NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Sponsor submission of evidence:
Evaluation title:
Sponsor:
Date sections A and B submitted:
Date section C submitted:

August 2011 (Version 1.1)

Contents

Instructions for sponsors

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) as part of the Medical Technologies Evaluation Programme process for developing NICE medical technologies guidance. Use of the submission template is mandatory.

The purpose of the submission is for the sponsor to collate, analyse and present all relevant evidence that supports the case for adoption of the technology into the NHS in England, within the scope defined by NICE. Failure to comply with the submission template and instructions could mean that the NICE cannot issue recommendations on use of the technology.

The submission should be completed after reading the 'Medical Technologies Evaluation Programme Methods guide' and the 'Medical Technologies Evaluation Programme Process guide' available at www.nice.org.uk/mt. After submission to, and acceptance by, NICE, the submission will be critically appraised by an External Assessment Centre appointed by NICE.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence'). When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly. For further information on disclosure of information, submitting cost models and equality issues, users should see section 11 of this document 'Related procedures for evidence submission'.

The submission should be concise and informative. The main body of the submission should not exceed 100 pages (excluding the pages covered by the template and appendices). The submission should be sent to NICE electronically in Word or a compatible format, not as a PDF file.

The submission must be a stand-alone document. Additional appendices may only be used for supplementary explanatory information that exceeds the level

of detail requested, but that is considered to be relevant to the case for adoption. Appendices will not normally be presented to the Medical Technologies Advisory Committee when developing its recommendations. Any additional appendices should be clearly referenced in the body of the submission. Appendices should not be used for core information that has been requested in the specification. For example, it is not acceptable to attach a key study as an appendix and to complete the economic evidence section with ‘see appendix X’.

All studies and data included in the submission must be referenced. Identify studies by the first author or trial ID, rather than by relying on numerical referencing alone (for example, ‘Trial 123/Jones et al.[126], rather than ‘one trial[126]’).Please use a recognised referencing style, such as Harvard or Vancouver.

The sponsor should provide a PDF copy of full journal articles or reports – in electronic or hard copy form – included in the submission, if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. This clearance must be wide enough to allow NICE to make further copies, store the article electronically for a limited period of time on a shared drive to be accessed by a limited number of staff. Additionally, any full article obtained and submitted in electronic format must be done so in a manner compliant with the relevant contractual terms of use permitting the sponsor electronic access to the article. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished research. NICE will then itself obtain full copies of all relevant papers or reports, paying a copyright fee where necessary. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

If a submission is based on preliminary regulatory recommendations, the sponsor must advise NICE immediately of any variation between the preliminary and final approval.

Document key

Boxed text with a grey background provides specific and/or important guidance for that section. This should not be removed.

Information in highlighted black italic is to help the user complete the submission and may be deleted.

The user should enter text at the point marked 'Response' or in the tables as appropriate. 'Response' text may be deleted.

List of tables and figures

Please include a list of all tables and figures here with page references.

Glossary of terms

If a glossary of terms is required to inform the submission of evidence include in the table. Delete if not required.

Term	Definition

Section A – Decision problem

Section A describes the decision problem, the technology and its clinical context. There is also information about ongoing studies, regulatory information and equality issues.

Sponsors should submit section A before the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

1 Statement of the decision problem

The decision problem is specified in the final scope issued by NICE. The decision problem states the key parameters that should be addressed by the information in the evidence submission. All statements should be evidence based and directly relevant to the decision problem.

Table A1 Statement of the decision problem

	Scope issued by NICE	Variation from scope	Rationale for variation
Population			
Intervention			
Comparator(s)			
Outcomes			
Cost analysis			
Subgroups to be considered			
Special considerations, including issues related to equality			

If the sponsor considers that additional parameters should be included in the submission, which are not stated in the decision problem, this variation from the scope and the rationale for it must be clearly described in the relevant columns in table A1.

2 Description of technology under assessment

2.1 Give the brand name, approved name and details of any different versions of the same device.

Response

All different versions/prototypes of the technology listed here must be CE marked or have equivalent UK regulatory approval.

2.2 What is the principal mechanism of action of the technology?

Response

3 Clinical context

3.1 Provide a brief overview of the disease or condition for which the technology is being considered in the scope issued by NICE.

Response

The disease or condition for which the technology is being considered in the scope must include an estimate of prevalence and/or incidence for the benefitting population. All estimates must be referenced.

3.2 Give details of any relevant NICE or other national guidance or expert guidelines for the condition for which the technology is being used. Specify whether the guidance identifies specific subgroups and make any recommendations for their treatment. If available, these should be UK based guidelines.

Response

3.3 Describe the clinical pathway of care that includes the proposed use of the technology.

Response

If a relevant NICE clinical guideline has been published, the clinical pathway of care should be consistent with the NICE guideline and described. If relevant, this should include comparator technologies.

3.4 Describe any issues relating to current clinical practice, including any uncertainty about best practice.

Response

If the clinical pathway of care described in response to question 3.3 is not consistent with the relevant NICE clinical guideline, this should be explained in response to question 3.4.

3.5 Describe the new pathway of care incorporating the new technology that would exist if the technology was adopted by the NHS in England.

Response

3.6 Describe any changes to the way current services are organised or delivered as a result of introducing the technology.

Response

3.7 Describe any additional tests or investigations needed for selecting or monitoring patients, or particular administration requirements, associated with using this technology that are over and above usual clinical practice.

Response

3.8 Describe any additional facilities, technologies or infrastructure that need to be used alongside the technology under evaluation for the claimed benefits to be realised.

Response

3.9 Describe any tests, investigations, interventions, facilities or technologies that would no longer be needed with using this technology.

Response

3.10 Describe how the NHS in England can disinvest from tests, investigations, interventions, facilities or technologies described in section 3.9 that would no longer be needed with using this technology.

Response

4 Regulatory information

4.1 Provide PDF copies of the following documents:

- instructions for use
- CE mark certificate or equivalent UK regulatory approval such as EC declaration of conformity
- quality systems (ISO 13485) certificate (if required).

PDF copies of these documents should be submitted at the same time as section A.

4.2 Does the technology have CE mark for the indication(s) specified in the scope issued by NICE? If so, give the date that authorisation was received. If not, state current UK regulatory status, with relevant dates (for example, date of application and/or expected approval dates).

Response

4.3 Does the technology have regulatory approval outside the UK? If so, please provide details.

Response

4.4 If the technology has not been launched in the UK provide the anticipated date of availability in the UK.

Response

4.5 If the technology has been launched in the UK provide information on the use in England.

Response

5 Ongoing studies

5.1 Provide details of all completed and ongoing studies on the technology from which additional evidence relevant to the decision problem is likely to be available in the next 12 months.

Response

This should include unpublished and ongoing studies, and studies awaiting publication. Also include post-marketing surveillance and register data.

5.2 If the technology is, or is planned to be, subject to any other form of assessment in the UK, please give details of the assessment, organisation and expected timescale.

Response

6 Equality

NICE is committed to promoting equality of opportunity and eliminating unlawful discrimination on the grounds of age, disability, gender reassignment, race, religion or belief, sex, and sexual orientation, and to comply fully with legal obligations on equality and human rights.

Equality issues require special attention because of NICE's duties to have due regard to the need to eliminate unlawful discrimination, promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others.

Any issues relating to equality that are relevant to the technology under assessment should be described. This section should identify issues described in the scope and also any equality issues not captured in the final scope.

Further details on equality may be found in section 11.3 of this document.

6.1.1 Describe any equality issues relating to the patient population and condition for which the technology is being used.

Response

6.1.2 Describe any equality issues relating to the assessment of the technology that may require special attention.

Response

6.1.3 How will the submission address these issues and any equality issues raised in the scope?

Response

Section B – Clinical evidence

7 Published and unpublished clinical evidence

Section B requires sponsors to present published and unpublished clinical evidence for their technology.

Sponsors should read section 6 of the Medical Technologies Evaluation Programme methods guide on published and unpublished evidence, available from www.nice.org.uk/mt

All statements should be evidence-based and directly relevant to the scope. Reasons for deviating from the scope should be clearly stated and explained in table A1.

Sponsors are required to submit section B in advance of the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

7.1 Identification of studies

Please note: sections 7.1 and 7.2 of the submission are divided into published and unpublished data. Responses must be split accordingly.

The sponsor's review of the clinical evidence should be systematic and transparent, and a suitable instrument for reporting such as the PRISMA statement (http://www.prisma-statement.org/statement.htm) should be used and CRD should be referred to (www.york.ac.uk/inst/crd).

The strategies used to retrieve relevant clinical data from the published literature and unpublished sources should be clearly described. The methods used should be justified with reference to the scope. Sufficient detail should be provided to enable the methods to be reproduced (the External Assessment Centre must be able to reproduce the search), and the rationale for any inclusion and exclusion criteria regarding search terms should be given.

Published studies

7.1.1 Describe the strategies used to retrieve relevant clinical data from the published literature. Exact details of the search strategy used should be provided in section 10, appendix 1.

Response

All published data relevant to the decision problem must be included.

Unpublished studies

7.1.2 Describe the strategies used to retrieve relevant clinical data from unpublished sources.

Response

The submission of unpublished evidence relevant to the decision problem is encouraged.

7.2 Study selection

Published studies

7.2.1 Complete table B1 to describe the inclusion and exclusion criteria used to select studies from the published literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B1 Selection criteria used for published studies

Inclusion criteria	
Population	
Interventions	
Outcomes	
Study design	
Language restrictions	
Search dates	
Exclusion criteria	
Population	
Interventions	
Outcomes	
Study design	
Language restrictions	
Search dates	

7.2.2 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Response

It is recommended that the number of published studies included and excluded at each stage is reported using the PRISMA statement flow diagram (available from *www.prisma-statement.org/statement.htm*)

Unpublished studies

7.2.3 Complete table B2 to describe the inclusion and exclusion criteria used to select studies from the unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B2 Selection criteria used for unpublished studies

Inclusion criteria	
Population	
Interventions	
Outcomes	
Study design	
Language restrictions	
Search dates	
Exclusion criteria	
Population	
Interventions	
Outcomes	
Study design	
Language restrictions	
Search dates	

7.2.4 Report the numbers of unpublished studies included and excluded at each stage in an appropriate format.

Response

It is recommended that the number of unpublished studies included and excluded at each stage is reported using the PRISMA statement flow diagram (available from *www.prisma-statement.org/statement.htm*)

7.3 Complete list of relevant studies

The sponsor should provide a PDF copy of all studies included in the submission if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished studies. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

7.3.1 Provide details of all published and unpublished studies identified using the selection criteria described in tables B1 and B2.

The details of all published and unpublished studies that compare the technology with other treatments for the relevant group of patients should be presented using tables B3 and B4 respectively. The studies that compare the intervention directly with the appropriate comparator(s) referred to in the decision problem should be clearly highlighted. If there are none, please state this. All types of studies should be considered, including observational studies such as cohort, case series and case-control studies, and single case reports and qualitative studies when relevant to the scope.

The list of relevant studies must be complete and will be validated by independent searches conducted by the External Assessment Centre.

Published studies should be referenced by first author name and year of publication. Unpublished studies should be referenced by first author and date of report. Full details of each reference should be provided in the reference list after section 9. In addition, list any trial short names if useful.

Table B3 List of relevant published studies

Primary study reference	Study name (acronym)	Population	Intervention	Comparator

Table B4 List of relevant unpublished studies

Data source	Study name (acronym)	Population	Intervention	Comparator

7.3.2 State the rationale behind excluding any of the published studies listed in tables B3 and B4.

The rationale for study exclusion must be provided by the sponsor for transparency. For example, if studies have been identified but there is no access to the level of study data needed, this should be indicated.

7.4 Summary of methodology of relevant studies

It is expected that all key aspects of the methodology will be in the public domain. If a sponsor wishes to submit aspects of the methodology in confidence, section 11.2 describes how to highlight confidential information.

7.4.1 Describe the study design and methodology for each of the published and unpublished studies using tables B5 and B6 as appropriate. A separate table should be completed for each study.

Table B5 Summary of methodology for randomised controlled trials

Study name
Objectives
Location
Design
Duration of study
Sample size
Inclusion criteria
Exclusion criteria
Method of randomisation
Method of blinding
Intervention(s) (n =) and comparator(s) (n =)
Baseline differences
Duration of follow-up, lost to follow-up information
Statistical tests
Primary outcomes (including scoring methods and timings of assessments)
Secondary outcomes (including scoring methods and timings of assessments)

Table B6 Summary of methodology for observational studies

Study name
Objective
Location
Design
Duration of study
Patient population
Sample size
Inclusion criteria
Exclusion criteria
Intervention(s) (n =) and comparator(s) (n =)
Baseline differences
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up
Statistical tests
Primary outcomes (including scoring methods and timings of assessments)
Secondary outcomes (including scoring methods and timings of assessments)

7.4.2 Provide details on data from any single study that have been drawn from more than one source (for example a poster and unpublished report) and/or when trials are linked this should be made clear (for example, an open-label extension to randomised controlled trial).

Response

7.4.3 Highlight any differences between patient populations and methodology in all included studies.

Response

Differences between study groups to consider include, but are not limited to, baseline patient characteristics, delivery of intervention and care setting.

7.4.4 Provide details of any subgroup analyses that were undertaken in the studies included in section 7.4.1. Specify the rationale and state whether these analyses were pre-planned or post-hoc.

Response

7.4.5 If applicable, provide details of the numbers of patients who were eligible to enter the study(s), randomised, and allocated to each treatment in an appropriate format.

Response

It is recommended that details of the numbers of patients that were eligible to enter the study(s), randomised and allocated to each treatment are presented as CONSORT flow charts if possible (see www.consort-statement.org/consort-statement/).

7.4.6 If applicable provide details of and the rationale for, patients that were lost to follow-up or withdrew from the studies.

Response

7.5 Critical appraisal of relevant studies

The validity of the results of an individual study will depend on the robustness of its overall design and execution, and its relevance to the scope. Each study that meets the criteria for inclusion should therefore be critically appraised. Whenever possible, the criteria for assessing published studies should also be used to assess the validity of unpublished and part-published studies.

For the quality assessments use an appropriate and validated quality assessment instrument. Key aspects of quality to be considered can be found in 'Systematic reviews: CRD's guidance for undertaking reviews in health care' (www.york.ac.uk/inst/crd).

The critical appraisal will be validated by the External Assessment Centre.

7.5.1 Complete a separate quality assessment table for each study. A suggested format for the quality assessment results is shown in tables B7 and B8.

Table B7 Critical appraisal of randomised control trials

Study name		
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?		
Was the concealment of treatment allocation adequate?		
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?		
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?		
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or		

adjusted for?		
Is there any evidence to suggest that the authors measured more outcomes than they reported?		
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?		
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table B8 Critical appraisal of observational studies

Study name		
Study question	**Response yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?		
Was the exposure accurately measured to minimise bias?		
Was the outcome accurately measured to minimise bias?		
Have the authors identified all important confounding factors?		
Have the authors taken account of the confounding factors in the design and/or analysis?		
Was the follow-up of patients complete?		
How precise (for example, in terms of confidence interval and p values) are		

the results?		
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

7.6 Results of the relevant studies

All outcomes pertinent to the scope and the measures used to assess those outcomes should be presented.

7.6.1 Complete a results table for each study with all relevant outcome measures pertinent to the decision problem. A suggested format is given in table B9.

A separate table for each study must be completed. State N/A or unknown if appropriate. Any outcomes not tested statistically can be included in the comments section.

For each outcome for each included study, provide the following information:

- *The primary hypothesis under consideration and the statistical analysis used for testing hypotheses. Provide details of the power of the study and a description of sample size calculation, including rationale and assumptions.*
- *The outcome name and unit of measurement. Indicate the outcomes that were specified in the study protocol as primary or secondary, and whether they are relevant with reference to the decision problem.*
- *The size of the effect. For dichotomous outcomes, the results ideally should be expressed as both relative risks (or odds ratios) and risk (or rate) differences. For time-to-event analysis, the hazard ratio is an equivalent statistic. Both absolute and relative measures should be presented.*
- *A 95% confidence interval.*
- *The number of participants in each group included in each analysis and whether the analysis was by 'intention to treat'. State the results in absolute numbers if feasible.*
- *Details of how the analysis took account of patients who withdrew and if patients were excluded from the analysis, give the rationale for this.*

- *Data from pre-specified outcomes rather than post-hoc analysis. If appropriate, provide evidence of reliability or validity, and current status of the measure (such as use in current clinical practice).*
- *Clear statements of when interim study data are quoted, along with the point at which data were taken and the time remaining until completion of that study. Analytical adjustments should be described to cater for the interim nature of the data.*
- *Other relevant data that may assist in interpretation of the results, such as adherence to medication and/or study protocol.*
- *Discussion and justification of definitions of any clinically important differences.*
- *Reports of any other analyses performed, including subgroup analysis and adjusted analyses, indicating whether they are pre-specified or exploratory.*
- *Graphs or figures to supplement text and tabulated data if available.*

Table B9 Outcomes from published and unpublished studies

Study name		
Size of study groups	**Treatment**	
	Control	
Study duration	**Time unit**	
Type of analysis	**Intention-to-treat/per protocol**	
Outcome	**Name**	
	Unit	
Effect size	**Value**	
	95% CI	
Statistical test	**Type**	
	p value	
Other outcome	**Name**	
	Unit	
Effect size	**Value**	
	95% CI	
Statistical test	**Type**	
	p value	
Comments		

7.6.2 Justify the inclusion of outcomes in table B9 from any analyses other than intention-to-treat.

7.7 Adverse events

In section 7.7 the sponsor is required to provide information on the adverse events experienced with the technology being evaluated in relation to the scope.

For example, post-marketing surveillance data may demonstrate that the technology shows a relative lack of adverse events commonly associated with the comparator.

7.7.1 Using the previous instructions in sections 7.1 to 7.6, provide details of the identification of studies on adverse events, study selection, study methodologies, critical apprasial and results.

For studies that have already been identified as relevant and appraised in sections 7.1 to 7.6 of the submission that were designed primarily to assess safety outcomes (for example, they are powered to detect significant differences between treatments with respect to the incidence of an adverse event), should be presented as a list of studies with the relevant study reference used in the submission.

Examples of search strategies for specific adverse effects and/or generic adverse-effect terms and key aspects of quality criteria for adverse-effects data can found in 'Systematic reviews: CRD's guidance for undertaking reviews in health care' (available from www.york.ac.uk/inst/crd).

Exact details of the search strategy used should be provided in section 10 appendix 2.

The sponsor's search strategy will be replicated by the External Assessment Centre.

7.7.2 Provide details of all important adverse events reported for each study. A suggested format is shown in table B10.

When providing details of important adverse events reported for each study, for each group, give the number of people with the adverse event, the total number of people in the group and the percentage with the event. Present the relative risk and risk difference and associated 95% confidence intervals for each adverse event.

Table B10 Adverse events across patient groups

	Time period 1			***Time period 2 etc.***		
	Intervention **% of patients (n = *x*)**	***Comparator*** **% of patients (n = *x*)**	**Relative risk (95% CI)**	***Intervention*** **% of patients (n = *x*)**	***Comparator*** **% of patients (n = *x*)**	**Relative risk (95% CI)**
Class 1 (for example, nervous system disorders)						
Adverse event 1						
Adverse event 2						
Class 2 (for example, vascular disorders)						
Adverse event 3						
Adverse event 4						

CI, confidence interval
Adapted from European Public Assessment Reports published by the European Medicines Agency

7.7.3 Describe all adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude).

Response

7.7.4 Provide a brief overview of the safety of the technology in relation to the scope.

Response

7.8 Evidence synthesis and meta-analysis

When more than one study is available and the methodology is comparable, a meta-analysis should be considered.

Section 7.8 should be read in conjunction with the 'Medical Technologies Evaluation Programme Methods Guide', available from www.nice.org.uk/mt

When direct comparative evidence about two key treatments is not available, indirect treatment comparison methods can be used to derive comparative estimates of the effectiveness of these two treatments. For example, if there is evidence comparing A with B, and B with C, indirect treatment comparison techniques could be used to help compare A with C. This option should be considered even though it may be less suitable for the evaluation of many new medical technologies, either because of lack of multiple comparators in the evidence base, or limitations in the evidence base/study designs.

7.8.1 Describe the technique used for evidence synthesis and/or meta-analysis. Include a rationale for the studies selected, details of the methodology used and the results of the analysis.

Response

Details should include the selection and quality assessment of the studies, the methodology used for combining the outcomes from the studies, including any tests for heterogeneity, and the results of the analysis including an assessment of the uncertainty associated with these results.

7.8.2 If evidence synthesis is not considered appropriate, give a rationale and provide a qualitative review. The review should summarise the overall results of the individual studies with reference to their critical appraisal.

Response

7.9 Interpretation of clinical evidence

7.9.1 Provide a statement of principal findings from the clinical evidence highlighting the clinical benefit and any risks relating to adverse events from the technology.

Response

7.9.2 Provide a summary of the strengths and limitations of the clinical-evidence base of the technology.

Response

7.9.3 Provide a brief statement on the relevance of the evidence base to the scope. This should focus on the claimed patient- and system-benefits described in the scope.

Response

7.9.4 Identify any factors that may influence the external validity of study results to patients in routine clinical practice.

Response

7.9.5 Based on external validity factors identified in 7.9.4 describe any criteria that would be used in clinical practice to select patients for whom the technology would be suitable.

Response

Section C – Economic evidence

Section C requires sponsors to present economic evidence for their technology.

All statements should be evidence-based and directly relevant to the decision problem.

The approach to the de novo cost analysis expected to be appropriate for most technologies is cost-consequence analysis. Sponsors should read section 7 of the Medical Technologies Evaluation Programme Methods guide on cost-consequences analysis, available from www.nice.org.uk/mt

Sponsors are requested to submit section C with the full submission. For details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

8 Existing economic evaluations

8.1 Identification of studies

The review of the economic evidence should be systematic and transparent and a suitable instrument for reporting such as the PRISMA statement (www.prisma-statement.org/statement.htm).

A PDF copy of all included studies should be provided by the sponsor.

8.1.1 Describe the strategies used to retrieve relevant health economics studies from the published literature and to identify all unpublished data. The search strategy used should be provided as in section 10, appendix 3.

Response

Health economics studies should include all types of economic evaluation and cost studies, including cost analyses and cost-effectiveness and budget-

impact analyses. The methods used should be justified with reference to the decision problem.

Sufficient detail should be provided to enable the methods to be reproduced (the External Assessment Centre must be able to reproduce the search), and the rationale for any inclusion and exclusion criteria regarding search terms should be used.

8.1.2 Describe the inclusion and exclusion criteria used to select studies from the published and unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table C1 Selection criteria used for health economic studies

Inclusion criteria
Population
Interventions
Outcomes
Study design
Language restrictions
Search dates
Exclusion criteria
Population
Interventions
Outcomes
Study design
Language restrictions
Search dates

8.1.3 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Response

It is recommended that the number of published studies included and excluded at each stage is reported using the PRISMA statement flow diagram (available from *www.prisma-statement.org/statement.htm*)

8.2 Description of identified studies

8.2.1 Provide a brief review of each study, stating the methods, results and relevance to the scope. A suggested format is provided in table C2.

Outcome measures should be included if applicable. Patient outcomes could include gains in life expectancy, improved quality of life, longer time to recurrence, and comparative costs.

Table C2 Summary list of all evaluations involving costs

Study name (year)	**Location of study**	**Summary of model and comparators**	**Patient population *(key characteristics, average age)***	**Costs *(intervention and comparator)***	***Patient outcomes (clinical outcomes, utilities, life expectancy, time to recurrence for intervention and comparator)***	***Results (annual cost savings, annual savings per patient, incremental cost per QALY)***
Study 1 (20xx)						
Study 2 (20xx)						
Study 3 (20xx)						

8.2.2 Provide a complete quality assessment for each health economic study identified. A suggested format is shown in table C3.

Table C3 Quality assessment of health economic studies

Study name		
Study design		
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?		
2. Was the economic importance of the research question stated?		
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?		
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?		
5. Were the alternatives being compared clearly described?		
6. Was the form of economic evaluation stated?		
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?		
8. Was/were the source(s) of effectiveness estimates used stated?		
9. Were details of the design and results of the effectiveness study given (if based on a single study)?		
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?		
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?		
12. Were the methods used to value health states and other benefits stated?		

13. Were the details of the subjects from whom valuations were obtained given?		
14. Were productivity changes (if included) reported separately?		
15. Was the relevance of productivity changes to the study question discussed?		
16. Were quantities of resources reported separately from their unit cost?		
17. Were the methods for the estimation of quantities and unit costs described?		
18. Were currency and price data recorded?		
19. Were details of price adjustments for inflation or currency conversion given?		
20. Were details of any model used given?		
21. Was there a justification for the choice of model used and the key parameters on which it was based?		
22. Was the time horizon of cost and benefits stated?		
23. Was the discount rate stated?		
24. Was the choice of rate justified?		
25. Was an explanation given if cost or benefits were not discounted?		
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?		
27. Was the approach to sensitivity analysis described?		
28. Was the choice of variables for sensitivity analysis justified?		
29. Were the ranges over which the parameters were varied stated?		
30. Were relevant alternatives		

compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)		
31. Was an incremental analysis reported?		
32. Were major outcomes presented in a disaggregated as well as aggregated form?		
33. Was the answer to the study question given?		
34. Did conclusions follow from the data reported?		
35. Were conclusions accompanied by the appropriate caveats?		
36. Were generalisability issues addressed?		
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

9 De novo cost analysis

Section 9 requires the sponsor to provide information on the de novo cost analysis.

The de novo cost analysis developed should be relevant to the scope.

All costs resulting from or associated with the use of the technology should be estimated using processes relevant to the NHS and personal social services.

Note that NICE cites the price of the product used in the model in the Medical Technology guidance.

9.1 Description of the de novo cost analysis

9.1.1 Provide the rationale for undertaking further cost analysis in relation to the scope.

Response

Patients

9.1.2 What patient group(s) is (are) included in the cost analysis?

Response

The patient group(s) included in the cost analysis must reflect the licensed indication/CE mark/marketing authorisation and be relevant to the scope.

The sponsor should not deviate from the scope.

Technology and comparator

9.1.3 Provide a justification if the comparator used in the cost analysis is different from the scope.

Response

If the choice of comparator used in the cost analysis is different from the scope an explanation must be provided.

Model structure

9.1.4 Provide a diagram of the model structure you have chosen.

Response

The model structure must be supplied to NICE in a legible format when printed on A4 paper.

9.1.5 Justify the chosen structure in line with the clinical pathway of care identified in response to question 3.3.

Response

Consider how the model structure captures the main aspects of the condition for patients and the NHS. What was the underlying disease progression implemented in the model? Or what treatment was assumed to reflect underlying disease progression? Cross-reference to section 3.3.

9.1.6 Provide a list of all assumptions in the cost model and a justification for each assumption.

Response

9.1.7 Define what the model's health states are intended to capture.

Response

9.1.8 Describe any key features of the cost model not previously reported. A suggested format is presented below.

Table C4 Key features of model not previously reported

Factor	Chosen values	Justification	Reference
Time horizon of model			
Discount of 3.5% for costs			
Perspective (NHS/PSS)			
Cycle length			
NHS, National Health Service; PSS, Personal Social Services			

9.2 Clinical parameters and variables

When relevant, answers to the following questions should be derived from, and be consistent with, the clinical evidence section of the submission (section 7). Cross-references should be provided. If alternative sources of evidence have been used, the method of identification, selection and synthesis should be provided as well as a justification for the approach.

9.2.1 Describe how the data from the clinical evidence were used in the cost analysis.

Response

In addition, if transition probabilities have been used in the model, explain how they were calculated from the clinical data. If appropriate, provide the transition matrix, details of the transformation of clinical outcomes or other details here. If the (transition) probabilities vary over time for the condition or disease, state how this has this been included in the evaluation and if it has not been included, provide an explanation of why it has been excluded. If transition probabilities have not been used, explain how the results of the clinical evidence were incorporated into the model.

9.2.2 Are costs and clinical outcomes extrapolated beyond the study follow-up period(s)? If so, what are the assumptions that underpin this extrapolation and how are they justified?

Response

In particular, consider what assumption was used regarding the longer term difference in effectiveness between the technology and its comparator.

Were any assumptions and/or techniques used for the extrapolation of longer term differences in clinical outcomes between the technology and its comparator?

9.2.3 Were intermediate outcome measures linked to final outcomes (for example, was a change in a surrogate outcome linked to a final clinical outcome)? If so, how was this relationship estimated, what sources of evidence were used and what other evidence is there to support it?

Response

9.2.4 Were adverse events such as those described in section 7.7 included in the cost analysis? If appropriate, provide a rationale for the calculation of the risk of each adverse event.

Response

9.2.5 Provide details of the process used when the sponsor's clinical advisers assessed the applicability of available or estimated clinical model parameter and inputs used in the analysis.

Response

This is a critical step and the names and professional titles of the clinical advisers should be included along with the following[1]:

[1] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

- *the criteria for selecting the experts*
- *the number of experts approached*
- *the number of experts who participated*
- *declaration of potential conflict(s) of interest from each expert or medical speciality whose opinion was sought*
- *the background information provided and its consistency with the totality of the evidence provided in the submission*
- *the method(s) used to collect and collate the opinions*
- *the medium used to collect opinions (for example, was information gathered by direct interview, telephone interview or self-administered questionnaire?)*
- *the questions asked*
- *whether iteration was used in the collation of opinions and if so, how it was used*
- *the uncertainly around these values should be addressed in the sensitivity analysis.*

9.2.6 Summarise all the variables included in the cost analysis. Provide cross-references to other parts of the submission. A suggested format is provided in table C5 below.

All parameters used to estimate cost should be presented clearly and include details of data sources. For continuous variables, mean values should be presented and used in the analyses. For all variables, measures of precision should be detailed.

Details should also include the values used, range (and distribution) and source.

Table C5 Summary of variables applied in the cost model

Variable	Value	Range or 95% CI (distribution)	Source
Age	*A years*	*x to y (normal)*	
Overall survival	*B months*	*x to y (Weibull)*	
Cost of *[X]*	£	*x to y (gamma)*	
[Insert other relevant variables]			
CI, confidence interval			

9.3 Resource identification, measurement and valuation

NHS costs

9.3.1 Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the payment by results (PbR) tariff.

Response

Provide Healthcare Resource Groups (HRG) and PbR codes and justify their selection.

9.3.2 State the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) codes for the operations, procedures and interventions relevant to the use of the technology for the clinical management of the condition.

Response

Resource identification, measurement and valuation studies

9.3.3 Provide a systematic search of relevant resource data for the NHS in England. Include a search strategy and inclusion criteria, and consider published and unpublished studies.

Response

9.3.4 Provide details of the process used when clinical advisers assessed the applicability of the resources used in the model[2].

Response

The details of the process should include:

- *the criteria for selecting the experts*
- *the number of experts approached*
- *the number of experts who participated*
- *declaration of potential conflict(s) of interest from each expert or medical speciality whose opinion was sought*
- *the background information provided and its consistency with the totality of the evidence provided in the submission*
- *the method(s) used to collect and collate the opinions*
- *the medium used to collect opinions (for example, was information gathered by direct interview, telephone interview or self-administered questionnaire?)*
- *the questions asked*
- *whether iteration was used in the collation of opinions and if so, how it was used*
- *the uncertainty around these values should be addressed in the sensitivity analysis.*

Technology and comparators' costs

9.3.5 Provide the list price for the technology.

Response

9.3.6 If the list price is not used in the de novo cost model, provide the alternative price and a justification.

A rationale must be provided for the choice of values used in the cost model. All prices should be referenced. Any uncertainty around prices should be

[2] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

addressed by sensitivity analysis. All costs must be cross-referenced to other sections of the submission if possible.

9.3.7 Summarise the annual costs associated with the technology and the comparator technology (if applicable) applied in the cost model. A suggested format is provided in tables C6 and C7. Table C7 should only be completed when the most relevant UK comparator for the cost analysis refers to another technology.

When completing tables C6 and C7 the price of the technology should refer to the list price stated in 9.3.4 unless a justification for using an alternative price has been provided in 9.3.5. If a technology is not for single use and consumables are needed to provide a treatment, these must be itemised and a breakdown of prices presented.

For all costs presented a source of the data must be stated.

Table C6 Costs per treatment/patient associated with the technology in the cost model

Items	Value	Source
Price of the technology per treatment/patient		
Consumables (if applicable)		
Maintenance cost		
Training cost		
Other costs		
Total cost per treatment/patient		

Table C7 Costs per treatment/patient associated with the comparator technology in the cost model

Items	Value	Source
Cost of the comparator per treatment/patient		
Consumables (if applicable)		
Maintenance cost		
Training cost		
Other costs		
Total cost per treatment/patient		

Health-state costs

9.3.8 If the cost model presents health states, the costs related to each health state should be presented in table C8. The health states should refer to the states in section 9.1.7. Provide a rationale for the choice of values used in the cost model.

Table C8 List of health states and associated costs in the economic model

Health states	Items	Value	Reference
Health state 1	**Technology cost**		
	Staff		
	Hospital costs		
	[Other items]		
	Total		
Health state 2			
Health state [X]			

Adverse-event costs

9.3.9 Complete table C9 with details of the costs associated with each adverse event referred to in 9.2.4 included in the cost model. Include all adverse events and complication costs, both during and after longer-term use of the technology.

Table C9 List of adverse events and summary of costs included in the cost model

Adverse events	Items	Value	Reference
Adverse event 1	**Technology**		
	Staff		
	Hospital costs		
	[Other items]		
	Total		
Adverse event 2	**Technology**		
	Staff		
Adverse event [X]			

Miscellaneous costs

9.3.10 Describe any additional costs and cost savings that have not been covered anywhere else (for example, PSS costs, and patient and carer costs). If none, please state.

Response

9.3.11 Are there any other opportunities for resource savings or redirection of resources that it has not been possible to quantify?

Response

Include a justification as to why it has not possible to quantify the resource use and/or costs.

9.4 Approach to sensitivity analysis

Section 9.4 requires the sponsor to carry out sensitivity analyses to explore uncertainty around the structural assumptions and parameters used in the analysis. All inputs used in the analysis will be estimated with a degree of imprecision. For technologies whose final price/acquisition cost has not been confirmed, sensitivity analysis should be conducted over a plausible range of prices.

Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

9.4.1 Has the uncertainty around structural assumptions been investigated? State the types of sensitivity analysis that have been carried out in the cost analysis.

Response

9.4.2 Was a deterministic and/or probabilistic sensitivity analysis undertaken? If not, why not? How were variables varied and what was the rationale for this? If relevant, the distributions and their sources should be clearly stated.

Response

All scenarios and/or ranges of variables must be justified.

9.4.3 Complete table C10.1, C10.2 and/or C10.3 as appropriate to summarise the variables used in the sensitivity analysis.

Table C10.1 Variables used in one-way scenario-based deterministic sensitivity analysis

Variable	Base-case value	Range of values

Table C10.2 Variables used in multi-way scenario-based sensitivity analysis

Variable	***Parameter 1***	***Parameter 2***	***Parameter 3***
Base case			
Scenario 1			
Scenario 2			

Table C10.3 Variable values used in probabilistic sensitivity analysis

Variable	Base-case value	Distribution

9.4.4 If any parameters or variables listed in section 9.2.6 were omitted from the sensitivity analysis, provide the rationale.

Response

It is acknowledged that some model parameters may be excluded from sensitivity analysis considerations, for example, because they can be considered 'constant' or because evidence exists about unbiased and accurate measurement.

9.5 Results of de novo cost analysis

Section 9.5 requires the sponsor to report the de novo cost analysis results. These should include the following:

- costs
- disaggregated results such as costs associated with treatment, costs associated with adverse events, and costs associated with follow-up/subsequent treatment
- a tabulation of the mean cost results
- results of the sensitivity analysis.

Base-case analysis

9.5.1 Report the total costs associated with use of the technology and the comparator(s) in the base-case analysis. A suggested format is presented in table C11.

Table C11 Base-case results

	Total per patient cost (£)
Technology	
Comparator 1	
...	

9.5.2 Report the total difference in costs between the technology and comparator(s).

Response

9.5.3 Provide details of the costs for the technology and its comparator by category of cost. A suggested format is presented in table C12.

Table C12 Summary of costs by category of cost per patient

Item	Cost *intervention (X)*	Cost *comparator (Y)*	Increment	Absolute increment	% absolute increment
Technology cost	*Xtech*	*Ytech*	*Xtech – Ytech*	*|Xtech – Ytech|*	*|Xtech – Ytech|/ (Total absolute increment)*
Mean total treatment cost	*Xtreat*	*Ytreat*	*Xtreat – Ytreat*	*|Xtreat – Ytreat|*	*|Xtreat – Ytreat|/ (Total absolute increment)*
Administration cost	*Xadmin*	*Yadmin*	*Xadmin – Yadmin*	*|Xadmin – Yadmin|*	*|Xadmin – Yadmin|/ (Total absolute increment)*
Monitoring cost	*Xmon*	*Ymon*	*Xmon – Ymon*	*|Xmon – Ymon|*	*|Xmon – Ymon|/ (Total absolute increment)*
Tests	*Xtests*	*Ytests*	*Xtests – Ytests*	*|Xtests – Ytests|*	*|Xtests – Ytests|/ (Total absolute increment)*
[Additional items]					
Total	*XTotal*	*YTotal*	*XTotal – YTotal*	*Total absolute increment*	*100%*

Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee

9.5.4 If appropriate, provide details of the costs for the technology and its comparator by health state. A suggested format is presented in table C13.

Table C13 Summary of costs by health state per patient

Health state	Cost *intervention (X)*	Cost *comparator (Y)*	Increment	Absolute increment	% absolute increment
Health state 1	*XHS1*	*YHS1*	*XHS1 – YHS1*	*|XHS1 – YHS1|*	*|XHS1 – YHS1|/ (Total absolute increment)*
Health state 2	*XHS2*	*YHS2*	*XHS2 – YHS2*	*|XHS2 – YHS2|*	*|XHS2 – YHS2|/ (Total absolute increment)*
Health state X					
Total	*XTotal*	*YTotal*	*XTotal – YTotal*	*Total absolute increment*	*100%*
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

9.5.5 If appropriate, provide details of the costs for the technology and its comparator by adverse event. A suggested format is provided in table C14.

Table C14 Summary of costs by adverse events per patient

Adverse event	Cost *intervention (X)*	Cost *comparator (Y)*	Increment	Absolute increment	% absolute increment
Adverse event 1	*XAE1*	*YAE1*	*XAE1 – YAE1*	*|XAE1 – YAE1|*	*|XAE1 – YAE1|/ (Total absolute increment)*
Adverse event 2	*XAE2*	*YAE2*	*XAE2 – YAE2*	*|XAE2 – YAE2|*	*|XAE2 – YAE2|/ (Total absolute increment)*
Total	*XTotal*	*YTotal*	*XTotal – YTotal*	*Total absolute increment*	*100%*
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

Sensitivity analysis results

9.5.6 Present results of deterministic one-way sensitivity analysis of the variables described in table C10.1.

Response

9.5.7 Present results of deterministic multi-way scenario sensitivity analysis described in table C10.2.

Response

9.5.8 Present results of the probabilistic sensitivity analysis described in table C10.3.

Response

9.5.9 What were the main findings of each of the sensitivity analyses?

Response

9.5.10 What are the key drivers of the cost results?

Miscellaneous results

9.5.11 Describe any additional results that have not been specifically requested in this template. If none, please state.

Response

9.6 Subgroup analysis

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. Sponsors are required to complete section 9.6 in accordance with the subgroups identified in the scope and for any additional subgroups considered relevant.

Types of subgroups that are not considered relevant are those based solely on the following factors.

- Subgroups based solely on differential treatment costs for individuals according to their social characteristics.
- Subgroups specified in relation to the costs of providing treatment in different geographical locations within the UK (for example, if the costs of facilities available for providing the technology vary according to location).

9.6.1 Specify whether analysis of subgroups was undertaken and how these subgroups were identified. Cross-reference the response to the decision problem in table A1 and sections 3.2 and 7.4.4.

Response

Consider if these subgroups were identified on the basis of a hypothesised expectation of differential clinical benefit or cost because of known, biologically plausible, mechanisms, social characteristics or other clearly justified factors.

9.6.2 Define the characteristics of patients in the subgroup(s).

Response

9.6.3 Describe how the subgroups were included in the cost analysis.

Response

9.6.4 What were the results of the subgroup analysis/analyses, if conducted? The results should be presented in a table similar to that in section 9.5.1 (base-case analysis).

Response

9.6.5 Were any subgroups not included in the submission? If so, which ones, and why were they not considered?

Response

9.7 Validation

9.7.1 Describe the methods used to validate and cross-validate (for example with external evidence sources) and quality-assure the model. Provide references to the results produced and cross-reference to evidence identified in the clinical and resources sections.

Response

9.8 Interpretation of economic evidence

9.8.1 Are the results from this cost analysis consistent with the published economic literature? If not, why do the results from this evaluation differ, and why should the results in the submission be given more credence than those in the published literature?

Response

9.8.2 Is the cost analysis relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope?

Response

9.8.3 What are the main strengths and weaknesses of the analysis? How might these affect the interpretation of the results?

Response

9.8.4 What further analyses could be undertaken to enhance the robustness/completeness of the results?

Response

References

Please use a recognised referencing style, such as Harvard or Vancouver.

Response

10 Appendices

10.1 Appendix 1: Search strategy for clinical evidence (section 7.1.1)

The following information should be provided:

10.1.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Response

10.1.2 The date on which the search was conducted.

Response

10.1.3 The date span of the search.

Response

10.1.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.1.5 Details of any additional searches, such as searches of company or professional organisation databases (include a description of each database).

Response

10.1.6 The inclusion and exclusion criteria.

Response

10.1.7 The data abstraction strategy.

Response

10.2 Appendix 2: Search strategy for adverse events (section 7.7.1)

The following information should be provided.

10.2.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Response

10.2.2 The date on which the search was conducted.

Response

10.2.3 The date span of the search.

Response

10.2.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.2.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

10.2.6 The inclusion and exclusion criteria.

Response

10.2.7 The data abstraction strategy.

Response

10.3 Appendix 3: Search strategy for economic evidence (section 8.1.1)

The following information should be provided.

10.3.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- EconLIT
- NHS EED.

Response

10.3.2 The date on which the search was conducted.

Response

10.3.3 The date span of the search.

Response

10.3.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example,

MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.3.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

10.4 Appendix 4: Resource identification, measurement and valuation (section 9.3.2)

The following information should be provided.

10.4.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- NHS EED
- EconLIT.

Response

10.4.2 The date on which the search was conducted.

Response

10.4.3 The date span of the search.

Response

10.4.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.4.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

10.4.6 The inclusion and exclusion criteria.

Response

10.4.7 The data abstraction strategy.

Response

11 Related procedures for evidence submission

11.1 Cost models

An electronic executable version of the cost model should be submitted to NICE with the full submission.

NICE accepts executable cost models using standard software – that is, Excel, TreeAge Pro, R or WinBUGs. If you plan to submit a model in a non-standard package, NICE should be informed in advance. NICE, in association with the External Assessment Centre, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the External Assessment Centre with temporary licences for the non-standard software for the duration of the assessment. NICE reserves the right to reject cost models in non-standard software. A fully executable electronic copy of the model must be submitted to NICE with full access to the programming code. Care should be taken to ensure that the submitted versions of the model programme and the written content of the evidence submission match.

NICE may distribute the executable version of the cost model to a consultee if they request it. If a request is received, NICE will release the model as long as it does not contain information that was designated confidential by the model owner, or the confidential material can be redacted by the model owner without producing severe limitations on the functionality of the model. The consultee will be advised that the model is protected by intellectual property rights, and can be used only for the purposes of commenting on the model's reliability and informing comments on the medical technology consultation document.

Sponsors must ensure that all relevant material pertinent to the decision problem has been disclosed to NICE at the time of submission. NICE may request additional information not submitted in the original submission of evidence. Any other information will be accepted at NICE's discretion.

When making a full submission, sponsors should check that:

- an electronic copy of the submission has been given to NICE with all confidential information highlighted and underlined
- a copy of the instructions for use, regulatory documentation and quality systems certificate have been submitted
- an executable electronic copy of the cost model has been submitted
- the checklist of confidential information provided by NICE has been completed and submitted.

- A PDF version of all studies (or other appropriate format for unpublished data, for example, a structured abstract) included in the submission have been submitted

11.2 Disclosure of information

To ensure that the assessment process is as transparent as possible, NICE considers it highly desirable that evidence pivotal to the Medical Technologies Advisory Committee's decisions should be publicly available at the point of issuing the medical technology consultation document and medical technology guidance.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').

When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly, and to provide reasons why they are confidential and the timescale within which they will remain confidential. The checklist of confidential information should be completed: if it is not provided, NICE will assume that there is no confidential information in the submission. It is the responsibility of the manufacturer or sponsor to ensure that the confidential information checklist is kept up to date.

It is the responsibility of the sponsor to ensure that any confidential information in their evidence submission is clearly underlined and highlighted

correctly. NICE is assured that information marked ‘academic in confidence’ can be presented and discussed during the public part of the Medical Technologies Advisory Committee meeting. NICE is confident that such public presentation does not affect the subsequent publication of the information, which is the prerequisite allowing for the marking of information as ‘academic in confidence’.

Please therefore underline all confidential information, and highlight information that is submitted under ‘commercial in confidence’ in blue and information submitted under ‘academic in confidence’ in yellow.

NICE will ask sponsors to reconsider restrictions on the release of data if there appears to be no obvious reason for the restrictions, or if such restrictions would make it difficult or impossible for NICE to show the evidential basis for its guidance. Information that has been put into the public domain, anywhere in the world, cannot be marked as confidential.

Confidential information submitted will be made available for review by the External Assessment Centre and the Medical Technologies Advisory Committee. NICE will at all times seek to protect the confidentiality of the information submitted, but nothing will restrict the disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

The Freedom of Information Act 2000, which came into force on 1 January 2005, enables any person to obtain information from public authorities such as NICE. The Act obliges NICE to respond to requests about the recorded information it holds, and it gives people a right of access to that information. This obligation extends to submissions made to NICE. Information that is designated as ‘commercial in confidence’ may be exempt under the Act. On receipt of a request for information, the NICE secretariat will make every effort to contact the designated company representative to confirm the status of any information previously deemed ‘commercial in confidence’ before making any decision on disclosure.

11.3 Equality

NICE is committed to promoting equality and eliminating unlawful discrimination, including paying particular attention to groups protected by equalities legislation. The scoping process is designed to identify groups who are relevant to the evaluation of the technology, and to reflect the diversity of the population. NICE consults on whether there are any issues relevant to equalities within the scope of the evaluation, or if there is information that could be included in the evidence presented to the Medical Technologies Advisory Committee to enable them to take account of equalities issues when developing guidance.

Evidence submitters are asked to consider whether the chosen decision problem could be impacted by NICE's responsibility in this respect, including when considering subgroups and access to recommendations that use a clinical or biological criterion.

For further information, please see the NICE website (www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp).