designed, manufactured or approved for intraocular use..."* . There has been an absence of appropriate efficacy and adequately powered safety studies to establish best practice bevacizumab for wAMD. Best supportive care is not an appropriate comparator as people with wAMD who are eligible for aflibercept solution for injection would receive ranibizumab as standard care in the NHS.	

Section	Consultees	Comments	Action
	NHS North Somerset	Bevacizumab is a valid comparator, as it is being studied for wet AMD; however, it is not licensed in UK and there have not been any studies that compared bevacizumab with aflibercept (VEGF trap-eye). It is not clear if 'best supportive care' includes (1) laser photocoagulation and (2) photodynamic therapy or if these are excluded. The term best supportive care should be further qualified.	Comment noted. Comparators should include technologies which constitute routine practice in the NHS even if they are unlicensed. During the scoping workshop it was confirmed by consultees that bevacizumab is currently being used in the NHS to treat wet age-related macular degeneration. Therefore, it was decided that bevacizumab should remain as a comparator in the scope. Ranibizumab is considered to be routine treatment for wet age-related macular degeneration in the NHS. Therefore, 'best supportive care' has now been removed as a comparator in the scope.
	The Royal College of Ophthalmologists	yes	Comment noted. No action required.

Section	Consultees	Comments	Action
	CSAS	Bevacizumab is a valid comparator, as it is being studied for wet AMD; however, it is not licensed in UK and there have not been any studies that compared bevacizumab with aflibercept (VEGF trap-eye). It is not clear if 'best supportive care' includes (1) laser photocoagulation and (2) photodynamic therapy or if these are excluded. The term best supportive care should be further qualified.	Comment noted. Comparators should include technologies which constitute routine practice in the NHS even if they are unlicensed. During the scoping workshop it was confirmed by consultees that bevacizumab is currently being used in the NHS to treat wet age-related macular degeneration. Therefore, it was decided that bevacizumab should remain as a comparator in the scope. Ranibizumab is considered to be routine treatment for wet age-related macular degeneration in the NHS. Therefore, 'best supportive care' has now been removed as a comparator in the scope.
Outcomes	**Royal National Institute of Blind People**	Experts tell us that contrast sensitivity is an inappropriate outcome measure and is not the standard measure used in clinical practice.	Comment noted. Contrast sensitivity has now been removed as an outcome measure in the scope.

Section	Consultees	Comments	Action
	Royal College of Nursing	Outcome measures - these are reasonable measures and we consider the one main benefit to the patients for Aflibercept is the fact that the frequency of injection is reduced due to the longer acting mechanism of the therapy, this means overall a reduced burden on patients and the units delivering the therapy.	Comment noted. No action required.
	Novartis Pharmaceuticals	Novartis suggests removing 'contrast sensitivity' as neither aflibercept or ranibizumab collected this data within clinical trials.	Comment noted. Contrast sensitivity has now been removed as an outcome measure in the scope.
	Bayer plc	Visual acuity in the study eye is the most relevant outcome for the measure of clinical effectiveness. Clinical outcomes measured in the VIEW I/II clinical trials of aflibercept solution for injection relate to the study eye only. Vision-related quality of life (i.e. the National Eye Institute Visual Function Questionnaire (NEI VFQ) 25) and health-related quality of life measures take account of the impact of visual acuity in both eyes. Contrast sensitivity is not an appropriate outcome. It is not an outcome measure in the VIEW I/II trials and is not the standard measure used in clinical practice.	Comment noted. Because some patients with wet age-related macular degeneration may require treatment in both eyes, visual acuity does not refer to the affected eye only. Contrast sensitivity has been removed as an outcome measure in the scope.
	The Royal College of Ophthalmologists	yes	Comment noted. No action required.

Section	Consultees	Comments	Action
	CSAS	The outcomes listed are appropriate but it would be useful to specifiy if short-term and/or long-term outcomes are to be considered and what the time period of interest might be. Few randomised trials have examined outcomes for longer than two years.	Comment noted. It was discussed at the workshop that the outcomes in the trials would be used and then extrapolated to an appropriate time horizon in the manufacturer's economic model.
Economic analysis	**Royal National Institute of Blind People**	The scope notes that: 'Costs will be considered from an NHS and Personal Social Services perspective'. By limiting considerations to NHS and Personal Social Services costs, NICE fails to recognise the full impact of sight loss on society and the Exchequer. By failing to focus on the whole picture - both mental, physical and social problems associated with blindness - there is a real danger of sub-optimal investment in new treatments.	Comment noted. During the scoping workshop, it was considered that the impact, in terms of mental, physical and social functioning, of ranibizumab and comparators on wet age-related macular degeneration would be captured in health-related quality of life measures.
	Bayer plc	No comment	Comment noted. No action required.
	The Royal College of Ophthalmologists	appropriate	Comment noted. No action required.

Section	Consultees	Comments	Action
Equality and Diversity	**Royal National Institute of Blind People**	Firstly, we would like NICE to be mindful of the risk factors mentioned in the background information. These show that older people, women and smokers are more at risk of developing wet AMD. Therefore, we would expect the use of aflibercept in these groups (including factors relating to assessment, delivery and follow up) to be thoroughly examined. Secondly, as the largest organisation of blind and partially sighted people in the UK, we would expect NICE to take steps to meet its legal obligations under the Equality Act 2011. This not only requires public bodies to have due regard to the need to promote disability equality in everything they do, including the provision of information to the public, but also requires such bodies to make reasonable adjustments for individual disabled people where existing arrangements place them at a substantial disadvantage. The Equality Act expressly includes a duty to provide accessible information as part of the reasonable adjustment duty. In relation to any materials produced as part of the STA we would expect: - online information to conform to the W3C's Web Accessibility Initiative Web Content Accessibility Guidelines (WCAG) 1.0, level AA, as required by the NHS Brand Guidelines and the Central Office of Information. - printed information, including downloadable content such as PDF files, should (wherever possible) comply with our "see it right" guidelines: http://www.rnib.org.uk/professionals/accessibleinformation/Pages/ see_it_right.aspx	Comment noted. These issues were discussed at the workshop and it was agreed that these were risk factors for wet AMD but these issues did not constitute an equality consideration for the proposed appraisal of this technology. With regard to any materials produced as part of the STA we have informed the NICE website team of your comments.

Section	Consultees	Comments	Action
	Bayer plc	As stated in the scope, wAMD is more prevalent in women and is a condition of those aged 50 years and over. There is evidence of variation in rates of intravitreal injections by age, gender, location and over time. National Hospital Episode Statistics rates of intravitreal injection after 2002 have consistently been highest in the 70 and older age group. Annual rates have increased most in women 70 years and over (1). Multiple comorbid conditions, such as hypertension, are also an issue in this increasingly older population and a majority of AMD patients in studies are prior or current smokers (2) which may consequently link AMD to socio-economic factors. 1 Keenan TDL, *et al*. Trends over time and geographical variation in rates of intravitreal injections in England. *British Journal of Ophthalmology* 2011; Aug; 10.1136/bjophthalmol-2011-300338 2 Wong T, *et al*. The natural history and prognosis of neovascular age-related macular degeneration: a systematic review and of the literature and meta-analysis. Ophthalmology 2008; Sep;115(9):1524	Comment noted. No action required.
	NHS North Somerset	There are no issues.	Comment noted. No action required.
	The Royal College of Ophthalmologists	none	Comment noted. No action required.
	CSAS	There are no issues.	Comment noted. No action required.
Innovation			
Other considerations	**Royal National Institute of Blind People**	Experts tell us that lesion type is an appropriate subgroup	Comment noted. No action required.

Section	Consultees	Comments	Action
	Novartis Pharmaceuticals	UK expert clinical feedback suggests that there is no treatment differentiation based on lesion type. ANCHOR and MARINA trials found similar outcomes based on lesion type and thus may not be a relevant subgroup for anti-VEGF agents.	Comment noted. During the scoping workshop it was agreed that that potential subgroups in the 'other considerations' section of the scope defined according to the composition of the lesion in terms of classic and occult choroidal neovascularisation and not the location of the lesion.
	Bayer plc	If evidence allows, lesion type is an appropriate subgroup. Location of the lesion was not a subgroup for efficacy analyses in the VIEW I/II trials.	Comment noted. During the scoping workshop it was agreed that that potential subgroups in the 'other considerations' section of the scope defined according to the composition of the lesion in terms of classic and occult choroidal neovascularisation and not the location of the lesion.
	The Royal College of Ophthalmologists	none	Comment noted. No action required.

Section	Consultees	Comments	Action
Questions for consultation	**Royal National Institute of Blind People**	Experts tell us that aflibercept solution for injection is innovative as it has a unique mode of action. As mentioned in comment one, the less onerous dosing regimen of aflibercept is expected to reduce the burden on patients/carers, and doctors' case load. This would improve the way that a current need is met. The impact on the carer and service capacity is unlikely to be captured in the QALY calculation.	Comment noted. These comments were discussed at the workshop and it was agreed that these potential benefits of aflibercept solution for injection would be likely to be captured in the QALY calculations and would result in a 'step-change' in the care pathway for people with wet age-related macular degeneration.

Section	Consultees	Comments	Action
	Bayer plc	*Have the most appropriate comparators for aflibercept solution for injection for the treatment wet age-related macular degeneration been included in the scope? Are the comparators listed routinely used in clinical practice?* *Is bevacizumab used for the first line treatment of age-related macular degeneration or only as second-line treatment for patients for whom treatment with ranibizumab has failed?* See response to 'comparators'. *Should subgroups defined by the location of the lesion and composition of the lesion (classic and occult choroidal neovascularisation) be considered?* See response to 'other considerations'. *Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?* *Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* Aflibercept solution for injection is innovative as it has a different mode of action to the other VEGF inhibitors. It addresses a wider range of growth factors and includes PIGF binding. It is expected that aflibercept solution for injection will provide for reductions in both case load and budget requirements.	Comment noted. No action required. These comments were discussed at the workshop and it was agreed that these potential benefits of aflibercept solution for injection would be likely to be captured in the QALY calculations and would result in a 'step-change' in the care pathway for people with wet age-related macular degeneration.

Section	Consultees	Comments	Action
		There would be cost and capacity savings in both number of intravitreal injections and frequency of monitoring compared with current licensed anti-VEGF treatments in an NHS which is currently under increasing pressure for its ophthalmology services. This impact on service capacity is unlikely to be captured by the QALY calculation. An STA is appropriate.	
	NHS North Somerset	Is there potential that this TA could save resource over existing therapies for this condition?	Comment noted. The proposed appraisal would consider the clinical and cost effectiveness of this technology compared with current treatments in the NHS.
	The Royal College of Ophthalmologists	yes Clinical trial data on VEGF -Trap (VIEW 2) study Clinical trial data on ranibizumab and bevacizumab - CATT study NICE TA155 May need to consider indirect costs of potentially less patient and carer visit than current standard therapy (i.e. transport for carer and patient and time off work for carer)	Comments noted. No action required.

Section	Consultees	Comments	Action
Additional comments on the draft scope.	**Royal College of Nursing**	There is a plethora of treatments now both for AMD and DMO and whilst this is excellent for patient choice it can also mean confusion around which agents maybe better and why, this may mean that the informed consent process may take longer. It is possible that patients may in the future have access to all intra-vitreal therapies and then depending upon patient response patients and clinicians may well need access to multiple agents in order to ensure that the therapy is matched to the individual.	Comments noted. During the scoping workshop it was discussed whether the appraisal should be an MTA in order to assess the clinical and cost-effectiveness of other treatments for wet AMD. However, it was agreed that because the appraisal process would take much longer if it were to be an MTA, that aflibercept solution for injection should be appraised within the STA process to allow timely guidance to be produced.

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

- Department of Health
- Healthcare Improvement Scotland
- Medicines and Healthcare products Regulatory Agency

Aflibercept solution for the treatment of wet age-related macular degeneration

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

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 Allied Health Professionals Federation to General Commentators	NICE Secretariat		Added	Allied Health Professionals Federation meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a general group commentator.
2.	Remove Association of Blind Asians (ASA) from patient/carer groups.	NICE secretariat		Removed	Association of Blind Asians (ASA) does not meet the inclusion criteria and has therefore been removed from patient/carer group consultees.

3.	Add Deafblind UK to patient/carer groups.	NICE Secretariat		Added	Deafblind UK meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a Patient/carer group consultee.
4.	Add Network of Sikh Organisations to patient/carer groups.	NICE Secretariat		Added	Network of Sikh Organisations meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a Patient/carer group consultee.
5.	Add British Opthalmic Anaesthesia Society (BOAS) to professional groups.	NICE Secretariat		Added	British Opthalmic Anaesthesia Society (BOAS) meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a professional group consultee.
6.	Add Eye Hope to relevant research groups.	NICE Secretariat		Added	Eye Hope meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a relevant research group commentator.

7.	We recommend that the following organisations are included in the "patient/carer groups" section under consultees: (a) The Alzheimer's Society - as people with dementia and sight loss often go unrecognised. 750,000 people in the UK have dementia (most are aged over 65), and around one in seven people over 65 is living with significant sight loss (of which AMD is the most common cause) (b) AgeUK - as AMD is the most common cause of visual impairment among older people	RNIB		Not Included	These organisation's interests are not directly related to the appraisal topic and as per our inclusion criteria The Alzheimer's Society and AgeUK have not been included in the matrix of consultees and commentators.
9.	If bevacizumab is included as a comparator, then the inclusion of manufacturers of intravitreal bevacizumab (e.g. Moorfields Pharmaceuticals) should be included.	Bayer		Added	Agreed