

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE
SPECIAL HEALTH AUTHORITY
CENTRE FOR HEALTH TECHNOLOGY EVALUATION
SINGLE TECHNOLOGY APPRAISALS PROCESS GUIDE

1.0 Background

In September 2005 the Board was presented with proposals for changes to the Technology Appraisal Process. These proposals included the development of a 'Single Technology Appraisal' (STA) process for the appraisal of single technologies for single indications. Key attributes of the proposed STA process were presented and the Board approved the proposals for implementation and consultation.

2.0 The development of the Single Technology Appraisal process

An interim process was developed for use by CHTE for the first STAs. The interim STA process was made available for public consultation in November 2005 to February 2006. Comments from public consultation were collated, presented to an internal Working Party and to members of the Appraisal Committees. A 'Specification for Manufacturer/Sponsor Submission' was also developed and made available for public consultation in conjunction with the interim STA process

This paper highlights the key themes from public consultation on the interim STA process and describes the subsequent changes to the proposals. The Board is asked to review the key themes from consultation and approve the final STA Process Guide. The final Manufacturer/Sponsor Specification Template has been signed off by the Centre Director and main comments from consultation are listed at the end of this paper.

The Board is also asked to note the hard work and dedication of the STA implementation team lead by Meindert Boysen, Associate Director STA, in developing the final STA Process Guide.

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May 2006

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FOR BOARD SIGN-OFF

Development of the STA process

1. Definition of STA and topic selection

The interim situation

The interim process was scarce in its reference to the definition of technologies that would be appropriate for STA.

Original proposal

1.1.2	The STA process is specifically designed for the appraisal of single products, with single indications. The process will result in formal NICE guidance. This process will normally be used to ensure that NICE is able to issue guidance to the NHS in England and Wales on new technologies close to their introduction into the UK market. The STA process may be applied to any single appraisal of a new pharmaceutical product, device, or other technology referred by ministers to the Institute.
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Key themes from public consultation

Although commentators generally recognised that topic selection was outside of the scope of the consultation on STA, comments were made on a number of related subjects.

There were comments on the definition of technologies that would be appropriate for STA and who would determine which technologies would follow which process; would stakeholders be asked to specify preference? Suggestions were made for STA to function as a 'screen' or 'triage' for topics to move between STA and MTA.

Questions were raised about the appropriateness for STA to deal with medical devices as development of technologies is so fast that new products reach the market while the process is ongoing.

Final proposals

The decision as to whether a topic is suitable for the STA process is made during topic selection and this undergoes consultation in line-with normal arrangements for topic selection. The final process guide gives more detail on the definition of an STA.

1.1.2	The STA process is specifically designed for the appraisal of a single product, with a single indication <u>where most of the relevant evidence lies with one sponsor – typically a new pharmaceutical close to launch. The decision as to whether a topic is suitable for the STA process is made during topic selection.</u> The process will result in formal NICE guidance. This process will normally be used to ensure that NICE is able to issue guidance to the NHS in England and Wales on new technologies close to their introduction into the UK market. The STA process may be applied to any appraisal of a single (new) pharmaceutical product, device, or other technology referred by Ministers to the Institute. <u>Once published guidance has the same status, regardless of whether it is the product of the multiple or single technology appraisals process.</u>
2.3	<u>In principle, any single technology for a single indication designated for referral by Ministers can be assigned to the STA programme for appraisal. In making decisions about the suitability of topics for the STA programme, consideration is also given to other factors, such as the complexity of current standard treatments and the probability of the evidence base being held primarily by the manufacturer/sponsor.</u>

2. Scoping.

The interim situation

No specific provisions were made for ‘scoping’ in the interim STA process.

Key themes from public consultation

Comments made in consultation called for the need of the STA process to be more specific on how questions to be answered by the appraisal will be defined and such issues as comparators decided. Scoping is seen to be a key component of the STA process as it is in the current technology appraisals programme.

Final proposals

We agree with consultees that scoping is a key component of a high quality STA process. The process now includes a ‘scoping’ phase in STA that aligns with the steps used in the multiple technology appraisal process for scoping during the topic selection process.

To allow for the Institute to further engage with the manufacturer or sponsor in developing the specification of the decision problem for the evidence submission we also propose to introduce a phase that allows for dialogue with the manufacturer to confirm the decision problem in advance of receipt of their evidence submission.

Final proposal – scoping

1.2.8	<u>An STA typically focuses on the use of a health technology within its licensed indication in comparison with current standard treatment in the NHS in England and Wales. The Institute will develop a scope for the STA in consultation with consultees and commentators. The approach for developing a scope is outlined in the 'Guide to the technology appraisal process' (section 3).</u>
3.1.1.1 And also 3.2.2	<u>The scope for the STA is developed during the consultation on proposed topics for referral to the NICE technology appraisal programme. Engagement with manufacturers and the wider consultee community in the selection process for appraisal topics ensures that stakeholders have advance notice that the STA is being planned (subject to referral). During this phase the final scope for the STA will be developed by the Institute in consultation with consultees and commentators on the basis of the remit issued by the Department of Health (see 'Guide to the technology appraisal process, Section 3, developing the scope for the technology appraisal').</u>
3.2.4	<u>The manufacturer or sponsor is required to submit to the Institute a summary of their 'decision problem for the Evidence Submission' 2 weeks after having been formally invited (see also section 3.2.3) to provide an Evidence Submission to the STA. This summary, which should include a specification of the population, the intervention, the comparators and outcomes relevant for the STA, is also a part of the STA submission template (see section 3.3.5) and will be used to ensure that the decision problem is specified appropriately with reference to the final scope as issued by the Institute (see also sections 1.2.8 and 3.3.7). On request, the Institute will be able to provide assistance in specifying the decision problem.</u>

3. Principal evidence for STA provided by manufacturer; assessment phase requires liaison with clinical experts; consultee and commentators not invited to make a submission of evidence.

The interim situation

The interim process specified that only the manufacturer would be requested to make an evidence submission. Only selected clinical specialists and patient experts from nominations would be requested to submit a personal statement.

Original proposal

1.2.6	The principal evidence for a STA is derived from an evidence submission by the manufacturer or sponsor of the technology. The review of this evidence submission is carried out by the Evidence Review Group. Selected clinical specialists and patient experts advise this group (see section 3.3) and submit their personal view to the Committee on the technology and the way it should be used in the NHS in England and Wales.
3.2.8	All healthcare professional groups and patient/carer groups that are consultees or commentators for the STA are invited to nominate clinical specialists or patient experts to advise the STA.

3.3.2	The evidence review phase requires liaison with clinical and patient experts. The experts are asked to advise the Institute and Evidence Review Group on the current management of the condition and the potential place of the new technology within current clinical practice.
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Key themes from public consultation

Respondents commented on two aspects of this interim proposal. On the one hand the practical implications for accepting only the manufacturer submission and on the other hand the missed opportunity of excluding a significant number of consultees in providing information to the STA.

Numerous comments were received relating to the quality of submissions to be received from manufacturers and the way the Institute would react to incomplete submissions and to those of low quality. Questions were also raised about the ability of the independent evidence review groups to deliver a high quality critique of a single evidence source without 'doing the work / analyses themselves'.

Finally, commentators suggested that it would be inappropriate to rely solely on input from clinical specialists and patient experts at the assessment phase of an STA and not allow for further – verbal – input in the meeting of the Appraisal Committee.

Final proposals

We remain convinced that the principal evidence for an STA should be submitted by the manufacturer or sponsor of the technology. However, we acknowledge that incomplete submissions or submissions of low quality could lead to challenges in presenting the appropriate evidence base to the Appraisal Committee for it to make decisions that could benefit patients in the NHS in England and Wales. The final STA process presented to the Board for sign-off includes a number of provisions to allow for the best possible evidence base to be presented to Committee within the constraints of the timelines inherent in the STA process.

1. Provide opportunities for iteration in the process to allow the manufacturer or sponsor to clarify the content of their evidence submission.
2. Allow for all consultees to submit statements to the STA by using templates specifically designed for clinical specialists, patient experts and other consultees.
3. Invite selected clinical specialist(s) and patient expert(s) to the Appraisal Committee meeting to answer questions the Committee may have during their proceedings.

The following detail is given for clarification. This forms the basis of the text in the final STA process (changes to the text are underlined).

Final proposal - introduction

1.2.6	The principal evidence for a STA is derived from an evidence submission by the manufacturer or sponsor of the technology. The review of this evidence submission is carried out by <u>an external organisation, independent of the Institute; the Evidence Review Group (ERG). All consultees to the STA are invited to submit a statement to the Committee on the technology and whether and how it should be used in the NHS in England and Wales. All healthcare professional groups and patient/carer groups that are consultees for the single technology appraisal are invited to nominate clinical specialists or patient experts to take part in the Appraisal Committee meeting.</u>
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Final proposal – ‘iteration’

3.3.7	<u>On receipt of the manufacturer or sponsor’s Evidence Submission, the Institute will assess whether the submission is complete and the decision problem is specified appropriately with reference to the final scope. If the submission is incomplete or the decision problem is not specified appropriately, the Institute will notify the manufacturer or sponsor within 2 weeks of receiving the submission and formally request clarification. If, following clarification, the Institute is not satisfied that the Evidence Submission will constitute a suitable basis for the Appraisal Committee to make a decision, manufacturers or sponsors may be asked to make a partial or full resubmission. Where such requests delay the published timeline, consultees and commentators will be advised of the reasons for the delay, and these will be posted on the Institute’s website.</u>
3.3.8	A <u>technical</u> review of the manufacturer or sponsor’s Evidence Submission will normally be undertaken by an external group, the Evidence Review Group. Their remit is to critically evaluate the Evidence Submission <u>and identify gaps in the evidence base that could lead the Institute to request further clarification from the manufacturer or sponsor (see section 0).</u> Normally, the Evidence Review Group is commissioned by the National Coordinating Centre for Health Technology Assessment (NCCHTA). However, the Institute may selectively choose to use its Decision Support Unit (DSU) in individual cases.
3.3.9	The Evidence Review Group prepares an Evidence Report (ERG Report). This is a review of the evidence for clinical and cost effectiveness of the technology based on a review of the Manufacturer Evidence Submission. This is prepared in accordance with the quality criteria of the HTA Programme (www.hta.nhsweb.nhs.uk) and is consistent with the Institute’s Guide to the Methods of Technology appraisal. The content and quality of the ERG Report is the responsibility of its authors.
3.4.2.9	Exceptionally, the Committee <u>may ask the Institute to seek clarification, within the period between the ACD and FAD meetings, on key uncertainties in the evidence base. Clarification will be sought from the manufacturer or sponsor.</u>
3.4.4.7	<u>The period of consultation on the ACD can, in exceptional circumstances, be used for further clarification (with the manufacturer or sponsor – see 3.4.2.9) on key uncertainties in the evidence base.</u>
4.1.6	The Evidence Review Group assesses the Manufacturer Evidence Submission and writes a report which forms part of the committee papers. <u>The Evidence Review Group may suggest to the Institute that the</u>

	<u>manufacturer or sponsor should undertake additional analyses. These will be reported as addenda to the manufacturer or sponsor submission. The Evidence Review Group's report will later be released to consultees and commentators and put on the NICE website either with the ACD (if any) or the FAD.</u>
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Final proposal – including all consultees

3.1.1.2	The <u>STA process begins after a topic has been referred to the Institute by Ministers and the first phase is initiated</u> either when NICE is notified that the manufacturer of the selected topic is applying to the regulatory authorities for a particular indication, or, when the STA is not tracking a regulatory submission, at a point determined by NICE. NICE will then contact the manufacturer or sponsor to notify them of the STA and request an Evidence Submission. <u>All other consultees will at the same time be invited to complete statements relevant to the group they are representing.</u> Manufacturers or sponsors are provided with a detailed template for this submission, called the Submission Template. Manufacturers <u>and other consultees</u> are given a minimum of 8 weeks to prepare the Evidence Submission <u>and complete the statements.</u> Depending on when a product is selected for STA and when regulatory approval, where relevant, is expected, this may be longer.
3.1.1.3	The <u>next phase begins with receipt of the Manufacturer Evidence Submission and includes the independent review of the Evidence Submission (a minimum of 8 weeks), appraisal (4 weeks), and preparation of the recommendations (2 weeks).</u> <u>Statements submitted by consultees other than the manufacturer or sponsor will not be formally reviewed in the independent review of the Evidence Submission. These statements are presented in full to the Appraisal Committee for their consideration alongside the Evidence Submission and Review</u>
3.3.4	<u>All consultees to the STA are invited to complete a statement on the implications (positive and negative) of the technology for the condition at the same time as the manufacturer/sponsor is invited to complete an Evidence Submission. These statements should be made using the appropriate templates available on the Institute's website (see ref <website>), which include information on the type and length of information that it should contain once completed.</u>

Final proposal – including clinical specialists and patient experts

3.3.2 in interim process	<u>Deleted.</u>
3.4.2.2	The Appraisal Committee undertakes its initial consideration and discussion about the evidence on a STA. The written evidence is presented in the manufacturer or sponsor's Evidence Submission, statements by consultees to the STA, the Evidence Review Group report and the pre-meeting briefing note of the NICE secretariat. <u>Oral evidence is drawn from discussions with invited clinical specialists and patient experts and the Evidence Review Group representatives.</u> More information about how the Appraisal Committee considers the evidence and makes its decision is available in the Guide to the Methods of Technology appraisal.

3.4.2.6	<u>Representatives from the National Collaborating Centre that is responsible for developing the Institute's clinical guidelines in areas related to the topic under appraisal are also invited to attend the meeting to observe and to contribute as advisors to the Committee.</u>
3.4.2.7	<u>Clinical specialists and patient experts are encouraged to interact fully in the debate with the Appraisal Committee whilst responding to questions posed by the Appraisal Committee. The clinical specialists and patient experts are asked to withdraw from the meeting before the Committee discusses the content of the FAD (or the ACD, if any).</u>
4.2.2	<p><u>Clinical specialists and patient experts are chosen from the nominations by the Chair of the Appraisal Committee in discussion with the Institute's project team on the basis of the extent and nature of their experience of the technology, the disease and the services provided by the NHS to patients with the condition(s) that the technology is designed to treat. Clinical specialists and patient experts are invited to attend meetings of the Appraisal Committee on the following conditions.</u></p> <ul style="list-style-type: none"> - <u>They agree to be bound by the terms and conditions of the Institute's Confidentiality Acknowledgement and Undertaking.</u> - <u>They agree to their name and affiliation appearing on the FAD, ACD and the final guidance.</u> - <u>They are prepared to declare, at the Appraisal Committee's meeting, any interests they have in the technology under appraisal.</u> - <u>They have no other conflict of interest that might preclude their involvement with the appraisal.</u>
4.2.3	<p><u>Additionally, the following criteria are used to inform the selection of clinical specialists.</u></p> <ul style="list-style-type: none"> - <u>They are in active clinical practice and have specialist expertise in the particular area of the appraisal.</u> - <u>Their principal place of work is within the NHS.</u> - <u>They hold no official office (that is, no paid employment, unpaid directorship or membership of a standing advisory committee) with any of the manufacturers of the technology or any manufacturer of a directly competing technology.</u>
4.2.4	<u>Usually, two clinical specialists and two patient experts are selected. In the context of Single technology Appraisals, they are not asked to submit a written personal view on the technology and the way it should be used in the NHS in England and Wales, and instead should be able to clarify the statement submitted by the consultee organisations that has nominated them. Further advice about the contribution of clinical specialists and patient experts is available in the specific guides for groups participating in an appraisal.</u>
4.1.8.5	<u>The Institute informs consultees and commentators of the names and affiliations of the selected clinical specialists and patient experts invited to take part in the Appraisal Committee meeting. This information is also posted on the NICE website.</u>

3. Publication of the FAD / guidance.

The interim situation

Original proposal

4.1.3	The Institute cannot issue guidance or an ACD on a technology before it receives UK regulatory approval. Where a STA begins before UK regulatory approval has been granted, it will only proceed past the point when the ACD or FAD is released, once UK regulatory approval has been granted, and once the price and the indication(s) for the technology are known.
5.1.15	If there is no appeal or an appeal is dismissed, the Institute makes arrangements for the FAD, as issued to consultees (subject to correction of any factual errors), to be published as guidance. Normally, the Institute will publish the guidance as part of its monthly schedule (on the last Wednesday of each month). In exceptional circumstances, guidance may be published outside this schedule.

Key themes from public consultation

Suggestions were made for it to be appropriate to hold the Appraisal Committee meeting to discuss the STA as soon as a positive opinion by the Committee for Medical Products for Human Use (CHMP) has been received.

Final proposals

We agree with this general approach and have amended the process but will determine appropriateness on a case by case basis. We also feel that it would be most appropriate for the Evidence Review Group to receive confirmation of the proposed licensed indication before issuing their final report to the Institute.

5.7	<u>The STA will be discussed by the Appraisal Committee at the earliest opportunity after the CHMP has published its positive opinion on the technology within the indication for which the technology is appraised by the Institute.</u>
5.16	If there <u>are</u> no appeals, or an appeal lodged is dismissed <u>with or without a hearing</u> , the Institute makes arrangements for the FAD, as issued to consultees (subject to correction of any factual errors), to be published as guidance. <u>The</u> Institute will publish the guidance as part of its monthly schedule (on the last Wednesday of each month). <u>The guidance, in its final form, will be put in the public domain for information through the Institute's website in advance of its formal publication.</u>

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**SINGLE TECHNOLOGY APPRAISALS PROCESS
FOR BOARD SIGN-OFF**

**Specification for manufacturer/sponsor submission of
evidence**

Key themes from public consultation that have led to amendments

1. Separation of section on specification of the decision problem for the evidence submission
2. Inclusion of the request for an executive summary
3. Explicit inclusion of provisions for non-randomised controlled trial evidence