NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD1)

Consultees – Organisations that accept an invitation to participate in the appraisal including the manufacturer or sponsor of the technology, national professional organisations, national patient organisations, the Department of Health and the Welsh Assembly Government and relevant NHS organisations in England. Consultee organisations are invited to submit evidence and/or statements and respond to consultations. They are also have right to appeal against the Final Appraisal Determination (FAD). Consultee organisations representing patients/carers and professionals can nominate clinical specialists and patient experts to present their personal views to the Appraisal Committee.

Clinical specialists and patient experts – Nominated specialists/experts have the opportunity to make comments on the ACD separately from the organisations that nominated them. They do not have the right of appeal against the FAD other than through the nominating organisation.

Commentators – Organisations that engage in the appraisal process but that are not asked to prepare an evidence submission or statement. They are invited to respond to consultations but, unlike consultees, they do not have the right of appeal against the FAD. These organisations include manufacturers of comparator technologies, NHS Quality Improvement Scotland, the relevant National Collaborating Centre (a group commissioned by the Institute to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups (for example, the NHS Confederation, NHS Information Authority and NHS Purchasing and Supplies Agency, and the *British National Formulary*).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but may be summarised by the Institute secretariat – for example when many letters, emails and web site comments are received and recurring themes can be identified.

Comments received from consultees

Consultee	Comment	Response
Roche products	**Summary** The ACD states: "*The Committee concluded that the cost-effectiveness estimates of bevacizumab as a first-line treatment of metastatic colorectal cancer (£36,400 and £31,500 per QALY gained) were at the lowest end of a range and plausible adjustments to the key model inputs would increase these ICERs substantially. The ICERs were therefore associated with a great deal of uncertainty.*" The areas of concern highlighted by the Committee can be summarized as follows: 1 The NHS resource costs of operating APAS and the subsequent impact on the ICERs. 2 The operation of the APAS in the context of an intermittent treatment strategy 3 Bevacizumab treatment duration in clinical practice compared with that observed in the NO16966 study 4 The incremental pharmacy and administration cost associated with adding bevacizumab to XELOX or FOLFOX 5 The health state utility values used in the economic model In order to fully address each of these points Roche has conducted further detailed research and analysis (described in detail in section 1	Comment noted. Please see detailed responses below.

<table>
<tr><th>Consultee</th><th>Comment</th><th>Response</th></tr>
<tr><td></td><td>below). This has resulted in revised base case ICERs for bevacizumab being presented which account for the criticisms listed within the ACD.

Revisions to base case ICERS
<table><tr><td rowspan="2">Revised parameter</td><td colspan="2">Marginal effect on ICERs of each revision</td></tr><tr><td>B-XELOX</td><td>B-FOLFOX</td></tr><tr><td>Utility Values
APAS Operating costs
Preparation and Pharmacy</td><td>+£647
+£164
- £678</td><td>+£560
+£113
- £1014</td></tr><tr><td>Cumulative impact</td><td>+£133</td><td>- £314</td></tr></table>
Upon further investigation of points 1 and 5 it was found that, as suggested by the Committee, the base case ICERs increased.

With regards to point 4, we have conducted a direct time and motion observation study, which demonstrated that preparation and administration of bevacizumab actually incurred less cost than we originally estimated, thus reducing the ICERs.

Based on the further research conducted to investigate point 2 and 3, no amendment to the economic modelling was considered necessary. Clarifications and discussion are provided in section 1 below regarding these points.</td><td></td></tr>
</table>

Consultee	Comment	Response
	The cumulative effect of each of the revisions to the model parameters (ie to APAS operating costs, utility values, pharmacy and drug administration costs) resulted in ICERs (£36,494 B-XELOX ; £31,122 B-FOLFOX) very similar to the original base case presented in the ACD. We hope that the findings of this additional research will serve to validate the robustness of the current ICERs and allay the concerns of the committee.	
Roche products	**WHETHER YOU CONSIDER THAT ALL OF THE RELEVANT EVIDENCE HAS BEEN TAKEN INTO ACCOUNT** **<u>1) The NHS resource cost of operating APAS and the subsequent effect on the ICER</u>** In section 4.14 of the ACD states: "*The Committee agreed that the impact of the scheme in practice was uncertain and that incorporating higher administration costs would increase the ICER estimates*" Following this feedback, Roche conducted extensive research with pharmacists, NHS business managers, and NHS finance and operations experts to identify the activities required to set up and administer the APAS and estimate the employee time required to conduct these activities. Full details of this research is supplied in appendix A.	Comment noted. The evidence section of the FAD includes a summary of the information provided by the manufacturer in response to ACD1. The Committee considered that the scheme was complex, with requirements for a number of financial transactions between the manufacturer, healthcare providers and commissioners . The Committee concluded the operating costs of the scheme were still likely to be greater than those presented by the manufacturer. The Committee noted the ERG's exploratory analysis showing that when the administration costs of the

Consultee	Comment	Response
	An activity based costing approach was taken to calculate a mean per patient cost of operating the APAS. The activities identified were split into 4 categories: 1 Initial set-up activities 2 Ongoing monthly activities 3 Per patient activities 4 Per treatment cycle activities The total estimated employee time is summarised in table 1 below, categorised by the frequency with which the activity would occur (see appendix A for more details) *Table provided, but not reproduced here.* The time required to complete each activity was allocated to a per patient time (shown in table 3) based on a three year time frame and the parameter estimates listed in table 2. The throughput of patients on the APAS per trust was calculated based upon the number of patients expected to be treated with bevacizumab between years one to three as calculated in the Budget Impact section of our original submission (section 8). The number of patients treated with bevacizumab is expected to be 2,186, 3,279, and 4,313 in years one, two and three respectively. *Tables provided, but not reproduced here.*	patient access scheme were increased to £100 the ICERs increased slightly. Please see the FAD section 4.17 for further details.

Consultee	Comment	Response
	The estimated time per patient of administering the APAS was 131 minutes and 152 minutes per patient for XELOX and FOLFOX based regimens respectively. The unit cost per minute for each of the professionals conducting the activities was calculated based on the mid-point salaries taken from the 2009 Agenda for Change pay scales combined with the overhead and salary on-costs taken from the PSSRU (PSSRU, 2008). Since overhead estimates for all the professionals involved were not available, overheads for these professional were assumed be the same as for a hospital pharmacist. As per assumed in the PSSRU, the calculation of unit costs per hour were based on 1565 working hours in a year. The resulting unit costs are shown in the table below. *Table provided, but not reproduced here.* Based on the above, the cost per patient of operating the APAS over years 1 to 3 is estimated to be £57 and £67 for B-XELOX and B-FOLFOX respectively. (calculations provided in appendix C) Using these revised estimates in the economic model increases the ICER's for B-XELOX and B-FOLFOX by £164 and £113 respectively.	
Roche Products	**WHETHER YOU CONSIDER THAT ALL OF THE RELEVANT EVIDENCE HAS BEEN TAKEN INTO ACCOUNT** **<u>2) The operation of the APAS in the context of an intermittent</u>**	

Consultee	Comment	Response
	<u>treatment strategy</u> The ACD states in section 4.14: *"The Committee understood that intermittent treatment is commonly used in UK clinical practice and chemotherapy treatment is often restarted if there are signs of disease progression. The Committee understood that in these circumstances (that is with any signs of disease progression) the patient access scheme would no longer apply."* Post the publication of the ACD Roche held a clinical expert advisory board with 6 leading UK oncologist specialising in the treatment of mCRC (Roche ACD ad-board, London 2009). The advisory board provided explicit input as to the nature of current treatment of mCRC in the UK. There was general agreement that intermittent treatment is used by some clinicians within the UK. Roche can now confirm the APAS scheme will still be applicable and available should clinicians choose to use intermittent treatment of oxaliplatin-based chemotherapy plus bevacizumab. The APAS would be applicable regardless of treatment breaks so long as patients are restarted on oxaliplatin-based treatment. For the avoidance of doubt, the 12 month cap will relate to 12 cumulative months of <u>treatment</u> and not 12 calendar months, therefore treatment breaks will be accounted for within the APAS should patients be treated intermittently.	Comment noted. The Committee noted that although intermittent treatment is commonly used in the UK, the sole evidence base for the addition of bevacizumab to first-line combination chemotherapy was reflective of a continuous treatment strategy. Therefore, the Committee concluded that the economic model reflected the clinical evidence that was available. Please see the FAD section 4.9 for further details. Comment noted.

Consultee	Comment	Response
	If a patient is transferred to an alternative chemotherapy regimen this would signify the start of second line therapy and thus they would no longer qualify for the APAS, as bevacizumab will not be recommended for second line therapy. This definition was suggested by the experts attending the advisory board with respect to intermittent treatment for patients in the UK.	
Roche Products	**WHETHER YOU CONSIDER THAT ALL OF THE RELEVANT EVIDENCE HAS BEEN TAKEN INTO ACCOUNT** **<u>3) Bevacizumab treatment duration in clinical practice and its effect on the ICERs</u>** The ACD suggests that in clinical practice bevacizumab may not be as cost effective as estimated based on the NO16966 study due to longer treatment duration of bevacizumab in UK clinical practice compared to the trial. The ACD states that the committee considered that *"the extra bevacizumab costs"…* associated with a longer treatment duration… *"would outweigh any additional survival benefits of bevacizumab, given its modest impact on progression-free and overall survival.*" Firstly, it is important to note that such a conclusion can not be drawn with any degree of certainty in the absence of the clinical data required for testing this hypothesis. Additionally it is unclear whether or not the committee considered the effect of the price cap on the cost of increasing treatment duration.	The Committee noted the information provided by the manufacturer and concluded that the economic model reflected the clinical evidence that was available (in terms of treatment duration). However, the Committee concluded that in practice bevacizumab treatment would be expected to continue until disease progression in patients treated with a continuous therapy policy. This could potentially increase the ICERs. Please see the FAD section 4.12 for further details.

Consultee	Comment	Response
	Secondly, we will present evidence below that suggests that in clinical practice treatment duration of bevacizumab is likely to be similar to or less than that observed and modeled on the NO16966 study. ***Clinical Advisory Board*** Following publication of the ACD, Roche facilitated an advisory board (Roche ACD ad-board, London 2009) to obtain the views from clinical experts on issues highlighted by the Committee. On the subject of treatment duration the main points of feedback from the experts were as follows: a) As recognised by the committee, intermittent treatment, such as that specified in the COIN study (Adams, 2009), is becoming more prevalent within UK clinical practice. This typically leads to a shorter treatment duration compared to the NO16966 study. b) It was considered that should bevacizumab be given positive NICE guidance it is likely to be added to the treatment strategy that is currently being employed, either intermittent treatment or continuous. c) Irrespective of whether a continuous or intermittent strategy was used bevacizumab would only likely be	

Consultee	Comment	Response
	given in combination with chemotherapy. It would also be expected that it treatment with oxaliplatin was stopped due to either a planned break or unacceptable toxicity then treatment with bevacizumab would also typically be stopped at this time. The feedback from the advisory board therefore suggests that treatment duration with bevacizumab in clinical practice would be similar to that of oxaliplatin, and the average duration of treatment is likely to be less that that observed in the NO16966 study due to a proportion of patients being treated with intermittent treatment strategies. ***Real world evidence of bevacizumab treatment duration*** Reassurance on the duration of continuous bevacizumab and chemotherapy (median 6 month in NO16966) treatment in clinical practice can be given based on the BRiTE and ARIES observational studies conducted in the USA. BRiTE (Kozloff et al 2009) is described fully in Section 6.8 of our original submission. This was a permissive programme recruiting patients requiring first-line chemotherapy for metastatic colorectal cancer (mCRC), other entry requirements were minimal, as was data collection, so that population would be expected to be fairly representative of a routine clinical cohort. Clinicians could use any first-line combination of chemotherapy plus bevacizumab. In practice	

Consultee	Comment	Response
	96% of the 1,953 patients recruited received a dose of 5mg/kg bevacizumab every 2 weeks (in accord with the NO16966 protocol and what Roche is seeking NICE endorsement for) and more than 60% of patients received a fluoropyrimidine plus oxaliplatin combination as their cytotoxic regimen. As shown in Table 5. the median bevacizumab treatment duration in BRiTE was shorter than in NO16966, but the median PFS and OS were actually longer indicating that any truncation of treatment was not at the expense of efficacy. ARIES was a prospective observational study. It was designed to investigate safety and efficacy in patients who would not necessarily satisfy the stringent entry criteria for conventional clinical trials. Patients from 244 sites were eligible if they had mCRC and received bevacizumab as part of their 1st or 2nd line treatment. This was the sole entry criterion. Between November 2006 and September 2008, 2041 patients with unresectable colorectal cancer were recruited (1538 first-line and 503 second-line). There was no protocol specified regimen, dose or duration stipulated, and no exclusions based on clinical characteristics. Data was collected via an electronic CRF at baseline and then quarterly from then on. Whilst only treatment duration of bevacizumab was captured in the BRiTE study treatment duration of both oxaliplatin and bevacizumab were recorded in ARIES. As presented in table 5, treatment durations of oxaliplatin and bevacizumab in patients that received 1st line B-FOLFOX (ARIES reports little use of B-XELOX) are consistent with the BRiTE study and less than that of the NO16966 study. Also as observed in the NO16966 study, the treatment durations of bevacizumab and oxaliplatin are very similar. PFS and OS was similar to that seen in	

Consultee	Comment	Response
	BRiTE and exceed those reported in the NO16966 study. *Table provided, but not reproduced here.*	
Roche Products	**WHETHER YOU CONSIDER THAT ALL OF THE RELEVANT EVIDENCE HAS BEEN TAKEN INTO ACCOUNT** **<u>4) The incremental pharmacy and administration cost associated with adding bevacizumab to XELOX or FOLFOX</u>** The ACD states: "*The Committee further noted that the administration costs of B−FOLFOX and B-XELOX were assumed to be very similar to the administration costs of FOLFOX and XELOX. The Committee considered that the addition of a bevacizumab infusion to either XELOX or FOLFOX would incur greater additional administration costs than those assumed by the manufacturer*." The economic model assumes that the incremental pharmacy and administration cost, per cycle, of adding bevacizumab to either XELOX or FOLFOX is £42. Roche notes, in TA176 the addition of cetuximab to FOLFOX or FOLFIRI was assumed to incur zero incremental pharmacy or drug administration costs. However given the concerns expressed by the committee Roche commissioned a time and motion study, following publication of the ACD, to gain a more precise estimate of the incremental resources consumed in preparing and administering	Comment noted. The evidence section of the FAD includes a summary of the information provided by the manufacturer in response to ACD1. The Committee considered that the addition of a bevacizumab infusion to either XELOX or FOLFOX could incur greater additional treatment administration costs than those stated by the manufacturer. The Committee concluded that if these higher administration costs were included, then this would result in an increase in the ICER estimates. Please see the FAD section 4.16 for further details

Consultee	Comment	Response
	bevacizumab. Three preparation episodes and three administration episodes of bevacizumab infusions were observed by an independent research group (pH Associates) at the Mount Alvernia Hospital in Guildford. The type of activity, start stop times, and the job title and grade of the healthcare professional performing the tasks were recorded. A summary of the results is provided in table 6 below (the full set of results is provided in Appendix B). *Table provided, but not reproduced here.* The estimated cost of hospital nurse and pharmacy time (accounting for overheads, qualifications, and salary on costs) taken from the PSSRU (PSSRU, 2008) and inflated to 2009 costs are provided below. *Table provided, but not reproduced here.* To estimate the cost of each infusion, the inflated PSSRU unit costs (see table 7 above) for patient contact time (nurses), or patient related activity time (pharmacists), were applied to the results of the time and motion study. It was assumed that nurses of band 5 through 7 would administer bevacizumab and so the average cost per hour across these bands was used (£63). In the absence of the cost per hour of a pharmacy technician it was assumed that a hospital pharmacist would perform all preparation activities. This will there overestimate the true cost of preparation as the results of the time and motion study indicate that preparation time is split between the pharmacist and the technician. *Table provided, but not reproduced here.*	

Consultee	Comment	Response
Roche Products	***Conclusion*** Whilst it was speculated by the committee that the preparation and administration of bevacizumab per cycle would cost more than that currently applied in the economic model (£42), the empirical evidence from this time and motion suggests the reverse. Amending the economic model to reflect the results of the time and motion study reduces the ICERs by £677 and £1,012 when adding bevacizumab to XELOX and FOLFOX-6 respectively.	Comment noted. The Committee considered that the addition of a bevacizumab infusion to either XELOX or FOLFOX could incur greater additional treatment administration costs than those stated by the manufacturer. The Committee concluded that if these higher administration costs were included, then this would result in an increase in the ICER estimates. Please see the FAD section 4.16 for further details.
Roche Products	**WHETHER YOU CONSIDER THAT ALL OF THE RELEVANT EVIDENCE HAS BEEN TAKEN INTO ACCOUNT** **<u>5) The health state utility values used in the economic model</u>** It is noted in the ACD that the utility values used within the economic model appeared to be high. There are 3 health state utility values used within the Roche economic model: 1. Progression free survival (PFS) whilst patients are on treatment – 0.77 2. PFS post cessation of chemotherapy – 0.79	Comment noted. The evidence section of the FAD includes a summary of the information provided by the manufacturer in response to ACD1. The Committee agreed that the utility value of 0.77 was still high because it was similar to the utility values of people in the UK general population rather than people with metastatic colorectal cancer. The Committee also noted that the utility values were obtained from a small study of patients with metastatic colorectal cancer receiving cetuximab and chemotherapy using the EQ-5D. In addition, the utility

Consultee	Comment	Response
	3. Post 1st line progression – 0.68 It is important to note that the ICERs are not sensitive to changes to the utility value used for the post progression health state. Reducing this parameter value from 0.68 to 0.60 alters the ICERs by less than £20, hence the validity of this assumption is not considered further within this response. The Guide to Methods for Technology Appraisals clearly states the most robust estimates of utility value would "*be reported directly from patients and the value of changes in patients' HRQL (that is, utilities) should be based on public preferences using a choice-based method. The EQ-5D is the preferred measure of HRQL in adults."* Ideally such EQ-5D results would come directly from the trial upon which the economic model is based. Quality of life data was not captured in NO16966 and thus the model uses the next most appropriate source, which is the EQ-5D results from a recent phase III study in 1st line mCRC in which patients received either FOLFIRI or cetuximab in combination with FOLFIRI. The subsequent figure of 0.77 is consistent with that accepted for use for PFS in both the previous NICE appraisal of bevacizumab, in the 1st line treatment of mCRC (TA 118, 2005) where a value of 0.80 was used for PFS in the analysis conducted by ScHARR, and recently in the appraisal of cetuximab (TA 176, 2009) where 0.77 is used for PFS.	values in the economic model were not regimen-specific. It further noted that decreasing the utility values by 20% had a large impact on increasing the ICERs Please see the FAD section 4.14 for further details.

Consultee	Comment	Response
	It is therefore reasonable to consider that the value of 0.77 is a robust estimate of the utility of patients in 1st line PFS with mCRC and is consistent with the NICE Guide to Methods. However in recognition of the concerns of the committee the new base case assumes that 0.77 applies throughout PFS i.e. the increase in utility for PFS patients off treatment has been removed and 0.77 represents the average utility value for PFS on and off treatment. Reducing the PFS off treatment utility value to 0.77 increased the ICERs by £647 and £560 for B-XELOX and B-FOLFOX respectively.	
Roche Products	**2 WHETHER YOU CONSIDER THAT THE SUMMARIES OF CLINICAL AND COST EFFECTIVENESS ARE REASONABLE INTERPRETATIONS OF THE EVIDENCE AND THAT THE PRELIMINARY VIEWS ON THE RESOURCE IMPACT AND IMPLICATIONS FOR THE NHS ARE APPROPRIATE** In section 4.14 the ACD states: "*Nevertheless, the Committee understood from the ERG that the ICERS for both B-XELOX and B-FOLFOX increased if bevacizumab treatment continued beyond that of oxaliplatin."* It appears that this conclusion was drawn based on the results of the sensitivity analysis conducted by the ERG (section 3.25, ACD). As discussed in section 1 above, the evidence does not allow for such a conclusion to be drawn given that this scenario has not been tested and therefore the benefit associated with an increase in treatment duration are unknown. Additionally it is not clear as to whether the committee considered the impact of the price cap on the cost of increasing treatment duration.	Comment noted. The Committee noted the information provided by the manufacturer and concluded that the economic model reflected the clinical evidence that was available (in terms of treatment duration). However, the Committee concluded that in practice bevacizumab treatment would be expected to continue until disease progression in patients treated with a continuous therapy policy. This could potentially increase the ICERs. Please see the FAD section 4.12 for further details.

Consultee	Comment	Response
Roche Products	**WHETHER YOU CONSIDER THAT THE PROVISIONAL RECOMMENDATIONS OF THE APPRAISAL COMMITTEE ARE SOUND AND CONSTITUTE A SUITABLE BASIS FOR THE PREPARATION OF GUIDANCE TO THE NHS** Several issues have been raised within the ACD that were assumed to increase the ICER, although alternative ICERs accounting individually or cumulatively were not reported. Roche has therefore attempted to address the concerns raised within the ACD and we have presented further cost effectiveness analysis, which we would like to request that the Committee consider at its next meeting, alongside the revised proposals for an accompanying patient access scheme. The patient access scheme that has been approved for NICE appraisal by DH has been designed to address all of the issues raised during the consultation on the scheme. Roche believes that the flexibility and logistical options available within the scheme will mean that it will be utilised effectively by NHS Trusts. The scheme is applicable both in the NHS setting and also for those NHS Trusts which require it in the homecare setting. Homecare provides a greater level of cost effectiveness to the NHS resulting in reduced ICERs compared to the hospital setting due to reductions in drug administration costs.	Comment noted. The evidence section of the FAD includes a summary of the information provided by the manufacturer in response to ACD1. The Committee considered that the scheme was complex, with requirements for a number of financial transactions between the manufacturer, healthcare providers and commissioners. The Committee concluded the operating costs of the scheme were still likely to be greater than those presented by the manufacturer. The Committee noted the ERG's exploratory analysis showing that when the administration costs of the patient access scheme were increased to £100 the ICERs increased slightly. Please see the FAD section 4.17 for further details.
Roche Products	**ARE THERE ANY EQUALITY RELATED ISSUES THAT NEED SPECIAL CONSIDERATION THAT ARE NOT COVERED IN THE ACD?** No	Comment noted.

Consultee	Comment	Response
Department of Health	I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Comment noted. No actions required.
Bowel Cancer UK	Many thanks for giving Bowel Cancer UK the opportunity to comment on NICE's Single Technology Appraisal of Bevacizumab in combination with Oxaliplatin and either 5FU or Capecitabine for the treatment of metastatic colorectal cancer. If I may, rather than answer your specific questions, can I make a few points with regard to your draft recommendations:	Comment noted. Please see detailed responses below.
Bowel Cancer UK	Firstly, may I reiterate what we said publically in response to the NICE announcement last month, namely that while we are disappointed by NICE's preliminary recommendations not to approve Bevacizumab in the treatment of advanced colorectal cancer, we understand that NICE, the manufacturers and the Department of Health are still in discussions to find a way to approve the drug on the NHS. We hope that these discussions are fruitful and that this highly effective treatment soon becomes available to the many bowel cancer patients who could benefit from it.	Comment noted. The amended patient access scheme was agreed by the Department of Health in time for the Committee meeting and was considered fully by the Committee. See FAD section 4.17.
Bowel Cancer UK	Secondly, we welcome the fact that NICE recognises the clinical efficacy of Bevacizumab in this setting, which is well proven and not in doubt. As your preliminary recommendations are therefore based solely upon cost grounds, we hope that your continuing discussions with DH and Roche will result in an agreement being reached that will enable NICE to approve the drug on the NHS, to the benefit of thousands of bowel cancer patients in the UK.	Comment noted. The Committee noted that bevacizumab gave modest clinical benefit as a first-line treatment and bevacizumab was clinically effective as part of second-line treatment. See FAD section 4.7. However, for both legal and bioethical reasons the Committee must take account economic considerations and

Consultee	Comment	Response
		cost effectiveness of the technologies (Social Value Judgments - Principles for the development of NICE guidance; principle 5). The Committee concluded that bevacizumab for the treatment of metastatic colorectal cancer would not be a cost-effective use of NHS resources. See FAD sections 4.21 and 4.22. The Committee is not able to make recommendations on the pricing of technologies to the NHS. See Guide to the methods of technology appraisal section 6.1.8.
Bowel Cancer UK	Thirdly, you will be aware that the UK is very much out of step with the rest of Europe as regards access to Bevacizumab and that the treatment is widely available in most other European countries. In view of this, and following NICE's positive guidance regarding Cetuximab first line, we hope that the Institute will come to a positive conclusion and approve this treatment as well, so that all patients who could benefit from a biological agent have the opportunity to do so.	The Institute recognises that guidance from other organisations may differ from its own guidance, because of different criteria for making decisions. The Committee considered all the evidence submitted, including evidence from clinical trials, patient and clinical experts, the manufacturer's submission and the Evidence Review Group Report. The Committee noted that bevacizumab gave modest clinical benefit as a first-line treatment and bevacizumab was clinically effective as part of second-line treatment. See FAD section 4.7. However, for both

Consultee	Comment	Response
		legal and bioethical reasons the Committee must take account economic considerations and cost effectiveness of the technologies (Social Value Judgments - Principles for the development of NICE guidance; principle 5). The Committee concluded that bevacizumab for the treatment of metastatic colorectal cancer would not be a cost-effective use of NHS resources. See FAD sections 4.21 and 4.22.
	Fourthly, can I reiterate the point that I made at the recent NICE appraisal meeting, namely that no-one, including I'm sure NICE, will wish to see a continuation of the climate of misery and inequity that patients and those who care for them have faced over the last three years in trying to gain access to Bevacizumab, after NICE refused to approve it first time around.	Comment noted. Please see detailed responses above and below.
	There is nothing more precious than life nor more natural than a person's desire to stay alive, both for themselves and for their loved ones. Consequently, there should be no place in our society for a system that treats patients in the advanced stages of bowel cancer with such disrespect and, frankly, cruelty by forcing them to make financial hardships and have to fight bureaucracy in their efforts to get this treatment, which gives them the chance to live longer and feel better when they are fighting what for many is a terminal disease. In conclusion, let me quote our patient [redacted], who also took part in NICE's appraisal of Bevacizumab and is living proof of the	The Committee considered all the evidence submitted, including evidence from clinical trials, patient and clinical experts, the manufacturer's submission and the Evidence Review Group Report. The Committee noted that bevacizumab gave modest clinical benefit as a first-line treatment and bevacizumab was clinically effective as part of second-line treatment. See FAD section 4.7. However, for both legal and bioethical reasons the Committee

Consultee	Comment	Response
	drug's efficacy. As she said at the time of the announcement: "My feelings are obviously of disappointment. However, I hope that NICE will do their utmost to find a way to approve Bevacizumab on the NHS, so that thousands of people in England and Wales can benefit from the drug like I did, while avoiding the financial hardships and bureaucratic procedures that I and many other patients have had to endure in their efforts to get the treatment".	must take account economic considerations and cost effectiveness of the technologies (Social Value Judgments - Principles for the development of NICE guidance; principle 5). The Committee concluded that bevacizumab for the treatment of metastatic colorectal cancer would not be a cost-effective use of NHS resources. See FAD sections 4.21 and 4.22.
Royal College of Nursing	Nurses working in this area of health have reviewed the Appraisal Consultation Document of the use of bevacizumab in combination with oxaliplatin and either 5FU or capecitabine for the treatment of metastatic colorectal cancer. There are no further comments to make on this document at this stage on behalf of the Royal College of Nursing. Thank you for the opportunity to review this document.	Comment noted.