NHS
National Institute for Health and Clinical Excellence

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Guide to the single technology appraisal process

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This document is one of a series describing the processes and methods that NICE uses to undertake technology appraisals. For further information, please go to www.nice.org.uk

It replaces the 'Guide to the single technology appraisal (STA) process' published in September 2006.

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Contents

Acknowledgements

NICE is very grateful to everyone who contributed to the development of this guide (see appendix A).

List of abbreviations

ACD	Appraisal consultation document
CHTE	Centre for Health Technology Evaluation
ERG	Evidence Review Group
FAD	Final appraisal determination
HTA	Health technology assessment
MTA	Multiple technology appraisal
NICE	National Institute for Health and Clinical Excellence
STA	Single technology appraisal

See appendix C for a glossary of terms used in this document.

Foreword

This document is one of a series describing the processes and methods that the National Institute for Health and Clinical Excellence (NICE) uses to undertake technology appraisals. It focuses on the single technology appraisal (STA) process and provides an overview for the organisations invited to contribute to an STA.

The documents in the series are:

- Guide to the multiple technology appraisal process
- Guide to the single technology appraisal process
- Guide to the methods of technology appraisal
- Technology appraisal process: guidance for appellants.

Organisations invited to contribute to NICE technology appraisals (consultees and commentators) should read this guide in conjunction with the documents listed above. All documents are available on NICE's website (www.nice.org.uk).

1 Introduction

This guide describes the standard, open and transparent process, including expected timescales, that NICE follows when undertaking a single technology appraisal (STA). The process is designed to produce robust guidance for the NHS with appropriate contribution from stakeholders.

This guide should be read in conjunction with the 'Guide to the methods of technology appraisal', available on NICE's website (www.nice.org.uk).

General description of NICE and the STA process

1.1 NICE is part of the NHS. It is an independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health.

1.2 The Centre for Health Technology Evaluation (CHTE), within NICE, develops STAs.

1.3 The STA process is designed to provide recommendations, in the form of NICE guidance, on the use of new and existing medicines, products and treatments in the NHS. These include:

- drugs
- medical devices (for example, hearing aids, inhalers, cochlear implants, pacemakers)
- diagnostic techniques (tests used to identify diseases, measure the severity of disease or the progression of disease)
- surgical procedures (for example, repairing hernias).

1.4 The STA process is specifically designed to appraise a single product, device or other technology, with a single indication. The process normally covers new technologies (typically, new pharmaceutical products or licensed indications) and enables NICE to produce guidance soon after the technology is introduced in the UK. NICE seeks relevant evidence from several sources. The manufacturer or sponsor of the technology submits the principal evidence. The Evidence Review Group (ERG), an external academic organisation independent of NICE, produces a review of the evidence submission (see section 3.4.8). Consultees provide further information (see table 1) and selected clinical specialists, NHS commissioning experts and patient experts also give evidence (see section 3.4.12).

1.5 The decision to appraise a technology through the STA process is made during topic selection. Once published, NICE technology appraisal guidance has the same status, regardless of whether it followed the STA or the multiple technology appraisal (MTA) process (please see the 'Guide to the multiple technology appraisal process' for more details on MTAs).

1.6 The Secretary of State for Health formally refers technologies to NICE for appraisal either as an MTA or an STA.

1.7 The purpose of STAs, which is described in the directions of the Secretary of State for Health (www.nice.org.uk/aboutnice/whatwedo/niceandthenhs/directions_from_the_secretary_of_state.jsp), is to appraise the health benefits and the costs of those technologies referred by the Secretary of State for Health and to make recommendations to the NHS in England and Wales.

1.8 An STA is based on a review of clinical and economic evidence principally provided by the manufacturer or sponsor. Clinical evidence measures how well the medicine or treatment works – the health benefits. The evidence includes the impact on quality of life (for example, pain relief, side effects and disability), and the likely effects on mortality. NICE also considers estimates of the associated costs, concentrating on costs to the NHS and personal social services (for example social services). The economic evidence shows how well the medicine or treatment works in relation to how much it costs the NHS and whether it represents value for money. Specific methods used for STAs are described in the 'Guide to the methods of technology appraisal'.

1.9 The Appraisal Committee (see table 1) considers the evidence and makes a judgement on whether or not the technology should be recommended as a clinically and cost-effective use of NHS resources, or whether it should only be recommended for specific subgroups of patients.

1.10 The Appraisal Committee submits its recommendations to NICE in one of two forms: an appraisal consultation document (ACD) or a final appraisal determination (FAD). Normally, the Appraisal Committee submits an ACD only if its provisional recommendations are substantially more restrictive than the terms of the marketing authorisation (or equivalent, for example, CE marking for devices) of the technology being appraised. If the Committee submits an ACD then NICE invites consultees, commentators and the public to comment on the ACD. After considering these comments, the Committee finalises its recommendations and submits them to NICE in the form of a FAD. If the Committee's recommendations are generally in line with the licensed indication (or equivalent), it submits a FAD. The FAD forms the basis of the guidance that NICE issues to the NHS in England and Wales.

1.11 When formulating its recommendations, the Appraisal Committee considers the factors that are most appropriate to each appraisal. The Appraisal Committee takes into account legislation on human rights, discrimination and equality, and the directions from the Secretary of State. These directions include:

- the broad balance of clinical benefits and costs
- the degree of clinical need of patients with the disease or condition under consideration

- any guidance issued to the NHS by the Secretary of State that is specifically drawn to the attention of NICE by the Secretary of State and any guidance issued by the Secretary of State
- the potential for long-term benefits to the NHS of innovation.

1.12 NICE gives the Appraisal Committee advice on making scientific and social value judgements. This advice is informed by the work of the Citizens Council. The Appraisal Committee considers the social value judgements provided in 'Social value judgements: principles for the development of NICE guidance' (see www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp).

Table 1 Participants in the STA process

Appraisal Committee	The Appraisal Committee is an independent standing committee that produces recommendations. NICE recruits Committee members through open advertising and appoints members initially for a 3-year term. Committee members are from: • the NHS • lay backgrounds (with an understanding of patient and public perspectives on healthcare issues) • academia • pharmaceutical and medical devices industries. Full details of how NICE recruits members can be found at www.nice.org.uk/getinvolved/joinnwc/advisorybodyrecruitmentpack.jsp NICE is committed to equality and diversity and welcomes applications for membership from all sectors of the community. NICE allocates Committee members to one of four standing Appraisal Committees. Members will normally remain in the same Committee for the duration of their membership. Although the Appraisal Committee seeks the views of organisations representing healthcare professionals, patients, carers, manufacturers and government, its advice is independent. Names of Appraisal Committee members are posted on NICE's website. See www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalcommittee/technology_appraisal_committee.jsp for the Appraisal Committee's standing order and terms of reference.

Table 1 continued

Consultees	NICE invites consultees to take part in the STA. They include: • national groups representing patients and carers • organisations representing healthcare professionals • manufacturer(s) or sponsor(s) of the technology • the Department of Health • the Welsh Assembly Government • specialised commissioning groups • primary care trusts and local health boards. As part of the scoping process, NICE invites consultees to comment on draft remits and draft scopes. Consultees can submit a statement and participate in the consultation on the ACD (if produced). All non-manufacturer consultees can nominate clinical specialists and/or patient experts to verbally present their personal views to the Appraisal Committee. Manufacturer or sponsor consultees can also nominate clinical specialists. Representatives from the primary care trusts and local health boards invited to participate in the appraisal may also attend the Appraisal Committee as NHS commissioning experts. All consultees have the opportunity to appeal against the FAD. Consultees can also comment on the proposal for reviewing the guidance.
Commentators	NICE invites commentator organisations, with an interest in the technology, to take part in the STA. They include: • manufacturers or sponsors of comparator technologies • NHS Quality Improvement Scotland • any relevant National Collaborating Centres (groups commissioned by NICE to develop clinical guidelines) and/or the relevant Programme Development Group for public health guidance • other related research groups (for example, the Medical Research Council and the National Cancer Research Institute) • other groups (such as the NHS Confederation, the NHS Purchasing and Supplies Agency, the Scottish Medicines Consortium, the Medicines and Healthcare Products Regulatory Agency, the Department of Health, the Ministry of Defence, Social Services and Public Safety for Northern Ireland).

Table 1 continued

Commentators (continued)	As part of the scoping process, NICE invites commentators to comment on draft remits and draft scopes. Commentators can participate in the consultation on the ACD (if produced), but NICE does not ask them to make any submission to the appraisal. Commentator organisations representing non-manufacturers can nominate clinical specialists and patient experts to verbally present their personal views to the Appraisal Committee. Commentator organisations representing comparator manufacturers or sponsors can also nominate clinical specialists. These organisations receive the FAD for information only, without right of appeal. Commentators can also comment on the proposal for reviewing the guidance.
Clinical specialists and patient experts	The Chair of the Appraisal Committee and the NICE project team select clinical specialists and patient experts from nominations by non-manufacturer consultees and commentators. They attend the Appraisal Committee meeting to answer questions to help clarify issues about the submitted evidence. Before they attend the meeting, all experts must either submit a written statement (using a template) or indicate they agree with the statement made by their nominating organisation.
NHS commissioning experts	NICE selects at random two primary care trusts or local health boards to be consultees. NICE invites two of their representatives to attend the Appraisal Committee meeting to offer their view, answer questions and help clarify issues about the submitted evidence and the impact of the technology on the NHS. Before they attend the meeting, NICE asks them to submit a written statement explaining their views and experiences of the technology and/or condition from an NHS perspective.
Evidence Review Group (ERG)	The ERG is an independent academic group that reviews the manufacturer or sponsor's evidence submission. The ERG may also prepare some additional analyses. The ERG is normally commissioned by the National Institute for Health Research – Health Technology Assessment Programme.

Table 1 continued

NICE staff	
Centre Director	The Centre Director is responsible for delivering all outputs of the CHTE. The Centre Director must also ensure that appraisals are conducted in accordance with the published appraisal process and methods.
Programme Director	The Programme Director is responsible for all aspects of managing and delivering the STA work programme. The Programme Director interacts with the NICE sponsor branch at the Department of Health and other national bodies, and with healthcare industry bodies. The Programme Director is responsible for signing off guidance at specific stages of an individual appraisal. The Programme Director is also responsible for ensuring that appraisals are conducted in accordance with the published appraisal process and methods.
Associate Director	The Associate Director is responsible for developing individual appraisals within the appraisal programme and has delegated responsibility, from the Programme Director, for signing off guidance at specific stages of an individual appraisal.
Project manager	The project manager is responsible for planning individual appraisal timelines, ensuring the timelines and process are followed, and liaising with consultees, commentators and other individuals and organisations contributing to the appraisal.
Technical lead	The technical lead is the analyst responsible for the technical aspects of the STA, including liaising with the ERG, scoping the appraisal, preparing drafts of guidance and advising the Appraisal Committee. There may be more than one technical lead for an appraisal.
Technical adviser	The technical adviser is responsible for the technical quality of the appraisal. This involves providing leadership on technical issues, and reviewing and quality assuring the work of the technical lead. The technical adviser also ensures a consistent approach is taken across the appraisal programme.
Executive lead	The executive lead is allocated from NICE's Executive Directors. It is an advisory role and involvement is limited to dealing with particularly complex issues.

Table 1 continued

Communications lead	The communications lead is responsible for circulating and communicating the guidance to appropriate groups within the NHS in England and Wales, and to patients and the public.
Information services lead	The information services lead is responsible for supporting the technical lead in scoping the appraisal. The information services lead gathers information to support the production of a draft scope and continues to track key information throughout the life cycle of the appraisal to support the work of the technical lead.
Editorial lead	The editorial lead is responsible for ensuring that all STA guidance documents are accurate, clear and consistent. The editorial lead prepares the final versions of the guidance for healthcare professionals (the quick reference guide) and patients and carers ('Understanding NICE guidance'), and works with the implementation, audit and costing leads to make sure the tools that help the NHS put the guidance into practice are clear and understandable.
Patient and Public Involvement Programme (PPIP) project manager	The PPIP is the team at NICE that supports and develops patient and public involvement across NICE's work programme. A PPIP project manager is assigned to each appraisal and supports patient and carer consultee organisations, their representatives, and individual patients or carers throughout the appraisal. This may include making it easier to attend workshops or meetings, giving advice on completing submissions, consultation responses or other documentation, and nominating experts. The PPIP project manager also supports the lay members of the Appraisal Committees and supplies the patient and carer group information for the 'Understanding NICE guidance'.
Costing lead	The costing lead works with the technical lead and clinical experts to produce guidance-related costing tools. The costing tools consist of a costing report and template to help organisations assess the financial impact of implementing NICE guidance. They are published at the same time as the appraisal and are subject to a limited consultation. The costing lead also provides input at the topic selection stage, assessing the potential financial impact of each topic scoped.

Table 1 continued

Audit lead	The audit lead is allocated from the implementation support team and is responsible for the development of audit support through the provision of ready-to-use criteria, including exceptions, definitions and data source suggestions, and a data collection tool. Audit support is externally validated and developed in collaboration with the technical lead.
Implementation adviser	The implementation adviser provides support from the scoping stage through to post-publication activities, liaising with the internal NICE teams, development teams and external organisations to support the implementation of NICE guidance, including the development of implementation support tools. A quarterly meeting is held with the appraisals and implementation team to identify STAs that might require additional implementation support.

2 Selection of technologies

NICE can only begin to appraise a technology when it has been formally referred by the Secretary of State for Health. A technology is referred as an MTA or an STA depending on various factors, such as the complexity of current standard treatment pathways and treatment options, and whether most of the evidence is held by the manufacturer or sponsor. In principle, any single technology for a single indication referred by the Secretary of State for Health can be assigned to the STA programme for appraisal.

Details of how topics are selected for appraisal can be found on NICE's website (www.nice.org.uk/aboutnice/howwework/howguidancetopicsarechosen/how_guidance_topics_are_chosen.jsp).

Developing the remit and scope

2.1 Developing the draft scope

2.1.1 Before NICE receives a formal referral, it is asked to consider a list of possible appraisals, in the form of draft remits, and to seek the views of interested parties. At this stage, NICE develops a draft scope for each possible appraisal. The steps involved in developing a draft scope are shown in figure 1.

2.1.2 The draft scope sets out what the appraisal will cover and the questions that need to be addressed. It will steer and focus the appraisal if the technology is formally referred to NICE for appraisal.

2.1.3 The first step in the scoping process is to identify information relating to the technology. NICE's information specialists, working with the appraisal team's technical leads, undertake this task, which includes conducting a literature search, identifying the availability of relevant evidence and contacting the manufacturer or sponsor of the technology. NICE uses this information to prepare a draft scope.

2.1.4 The draft scope defines a number of elements, including:

- the clinical problem, the population(s) and any relevant subgroups in whom treatment with or use of the technology would be appraised
- the clinical setting – where the technology will be used
- the relevant comparator technologies – usually the treatment(s) used in current clinical practice in the NHS to manage the disease or condition (this may include non-licensed technologies if they are used in current clinical practice); sometimes the comparator is best supportive care, palliative therapy or no intervention (for further details, see the 'Guide to the methods of technology appraisal')
- the principal health outcome measures appropriate for analysis

- the measures of costs to be assessed
- the length of time over which the benefits and costs will be considered
- special considerations and issues that are likely to affect the potential STA, including equality and diversity issues.

2.1.5 For further information on how scopes are developed, see the 'Guide to the methods of technology appraisal'.

2.1.6 Unless the Department of Health specifically indicates otherwise, NICE will not publish guidance on the use of a technology for indications for which regulatory approval has not been granted in the UK (that is, off-licence use).

2.2 Identifying interested parties

2.2.1 Identifying interested parties (known as consultees and commentators; see table 1) is an important stage of the process. NICE identifies consultees and commentators before it consults on the draft remit and draft scope.

2.2.2 A patient or professional group can be a consultee if it works at a national level (covering the UK or England, or a UK branch of an international body) and represents patients, carers or healthcare professionals either broadly or directly related to the technology being considered. Other consultees include specialised commissioning groups – two primary care trusts or local health boards selected at random, and the manufacturer or sponsor of the technology.

2.2.3 Commentators include research organisations with an interest in the technology being considered, organisations that cover the NHS as a whole, such as the NHS Confederation, patient and professional groups covering Wales only, and the manufacturers or sponsors of relevant comparator technologies.

2.2.4 During the scoping phase, NICE aims to identify the widest range possible of relevant consultees and commentators who have an interest in the technology or disease area being considered. This includes, but is not restricted to, national organisations representing relevant specific ethnic groups, people with disabilities, mental health problems and/or learning disabilities.

2.2.5 Any organisation meeting the criteria that wishes to become a consultee or commentator for a proposed appraisal can contact the relevant project manager (see NICE's website for details). An application to join the appraisal as a consultee or commentator can be made at any point during the scoping and appraisal phases of the process.

2.3 Consultation on the draft remit and draft scope

2.3.1 The next step is a consultation stage on the list of consultees and commentators, draft remit and draft scope for the potential appraisal with identified provisional consultees and commentators. The aim of this consultation is to gather views on whether NICE should appraise the technology, as well as to ensure that all the relevant areas and issues are covered if the technology is referred to NICE for appraisal. It is important that all the relevant organisations and interested parties are included in these consultations. NICE therefore asks identified provisional consultees and commentators if there are other organisations that need to be included in the consultation.

2.3.2 NICE sends the draft remit and draft scope to the identified provisional consultees and commentators, together with the list of consultees and commentators, for comment. NICE must receive comments within 20 working days of the date of sending.

2.3.3 NICE asks the manufacturer or sponsor to provide information about the expected timing of pending licence applications (or equivalent) for their technology in the UK. This must include, if applicable, the expected date for Committee for Medicinal Products for Human Use (CHMP) opinion and the date of receipt of regulatory approval (or equivalent). The manufacturer or sponsor should also state whether they expect the launch date for their technology in the UK to differ from the regulatory approval date. Medical devices go through a different regulatory approval process than pharmaceuticals with different timelines and data requirements. It is important that the manufacturer or sponsor informs NICE of any change in the regulatory approval timelines as soon as possible. NICE uses this information to plan the appraisal.

2.3.4 NICE publishes the draft remit, draft scope and list of consultees and commentators on its website, for information, 5 working days after it sends these documents to the provisional consultees and commentators.

2.4 The scoping workshop

2.4.1 After provisional consultees and commentators have submitted their comments on the draft remit, draft scope and list of consultees and commentators, NICE holds a meeting called the scoping workshop. NICE invites all provisional consultees and commentators, and the ERG, to send one or two representatives to this meeting.

2.4.2 The aims of the workshop are to:

- briefly explain the appraisal process
- ensure the scope is appropriately defined
- discuss the issues raised by provisional consultees and commentators during consultation on the draft remit and draft scope
- identify important evidence and any other issues relevant to the potential appraisal.

2.4.3 It is important that sufficient expertise is fed into the development of the scope. NICE welcomes and values all specialist input from patient groups, NHS commissioners and healthcare professionals provided at consultation and during the workshop discussions.

2.4.4 At the scoping workshop, NICE encourages the manufacturer or sponsor to provide preliminary details of the evidence it would submit if NICE were asked to appraise the technology. This may include details of trials in progress, for example the inclusion and exclusion criteria used. At the end of the workshop, the manufacturer or sponsor can discuss commercially sensitive information and technical issues relating to the potential appraisal with NICE, in confidence.

2.5 Final scope

2.5.1 NICE finalises the scope, taking into account comments received during the draft remit and draft scope consultation, and the discussions at the scoping workshop. This is in anticipation of receiving a formal referral to appraise the technology from the Secretary of State for Health.

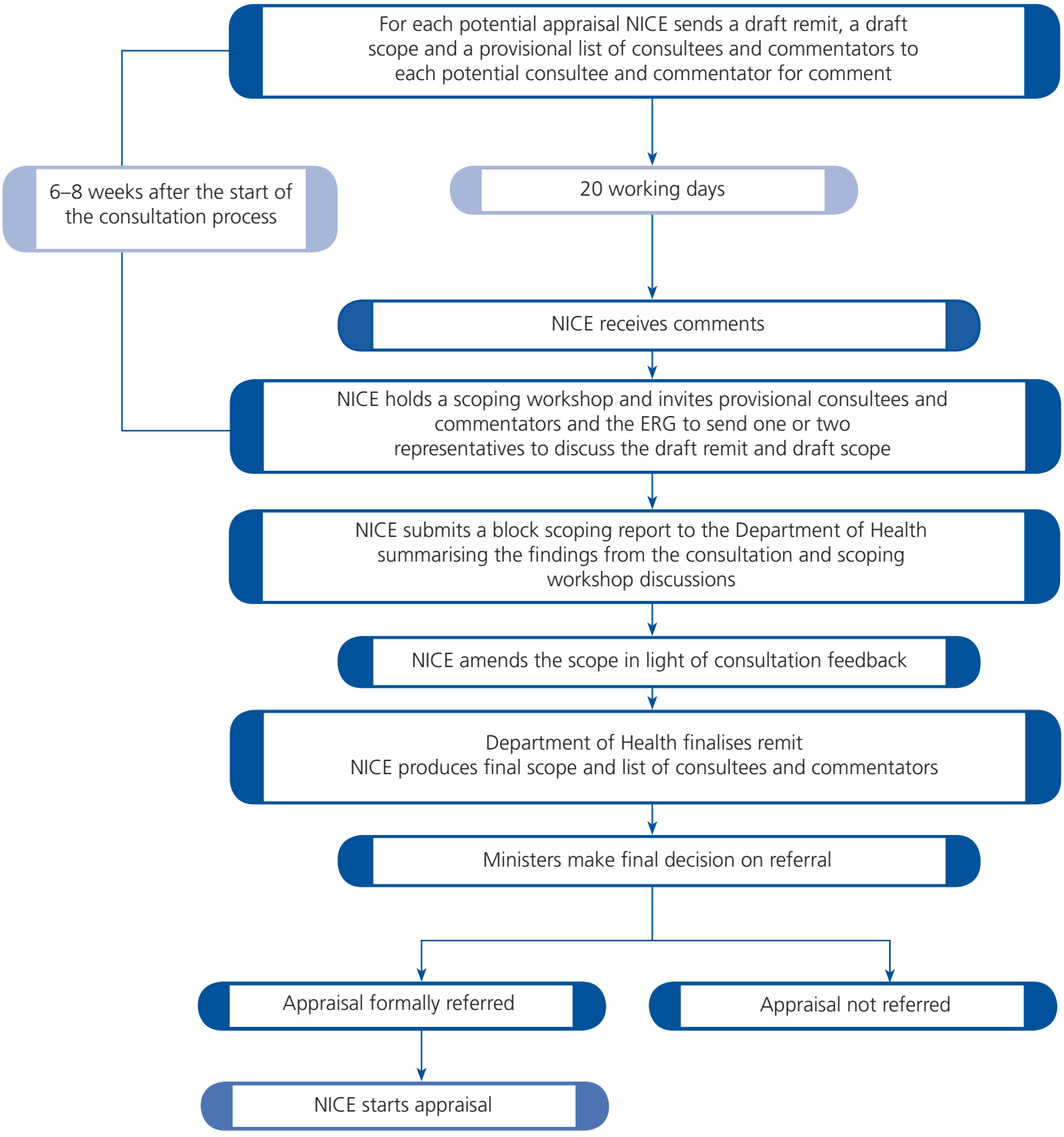
2.5.2 NICE submits a report to the Department of Health summarising the results of the consultation and scoping workshop discussions (known as the block scoping report). This information helps ministers to decide whether or not the technology should be formally referred to NICE for appraisal and whether it should be referred as an MTA or an STA. If ministers decide to refer a technology, the technology is formally referred to NICE for appraisal along with the final remit.

2.5.3 NICE publishes the block scoping report (with any 'commercial in confidence' information removed) on its website after formal referral.

2.5.4 If there is a significant length of time between scoping and the start of the appraisal, NICE may need to update the scope to ensure it is still relevant. Depending on the extent of this update, NICE may undertake further consultation with consultees and commentators.

2.5.5 NICE may need to refine the scope further at the request of ministers.

Figure 1 Steps in developing the scope



2.6 Planning the referred appraisals into the work programme

2.6.1 After formal referral, NICE plans the timelines for the STA and normally publishes them on its website within 6 weeks. NICE aims to hold the first Appraisal Committee meeting at the point the technology gains its positive opinion (or equivalent) from the licensing authority. It is therefore essential that the manufacturer or sponsor informs NICE of all developments in the regulatory approval process. This ensures that NICE publishes guidance on the use of the new technology as soon as possible after its introduction into the UK.

2.6.2 If possible, before the start of an STA, NICE informs the consultees and commentators of the expected timelines for the appraisal. Occasionally, timelines have to change, either before or during the appraisal. NICE will inform consultees and commentators about these changes and, if possible, explain the reasons for the changes. Sometimes, however, if the reasons are commercially sensitive, NICE cannot disclose them. NICE works with the manufacturer or sponsor of the technology to release as much information as possible to interested parties.

2.6.3 During the referral process of an STA, NICE asks the National Institute for Health Research – Health Technology Assessment Programme (NIHR HTA Programme) to formally commission the ERG to produce a report. The NIHR HTA Programme commissions the ERG report from one of a number of independent academic centres.

3 The STA process

Section 3 sets out the STA process under the following headings:

- General points
- Phase 1: initiation of the STA and evidence submission
- Phase 2: evidence review
- Phase 3: appraisal

See figure 2 and appendix B for an overview of the STA process and timelines.

3.1 General points

3.1.1 NICE sends the name and contact details of the project manager assigned to an individual STA to all consultees and commentators. Consultees and commentators should send all correspondence, including consultation responses, relating to an individual STA to the project manager to make sure it is dealt with effectively.

3.1.2 NICE sends correspondence for an appraisal by email or post to one key contact identified by each consultee and commentator organisation. It is therefore essential that consultees and commentators notify the project manager of any change in contact details or in organisation or company name throughout the appraisal process.

3.1.3 NICE's website has a page for each STA giving information about the timelines and progress of the appraisal. Further information is available from the project manager.

3.2 Phase 1: initiation of the STA and evidence submission

3.2.1 The STA process consists of three distinct phases: phase 1: initiation of the STA and evidence submission (including the decision problem); phase 2: evidence review (including initial clarification); and phase 3: appraisal. Phase 1 begins after the scoping phase has been completed and NICE has received formal referral from the Secretary of State for Health (see figure 2 and appendix B for an overview of the STA process and timelines).

3.2.2 NICE publishes the final remit and final scope (see section 2.5), the name of the ERG and the list of consultees and commentators on its website at least 8 weeks before the manufacturer or sponsor's evidence submission deadline. Each STA is assigned to a project team at NICE; the members are listed on NICE's website. The roles of key members of the project team are summarised in table 1.

3.2.3 Phase 1 starts when NICE invites consultees and commentators to participate in the STA. NICE sends consultees and commentators a list of key dates for the STA along with their invitation to participate.

Evidence submission from the manufacturer or sponsor

3.2.4 NICE invites the manufacturer or sponsor of the technology to provide an evidence submission using a detailed template and specification (see www.nice.org.uk/aboutnice/howwework/devnicetech/singletechnologyappraisalsubmissiontemplates.jsp). The deadline for receipt of the evidence submission is at least 8 weeks from invitation. On receipt, NICE sends the evidence submission to the ERG for review.

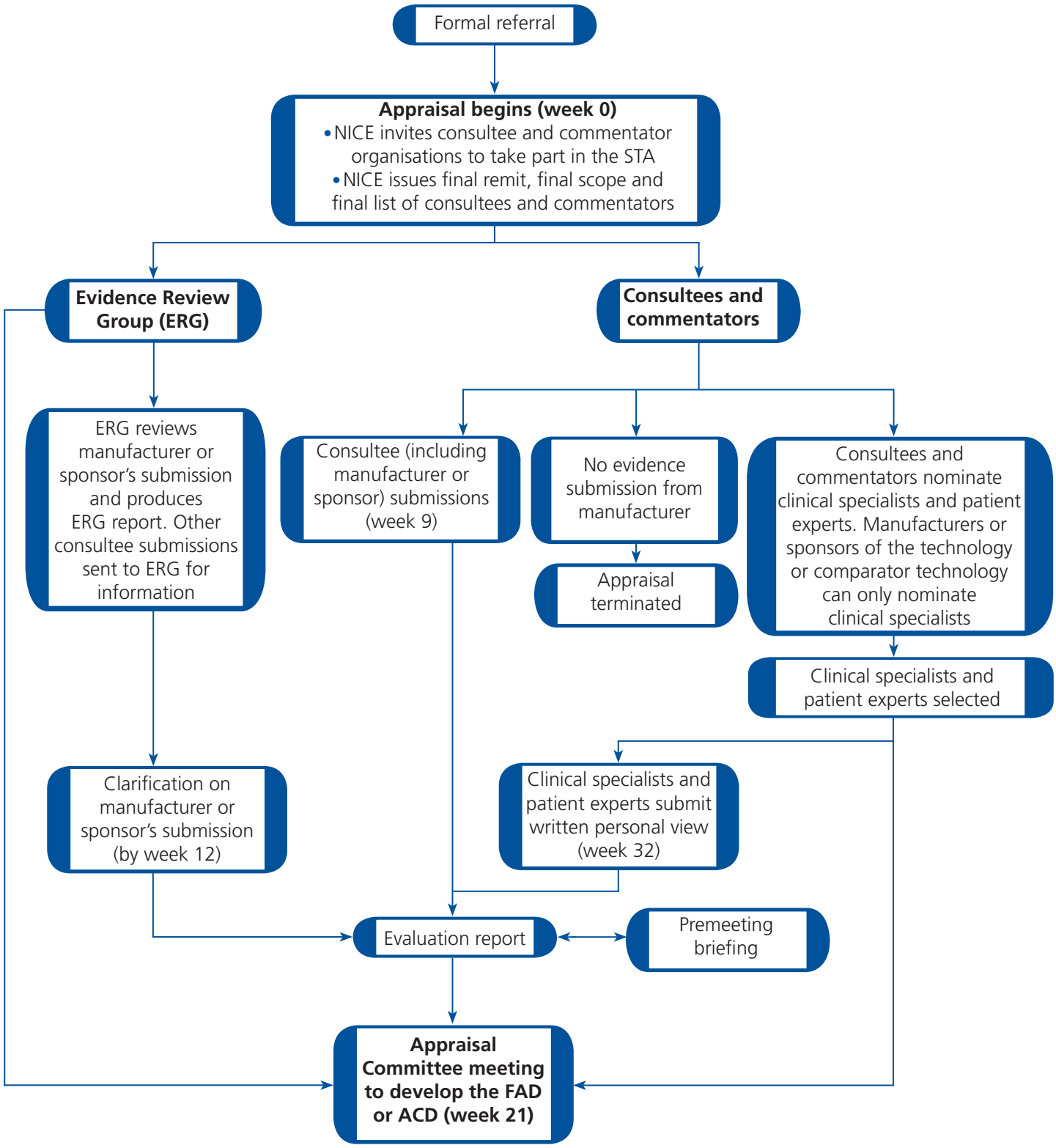
3.2.5 The specification for the evidence submission is derived from the decision-analytical approach NICE uses to evaluate the clinical and cost effectiveness of health technologies. This approach is outlined in the 'Guide to the methods of technology appraisal'. Page limits and instructions on the use of appendices are given in the specification for evidence submission. Submission appendices are not normally given to the Appraisal Committee.

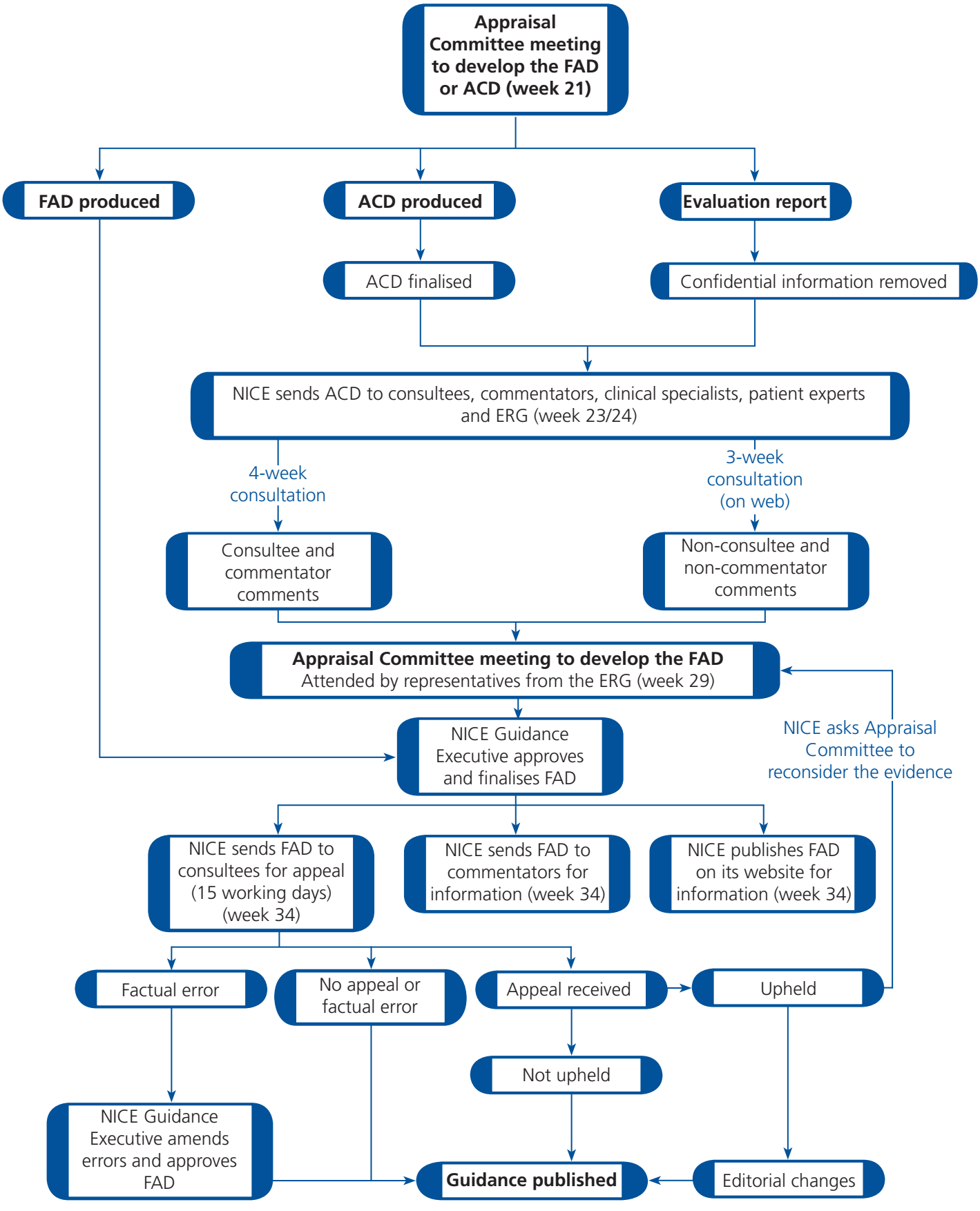
3.2.6 If the manufacturer or sponsor plans to submit an economic model, they should inform NICE what software will be used. NICE accepts fully executable economic models using standard software, that is, Excel, DATA, R or WinBUGs. If the manufacturer or sponsor plans to submit a model in a non-standard package, they should tell NICE in advance. NICE, in association with the NIHR HTA and the ERG, will then investigate whether the requested software is acceptable. When the manufacturer or sponsor submits a fully executable electronic copy of the model, they must give NICE full access to the programming code. Care should be taken to ensure that the submitted versions of the model program and the written content of the evidence submission match.

3.2.7 If the manufacturer or sponsor wishes to include a patient access scheme as part of their submission, they must agree this scheme with the Department of Health before submission to NICE. The Department of Health asks the Patient Access Scheme Liaison Unit (PASLU) at NICE to advise them on the feasibility of implementing a patient access scheme in the NHS in England and Wales. The PASLU provides advice to the Department of Health that will inform ministerial decisions on referring an agreed patient access scheme to NICE for consideration with the submission. NICE includes details of the scheme in the evaluation report (see section 5 of this guide for further details).

3.2.8 If the timelines of the STA are following the anticipated timeframe for regulatory approval, the manufacturer or sponsor must notify NICE when it makes a submission for regulatory approval of the indication being appraised. The notification should also specify when an opinion is expected from the CHMP (or equivalent), when it expects to receive regulatory approval and the expected wording of the marketing authorisation. Manufacturers or sponsors are required to inform NICE immediately if there are changes in the regulatory approval process that will affect the timeframe or have implications for the wording of the marketing authorisation.

Figure 2 Summary of the STA process




Appraisal Committee meeting to develop the FAD or ACD (week 21)
FAD produced
ACD produced
Evaluation report
ACD finalised
Confidential information removed
NICE sends ACD to consultees, commentators, clinical specialists, patient experts and ERG (week 23/24)
4-week consultation
3-week consultation (on web)
Consultee and commentator comments
Non-consultee and non-commentator comments
Appraisal Committee meeting to develop the FAD
Attended by representatives from the ERG (week 29)
NICE Guidance Executive approves and finalises FAD
NICE asks Appraisal Committee to reconsider the evidence
NICE sends FAD to consultees for appeal (15 working days) (week 34)
NICE sends FAD to commentators for information (week 34)
NICE publishes FAD on its website for information (week 34)
Factual error
No appeal or factual error
Appeal received
Upheld
Not upheld
NICE Guidance Executive amends errors and approves FAD
Guidance published
Editorial changes

3.2.9 NICE asks the manufacturer or sponsor to submit a summary of the decision problem for their evidence submission 2 weeks after formally inviting them to provide an evidence submission for the STA. NICE sends this document to the ERG. It should summarise the analyses that will be performed, including details of the study population, the intervention, the comparators and the outcomes. The STA submission template ensures that the decision problem is specified appropriately in relation to the final scope. NICE invites the manufacturer or sponsor to attend a meeting to discuss the decision problem and to ensure that it is specified appropriately. This meeting also provides an opportunity for the manufacturer or sponsor to ask questions. NICE reports a summary of discussions from the decision problem meeting to the ERG.

3.2.10 NICE is unable to review or approve submissions during their preparation.

Statements from non-manufacturer consultees

3.2.11 NICE invites all non-manufacturer consultees to submit a statement providing information on the potential clinical and cost effectiveness of a treatment using the appropriate templates available on NICE's website (www.nice.org.uk/aboutnice/howwework/devnicetech/singletechnologyappraisalsubmissiontemplates.jsp). The statement should reflect the patient or clinician's experience of current standard treatment in the NHS in England and Wales and the potential impact of treatment on health-related quality of life. Implementation issues, such as staffing and training requirements, should also be included. Consultees have at least 8 weeks to provide their statements to NICE. On receipt, NICE sends the evidence submission to the ERG for information.

3.2.12 The Patient and Public Involvement Programme (PPIP) project manager at NICE offers support throughout the STA process to consultee groups representing patient or carer organisations and patient experts (see table 1 for further information).

3.2.13 NICE offers consultee groups representing patients, carers and healthcare professionals a financial contribution towards the cost of participating in the appraisal. Payments will normally be made only into a corporate bank account of the consultee organisation. Under exceptional circumstances, a payment may be made into a personal bank account but only after written authorisation has been received from the consultee organisation.

3.2.14 NICE is unable to review or approve statements during their preparation.

Information handling

3.2.15 NICE adheres to the principles and requirements of the Data Protection Act and the Freedom of Information Act when dealing with information received during an appraisal.

3.2.16 With the exception of the draft scope, NICE will not make public, or circulate among consultees and commentators, any documents for consultation before the technology has received regulatory approval.

3.2.17 Care should be taken when submitting information relating to individuals. Personal and sensitive information, for example identifying an individual's clinician, should be removed from submissions.

3.2.18 If an evidence submission from a manufacturer or sponsor, or a statement from a non-manufacturer consultee contains confidential information, it is the responsibility of the submitter to provide two versions, one complete (including the confidential information) and one for publication (with the confidential information removed), together with a checklist of the confidential information. Detailed instructions on submitting confidential information relating to an STA are available from the project manager.

3.2.19 NICE is required to meet the requirements of copyright legislation. If a manufacturer or sponsor of a technology cites journal articles in their submission, they must include the full journal articles in their submission and have copyright clearance for these articles. NICE will accept journal articles in electronic format only if they are provided on CD-ROM separate to the main submission and economic model. Copyright-controlled material may not be submitted by email or other Internet-based means. NICE will pass journal articles to the ERG in the format they are received (printed or electronic). NICE will not copy, print or store submitted references as this would breach copyright legislation.

3.2.20 NICE requires manufacturers and sponsors of technologies under appraisal to sign a statement declaring that all material relevant to the STA has been disclosed to NICE.

3.2.21 To ensure that the appraisal process is as transparent as possible, NICE considers it essential that evidence on which the Appraisal Committee's decisions are based is publicly available. Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information (for example, the findings of a research project defined as 'confidential' because its public disclosure could have an impact on the commercial interests of a particular company) and evidence that is awaiting publication ('academic in confidence').

3.2.22 NICE considers that evidence designated as 'academic in confidence' (but not 'commercial in confidence') can be presented at Appraisal Committee meetings with members of the public and press present. This should be highlighted to third party providers of 'academic in confidence' information.

3.2.23 NICE expects consultees to keep confidential material within a submission to an absolute minimum. When consultees believe that part of a submission should be

treated as confidential, they must clearly state the reason for this according to the following principles:

- Information that has been put into the public domain, in written form, anywhere in the world may not be marked as confidential.
- The list price of a technology (after launch) and incremental cost-effectiveness ratio (ICER) estimates cannot be marked as 'commercial in confidence'.
- The results of clinical trials relating to products that have received regulatory approval should be available. When NICE documentation quoting evidence from a clinical trial is released before the results are published in a journal, as a minimum, a structured abstract should be made available for public disclosure. This abstract should follow a recognised format for a full trial report, such as that provided by the CONSORT statement (www.consort-statement.org).
- Manufacturers or sponsors can seek further information on guidelines for the release of data into the public domain during an STA from the agreement between the Association of the British Pharmaceutical Industry (ABPI) and NICE (www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/agreement_of_the_british_pharmaceutical_industry.jsp).

3.2.24 The same principles apply to the manufacturer or sponsor's economic model. The manufacturer or sponsor should make available to NICE and the ERG the fully executable economic model used in the cost-effectiveness analysis, in electronic format. In addition, as a minimum, the manufacturer or sponsor should provide a structured abstract describing the economic model for public disclosure.

3.2.25 The ERG and the Appraisal Committee, and the clinical specialists, NHS commissioning experts and patient experts invited to attend the Appraisal Committee meeting can review confidential information submitted by consultees. NICE distributes confidential information to consultees and commentators only with permission from the evidence owners.

3.2.26 NICE releases the documents listed in table 2 to consultees and commentators during the STA process. NICE publishes these documents on its website at least 5 working days after they have been sent to consultees and commentators. After NICE has published these documents on its website they are no longer confidential.

3.2.27 NICE encourages consultees to make their individual submissions accessible – for example, by placing them on their own websites after they have sent their submission to NICE.

3.2.28 NICE will not comment on the content of an STA until the process has been completed and its guidance has been produced, except in the following circumstances:

- NICE reserves the right to make public comment if there has been an unauthorised disclosure from a confidential NICE document before it has been published on its website. The Chair or Vice Chair of NICE will take this decision on the recommendation of two Executive Directors. NICE will inform consultees and commentators of this decision as soon as possible.
- NICE reserves the right to issue a correction if a public comment is made on an ACD or FAD that could mislead or misinform.

3.2.29 Organisations participating in an STA must sign a confidentiality agreement before they are recognised as formal consultees and commentators. After this, NICE can release appraisal documents to them.

3.2.30 It is the responsibility of the consultees and commentators, and any other party that has signed a confidentiality agreement for the appraisal, to treat appraisal documents that are not in the public domain as confidential until NICE makes those documents public. NICE considers individuals within a consultee or commentator organisation who see appraisal documents to be bound by the terms of the confidentiality agreement signed by the consultee or commentator organisation.

3.2.31 Any organisation or individual not directly employed by the consultee or commentator organisation is a third party. Consultees and commentators may release the appraisal documents to third parties when:

- it is necessary to enable the consultee or commentator to contribute to the appraisal, and
- the third party has seen and agreed to be bound by the terms of the confidentiality agreement.

3.2.32 Consultees and commentators may discuss confidential appraisal documents with other consultees and commentators but, before doing so, they must be satisfied that the other consultees and commentators have signed and returned their confidentiality agreements to NICE.

3.2.33 In the evaluation report (see section 3.5.3), ACD and FAD, NICE reserves the right to use any material submitted during the STA process that is not marked as 'confidential' by the consultee, or which ceases to be so under sections 3.2.26 or 3.2.39. Reference will be made in the evaluation report to documents or information that have been marked as confidential by the consultee.

3.2.34 If changes are made to the expected summary of product characteristics during the regulatory approval process, NICE will discuss the implications with the ERG and the manufacturer or sponsor and agree how to incorporate the changes into the submission and the ERG report.

3.2.35 An STA may begin before UK regulatory approval has been granted. NICE will not issue consultation documents or guidance on a technology until UK regulatory approval has been granted and the technology's price is known.

Table 2 Documents NICE releases during the appraisal process

Document	For further information, see section
List of consultees and commentators	2.2.1
Final scope and remit for the appraisal	2.5
Manufacturer or sponsor's evidence submission (confidential information removed)*	3.2.4
Statements from non-manufacturer consultees*	3.2.11
Clarification letters sent to the manufacturer or sponsor and the response to these letters*	3.4.2
Evidence Review Group (ERG) report*	3.4.8
Premeeting briefing*	3.5.2
If produced, the appraisal consultation document (ACD)	3.5.22
Comments from consultees and commentators on the ACD, if produced, and responses from NICE	3.5.30
Final appraisal determination (FAD)*	3.5.38

*NICE releases these documents to consultees and commentators who have signed a confidentiality agreement before publishing them on its website (5 working days later).

Submitting confidential information

3.2.36 All confidential information NICE receives (in evidence submissions, statements, responses to consultation and general correspondence) must be clearly underlined and highlighted. A checklist must also be provided explaining why the information is marked as confidential and when it will be made publicly available.

3.2.37 Confidential information in a submission should be kept to a minimum. It is not acceptable to mark a whole evidence submission as confidential.

3.2.38 If NICE does not receive a completed checklist with a document, none of the information will be considered confidential. If a document contains confidential information, it is the responsibility of the submitter to provide two versions, one complete (including the confidential information) and one for publication (with the confidential information removed).

3.2.39 NICE aims to provide a complete audit trail for all of its guidance. To make sure that the appraisal process is transparent, NICE considers it essential that evidence on which the Appraisal Committee's decisions are based is publicly available. All the evidence seen by the Committee should be available to all consultees and commentators. This includes an executable version of the economic model. Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. It is important to consider carefully the information that is marked as confidential and therefore not releasable because it may be difficult to identify how evidence has been used and interpreted. NICE will ask for restrictions on release of evidence to be reconsidered if there appears to be no obvious reason for the restrictions, or when such restrictions would make it difficult or impossible for NICE to show the evidence on which the guidance is based.

3.3 Process timelines

3.3.1 It is not possible to set absolute timelines for all stages of the appraisal process. The length of time needed for each stage can vary depending on the nature of the particular appraisal. The timelines set out in tables 3–5 and appendix B indicate the minimum number of weeks for each stage of the STA process.

3.3.2 Throughout an appraisal, up-to-date information about timelines and progress is available on NICE's website. Further information is available from the project manager.

3.3.3 If possible, NICE informs the consultees and commentators about timeline changes and the reasons for these changes. Sometimes, however, if the reasons are commercially sensitive, NICE cannot disclose them. NICE works with the manufacturer or sponsor of the technology to release as much information as possible to interested parties.

3.4 Phase 2: evidence review

Evidence submission and clarification

3.4.1 On receipt of the manufacturer or sponsor's evidence submission, NICE and the ERG assess whether the submission is complete and whether the decision problem is specified appropriately with reference to the final scope.

3.4.2 If the evidence submission is incomplete or the decision problem is not specified appropriately, NICE consults with the ERG and sends a letter of clarification to the manufacturer or sponsor within 15 working days of receiving the submission. The manufacturer or sponsor has 10 working days from the date of the correspondence to respond. NICE will organise a face-to-face meeting to discuss any issues that cannot be resolved by other means.

3.4.3 If such requests for clarification delay the published timelines, NICE informs consultees and commentators, and publishes the reason for the delay on its website.

3.4.4 The response to the clarification request allows the manufacturer or sponsor to review the confidential status of information in its evidence submission before the Appraisal Committee meeting (see sections 3.2.36–3.2.39 for details on submission of confidential information).

3.4.5 The manufacturer or sponsor should not submit additional evidence during the evidence review phase unless NICE requests or agrees to this in advance.

Terminating an STA

3.4.6 NICE must ensure that the manufacturer or sponsor prepares the best possible evidence submission for the Appraisal Committee. NICE's technical leads do not validate the submission but they help to clarify substantive issues. If, after all reasonable requests for clarification, NICE is not satisfied that the evidence submission is adequate for the Appraisal Committee to make a decision or no evidence submission has been received, the Centre Director will recommend to NICE's Guidance Executive that the STA should be terminated. NICE will return an inadequate evidence submission to the manufacturer or sponsor noting that no submission has been received. NICE will subsequently advise the NHS that the appraisal has been terminated and that 'NICE is unable to recommend the use in the NHS of the technology because no evidence submission was received from the manufacturer or sponsor of the technology'. NICE will also provide an explanation to help the NHS make local decisions on making the technology available.

3.4.7 A terminated appraisal can be re-initiated if the manufacturer or sponsor indicates that they wish to make a full evidence submission.

Evidence Review Group report

3.4.8 When a manufacturer or sponsor submits an adequate evidence submission, the ERG reviews it.

3.4.9 The ERG prepares a report on the clinical and cost effectiveness of the technology consistent with the methodology of technology appraisal. The report is based on a review of the manufacturer or sponsor's evidence submission and advice from their clinical advisers. The ERG prepares the report in accordance with the NIHR HTA Programme quality criteria (www.hta.ac.uk/investigators/authorinstructions.shtml) and an agreed report template. The ERG is responsible for the content and quality of the report.

3.4.10 The ERG critically evaluates the evidence submission. The ERG may suggest to NICE, during initial clarification, that the manufacturer or sponsor should undertake additional analyses. The manufacturer or sponsor should include full descriptions of any additional analyses as appendices to the original submission. If changes are made to the submitted model, the ERG should include technical details of these amendments and their impact in the ERG report. If appropriate, the ERG may perform exploratory and sensitivity analyses using the manufacturer or sponsor's economic model. If undertaken, the ERG will include details of these analyses in their report. NICE sends the ERG report to consultees and commentators and publishes it on the website with either the ACD or the FAD.

3.4.11 NICE sends the ERG report to the manufacturer or sponsor before it is presented to the Appraisal Committee. The manufacturer or sponsor has 5 working days from the date of sending to check that the report (including confidential information provided by the manufacturer or sponsor) does not contain factual errors, for example, errors in the figures, incorrect quotes from the evidence submission or text that does not describe the facts accurately. NICE prepares a document highlighting any factual errors for the Appraisal Committee meeting and publishes the document on its website as part of the evaluation report. The manufacturer or sponsor cannot submit additional evidence during the evidence review phase unless NICE has agreed to this before the main evidence submission, or NICE asks for more evidence.

Participation of clinical specialists, NHS commissioning experts and patient experts

3.4.12 While the ERG is producing its report, and consultees are preparing their submissions, NICE organises phase 3 of the STA process. This involves planning the Appraisal Committee meetings (which are held in public). NICE encourages all consultees and commentators to nominate clinical specialists and patient experts to take part in the first

Appraisal Committee meeting discussions. NICE asks the two primary care trusts or local health boards selected at random to be consultees to nominate two NHS commissioning experts to attend the Appraisal Committee meeting.

3.4.13 The Chair of the Appraisal Committee, NICE's project team and PPIP team choose clinical specialists and patient experts from the nominations received.

3.4.14 The PPIP project manager gives advice and information to the organisations nominating patient experts. Individuals interested in being patient experts can also contact the PPIP project manager for information about how to be nominated. To do this, the individual and the nominating organisation complete a joint patient expert nomination form. This asks them to provide a short biography describing the nominee's experience and knowledge of the condition and/or technology, and describing any previous involvement with NICE.

3.4.15 The Chair and NICE's project team base their choice of clinical specialists and patient experts on the nominees' experience of the technology and the condition(s) that the technology is designed to treat. If possible, the clinical specialists and patient experts will have complementary rather than similar backgrounds and experiences. NICE invites clinical specialists, NHS commissioning experts and patient experts to attend Appraisal Committee meetings provided they meet the following criteria:

- They agree to be bound by the terms and conditions of NICE's confidentiality agreement.
- They agree to their name and affiliation appearing in the ACD and/or FAD.
- They have knowledge and/or experience of the condition and/or technology under appraisal and/or the way it is used in the NHS.
- They are willing and able to discuss the condition and the technology with members of a large committee at a meeting where there may be members of the public and press observing.
- They are familiar with the purpose and processes of NICE (the PPIP project manager at NICE can give patient experts an overview that enables them to contribute to the discussions at Appraisal Committee meetings).
- They are prepared to declare any interests they have in the technology under appraisal at Appraisal Committee meetings.
- They do not have any conflicts of interest that would prevent them from participating in the appraisal.

3.4.16 Additionally, the following criteria are used to select clinical specialists:

- They are in active clinical practice and have specialist expertise in the subject area of the appraisal.
- Their principal place of work is within the NHS.

- If they have acted as a clinical expert for the ERG, they agree to declare this in their personal statement and at Appraisal Committee meetings.
- They hold no official office (that is, no paid employment, unpaid directorship or membership of a standing advisory committee) with the manufacturer or sponsor of the technology or any manufacturers or sponsors of comparator technologies.

3.4.17 Usually, two clinical specialists and two patient experts are selected. NICE asks the clinical specialists, NHS commissioning experts and patient experts to submit a short (4-page maximum) written personal view on the technology and the way it should be used in the NHS in England and Wales using a standard template. NICE gives the written personal views to the Appraisal Committee and publishes them as part of the evaluation report. However, if the clinical specialists and patient experts support the statement made by their nominating organisation they do not need to submit a personal view. Further advice about the contribution of clinical specialists, NHS commissioning experts and patient experts is available from the project manager.

3.4.18 Clinical specialists, NHS commissioning experts and patient experts attend Appraisal Committee meetings as individuals and not as representatives of their nominating organisation. NICE aims to select a cross-section of individuals from the nominations received for clinical specialists and patient experts. For example, for patient experts, NICE would select a person with direct personal experience of the technology and a representative of a patient, carer or professional organisation.

3.4.19 NICE publishes details of consultee and commentator organisations, which have provided nominations for clinical specialists, NHS commissioning experts and patient experts, on the Appraisal Committee agenda. NICE includes the names and affiliations of the selected clinical specialists, NHS commissioning experts and patient experts in the ACD, FAD and in the minutes of Appraisal Committee meetings.

3.4.20 It is important that sufficient expertise feeds into the technology appraisal. NICE welcomes and values the input from patient experts, NHS commissioning experts and clinical specialists.

Participation of manufacturer or sponsor representatives

3.4.21 Two representatives of the manufacturer or sponsor (normally one with health economics expertise and one with medical expertise) of the technology being appraised can attend part 1 of the Appraisal Committee meeting discussions. The Chair will ask these representatives to respond to questions from the Appraisal Committee. The Chair will ask the representatives to comment on any matters of factual accuracy before concluding part 1 of the meeting. The Chair may ask the representatives to remain

for part of the closed session (part 2) of the Appraisal Committee meeting, specifically to respond to questions from the Committee about confidential information in the manufacturer or sponsor's submission. The project manager can give further advice on appropriate manufacturer or sponsor representation at Appraisal Committee meetings.

3.4.22 Each representative must:

- be an employee of the manufacturer or sponsor or have been contracted by the manufacturer or sponsor to develop the evidence submission
- have relevant detailed knowledge of the technology under appraisal to engage effectively with the Appraisal Committee
- be able to comment on the clinical and cost effectiveness of the technology
- agree to be bound by the terms and conditions of NICE's confidentiality agreement
- be willing and able to discuss the condition and the technology with members of a large committee at a meeting where there may be members of the public and press observing
- be familiar with the purpose and processes of NICE
- be prepared to declare any interests they have in the technology under appraisal at Appraisal Committee meetings.

3.4.23 The ACD, FAD and the minutes of Appraisal Committee meetings will report the industry representation at the Appraisal Committee meetings but will not name the individuals in attendance.

3.5 Phase 3: appraisal

3.5.1 The appraisal phase of the STA process has four possible stages:

- consideration of the evidence at an Appraisal Committee meeting to discuss the content of either the FAD or ACD
- if required, development of and consultation on the ACD
- review of the ACD (if produced) in the light of comments from consultation at a second Appraisal Committee meeting
- preparation of the FAD.

Preparing for the meeting to develop the FAD or ACD

3.5.2 A lead team, selected from the Committee members at the start of each STA, helps the NICE technical lead prepare a summary of the evidence, known as the premeeting briefing. One of the lay representatives on the Committee is also selected to advise the lead team when developing the premeeting briefing. At the Appraisal Committee meeting, the lead team makes a brief presentation, based on the premeeting briefing, to introduce the STA topic.

Table 3 Expected timelines for the STA process: starting the process and preparing the ERG report*

		Weeks (approx.) since process began
Step 1	NICE invites organisations to participate in the STA as consultees or commentators	0
Step 2	NICE receives evidence submissions and statements from consultees	8
Step 3	NICE requests clarification on the evidence submission	10–11
Step 4	NICE invites selected clinical specialists, NHS commissioning experts and patient experts to attend the Appraisal Committee meeting and asks them to submit a written personal view	10
Step 5	NICE sends the ERG report to the manufacturer or sponsor for fact checking	18
Step 6	Selected clinical specialists, NHS commissioning experts and patient experts submit written personal views	18
Step 7	NICE compiles the evaluation report (see section 3.5.3) and sends it to the Appraisal Committee	19

*Timelines may change in response to individual appraisal requirements.

3.5.3 In preparation for the Appraisal Committee meeting, the evaluation report is circulated to all attendees (except members of the public) usually 2 weeks before the meeting. The report consists of:

- the final scope of the appraisal and the list of consultees and commentators
- the manufacturer or sponsor's evidence submission plus responses to clarification requests
- statements from consultees, clinical specialists, NHS commissioning experts and patient experts attending the Appraisal Committee meeting
- the ERG report, containing confidential material, and any supplements to it
- factual errors in the ERG report identified by the manufacturer or sponsor
- a premeeting briefing written by NICE's technical lead for the appraisal.

3.5.4 Appraisal Committee meetings are open to members of the public and press. This supports NICE's commitment to openness and transparency. It enables stakeholders and the public to understand how evidence is assessed and interpreted and how consultation comments are taken into account.

3.5.5 To promote public attendance NICE publishes a notice and draft agenda on its website announcing each Appraisal Committee meeting at least 20 working days before the meeting. At this point, members of the public who wish to attend the meeting can register on NICE's website. Up to 20 places will be available, depending on the size of the venue. In the event that attendance at any meeting is oversubscribed, NICE will select attendees according to its allocation procedure (for further information, see www.nice.org.uk/media/FC7/9D/PublicMeetingsInformation.pdf). To allow wide public access, NICE reserves the right to limit attendees to one representative per organisation. The closing date for receipt of completed application forms is 10 working days before the meeting. NICE publishes the final agenda on its website 5 working days before the meeting. Once registration has closed, NICE will contact successful applicants to invite them to the meeting. Along with the invitation, applicants will receive a code of conduct for public attendees and frequently asked questions.

Appraisal Committee meeting to develop the FAD or ACD

3.5.6 When the Appraisal Committee meets for the first time to discuss an STA, it may develop a FAD or an ACD (see section 3.5.24 for an explanation of when an ACD is produced). The Appraisal Committee considers and discusses the evidence for a technology. Committee decisions are normally based on consensus. If a vote is taken, it will be noted in the minutes. More information on how the Appraisal Committee considers the evidence and makes its decision is available in the 'Guide to the methods of technology appraisal'. The evaluation report includes the written evidence (see section 3.5.3). The verbal evidence is drawn from discussions with invited clinical specialists, NHS commissioning experts, patient experts and ERG representatives.

3.5.7 Clinical specialists, NHS commissioning experts, manufacturer representatives and patient experts respond to questions from the Appraisal Committee and provide clarification. They contribute to the debate with the Appraisal Committee but do not make a formal presentation to the Committee.

3.5.8 NICE Appraisal Committee meetings are, in part, open to members of the public and press. There may be occasions when a meeting will be entirely closed because it is not possible to conduct any discussion without referring to confidential information.

Structure of the meeting

Part 1 (public session)

3.5.9 Members of the Committee and individuals having direct input into the discussions (including clinical specialists, NHS commissioning experts, patient experts and NICE staff) declare their interests, which are recorded in the minutes. For further information on how NICE deals with conflicts of interest, please see 'A code of practice for declaring and dealing with conflicts of interest' (www.nice.org.uk/getinvolved/joinnwc/patientsandlaypeople/guidelinereviewpanelsrecruitment/nice_code_of_practice_for_declaring_and_dealing_with_conflicts_of_interest_april_2007.jsp).

3.5.10 The lead team (selected from members of the Appraisal Committee) usually introduces the topic of the appraisal to the other Appraisal Committee members and attendees. A lay member advises the lead team and assists in the preparation of the lead team's introduction. This introduction does not pre-empt the Committee's debate or the formulation of the guidance. It does not include any 'commercial in confidence' information. See section 3.2.22 for further details on how 'academic in confidence' information is handled at Appraisal Committee meetings.

3.5.11 The Appraisal Committee considers the evidence during the public session. However, the Appraisal Committee will not discuss 'commercial in confidence' information, or information contained in a submission from a clinical specialist, NHS commissioning expert or patient expert that has been marked as confidential during this part of the meeting.

3.5.12 The ERG representatives answer questions from the Appraisal Committee and provide clarification on the ERG report.

3.5.13 Representatives from other guidance-producing teams (for example, clinical guidelines and public health) at NICE who are responsible for developing NICE guidance in areas related to the STA may also attend the meeting to observe and advise the Appraisal Committee. These representatives must declare their interests and satisfy NICE's conflict of interest policy as indicated in section 3.5.9.

3.5.14 NICE staff may present evidence, provide advice on NICE policies and procedures, and respond to questions from the Appraisal Committee.

Part 2 (closed session)

3.5.15 During the closed session, the Appraisal Committee considers 'commercial in confidence' information and agrees the recommendations. Members of the public and press are asked to leave the meeting before this discussion takes place.

3.5.16 Only members of the Appraisal Committee, the ERG and NICE staff are normally in attendance.

3.5.17 ERG representatives may remain during Committee discussions to answer any further questions; however, they play no part in decision-making.

3.5.18 The Chair may ask clinical specialists, NHS commissioning experts and patient experts to remain when confidential information is discussed, but the Chair will ask them to leave before the Committee agree the recommendations in the ACD or the FAD.

3.5.19 NICE staff and representatives from other guidance-producing teams at NICE who are responsible for developing NICE guidance in areas related to the STA may stay at the meeting while the Appraisal Committee agree the recommendations in the ACD or the FAD; however, they play no part in decision-making.

3.5.20 The Appraisal Committee concludes the discussions and agrees the content of either the ACD (see section 3.5.27), which sets out its provisional recommendations, or the FAD (see section 3.5.43), which sets out its final recommendations. After the meeting, the NICE project team drafts the ACD or the FAD based on the discussions at the meeting, including the provisional or final recommendations agreed by the Appraisal Committee.

Minutes

3.5.21 NICE publishes unconfirmed minutes of the Appraisal Committee meeting on its website within 15 working days of the meeting. When the Appraisal Committee has approved them, NICE publishes confirmed minutes on its website normally within 6 weeks of the meeting. The minutes of an Appraisal Committee meeting provide a record of the proceedings and a list of the issues discussed.

Consultation on the ACD (if produced)

3.5.22 The ACD summarises the evidence and views that have been considered by the Appraisal Committee and sets out provisional recommendations. The ACD is not NICE's final guidance on a technology. The recommendations may change after consultation. NICE cannot issue an ACD or a FAD on a technology before that technology receives UK regulatory approval. If an STA begins before UK regulatory approval has been granted, an ACD or FAD will only be released after UK regulatory approval has been granted, and after the technology's price and indication are known.

3.5.23 If the Appraisal Committee produces a FAD after its meeting, please refer to section 3.5.43.

3.5.24 Normally, formal consultation (when an ACD is produced) takes place only if the recommendations from the Appraisal Committee are restrictive or if the manufacturer or sponsor is requested to provide further clarification on their evidence submission. Restrictive recommendations limit the use of the product further than the licence for the indication being appraised. In the absence of a regulatory approval process (for example, for a device), a restrictive recommendation will be one that is more limited than the instructions for use that accompany the technology. Otherwise, formal consultation does not take place and a FAD is agreed.

3.5.25 NICE contacts consultees and commentators by email after the Appraisal Committee meeting to let them know when they can expect to receive a copy of the ACD.

3.5.26 NICE usually circulates the ACD to consultees and commentators within 15 working days of the Appraisal Committee meeting. In exceptional circumstances, this may take longer. If NICE expects a delay, consultees and commentators will be informed as soon as possible.

3.5.27 The ACD usually contains the following elements:

- The Appraisal Committee's provisional recommendations to the NHS on the technology and how it should be used.
- A description of the technology, including its licensed indication and dosage, mode of action and cost.
- A summary of the evidence submission from the manufacturer or sponsor.
- A summary of the key issues raised by the ERG.
- A description of how the Appraisal Committee has interpreted the evidence submission from the manufacturer or sponsor together with the key issues raised by clinical specialists, NHS commissioning experts and patient experts.
- Proposed recommendations for further research, if appropriate.
- A list of related NICE guidance.
- The proposed date for review of the guidance.

3.5.28 The ACD and the evaluation report (with confidential material removed) are sent to consultees, commentators, clinical specialists, NHS commissioning experts and patient experts for consultation. These documents are confidential until NICE publishes them on its website 5 working days after circulation.

3.5.29 If the manufacturer or sponsor has submitted an economic model, NICE offers to send it (in its executable form) to consultees and commentators during consultation on the ACD (if produced) or with the FAD. This offer is made if the economic model does not contain confidential information. If it does contain confidential material NICE will ask the manufacturer or sponsor to remove the confidential material if this can be done

without severely limiting the model's function. Consultees and commentators must make requests for a copy of the model in writing. NICE supplies the model on the basis that the consultee or commentator agrees, in writing, to the following conditions of use:

- The economic model and its contents are confidential and are protected by intellectual property rights, which are owned by the manufacturer or sponsor who created the model. It cannot be used for any other purpose than to inform the recipient's understanding of the evaluation report.
- The economic model cannot be published by consultees or commentators (except by the manufacturer or sponsor who owns the model), in whole or in part, or used to inform the development of other economic models.
- The model must not be run for purposes other than to test its reliability.

3.5.30 The purpose of the consultation is to seek views on the Appraisal Committee's provisional recommendations and to determine whether they are an appropriate interpretation of the evidence considered. NICE invites comments on whether:

- all the evidence available to the Appraisal Committee has been appropriately taken into account
- the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence
- the provisional recommendations are sound and constitute a suitable basis for guidance to the NHS
- there are any equality related issues that need special consideration that are not covered in the ACD.

3.5.31 Consultees and commentators have 20 working days from the date of sending to submit comments on the ACD. They must submit their comments in writing, preferably by email. They must not use the website comment facility.

3.5.32 NICE publishes the ACD with an electronic comment facility and the evaluation report with confidential material removed on its website 5 working days after circulation. NICE sends the comments received from this website consultation (in summary form if there are a large number of comments) to the Appraisal Committee for consideration.

3.5.33 If a comment contains confidential information, it is the responsibility of the responder to provide two versions, one complete and one with the confidential information removed (to be published on NICE's website), together with a checklist of the confidential information. Detailed instructions on sending NICE confidential information relating to an appraisal are available from the project manager.

3.5.34 At the ACD consultation stage, the Centre Director must agree to accept any new evidence before it is submitted. New evidence will only be accepted if it is likely to affect

the provisional recommendations in the ACD. The new evidence must be presented as a separate appendix to the comments on the ACD. NICE may need to extend timelines to allow for new evidence to be considered.

3.5.35 When consultees and commentators submit comments and/or new evidence that lead to a substantial revision of the ACD, involving a major change in the recommendations, considerations and/or evidence base, the Centre Director and the Chair of the Appraisal Committee will decide whether it is necessary to prepare another ACD. If so, the consultation process will be repeated. The decision to produce another ACD will extend the timelines for the appraisal. NICE will distribute the evaluation report with the second ACD, together with any new evidence not circulated with the previous ACD and consultation comments on the first ACD.

3.5.36 Between the meetings, the Appraisal Committee may ask NICE to seek clarification from the manufacturer or sponsor on the key evidence submitted. NICE will ask the manufacturer or sponsor to submit its response to this request (as a separate appendix) along with its comments on the ACD and the evaluation report. If the manufacturer or sponsor has undertaken new analyses, it must submit an updated version of the economic model.

3.5.37 If comments received from the consultation on the economic model require a response from the manufacturer or sponsor, the response made will be tabled at the next Appraisal Committee discussion.

Appraisal Committee meeting to develop the FAD

3.5.38 If an ACD is produced, the Appraisal Committee meets again, with members of the public and press observing, to consider the ACD in the light of the comments received. Before the meeting, NICE sends the Appraisal Committee members the full text of the comments from the consultees and commentators and a summary of any comments received from other individuals or organisations.

3.5.39 Representatives from the ERG and from other guidance-producing teams at NICE (for example clinical guidelines and public health) who are responsible for developing NICE guidance in areas related to the STA may attend the meeting. If clarification of issues raised during the consultation period is required, the Chair of the Appraisal Committee can, at their discretion, invite one or more of the clinical specialists, NHS commissioning experts or patient experts to attend.

3.5.40 The Appraisal Committee discusses the responses to the ACD consultation in part 1 of the meeting (see section 3.5.9) and moves to a closed session (part 2, see section 3.5.15) to consider any confidential information and to agree the content of the FAD, which sets

out the final recommendations. After the meeting, the NICE project team drafts the FAD based on the discussions at the meeting and the final recommendations agreed by the Appraisal Committee.

3.5.41 Because the Appraisal Committee usually considers more than one appraisal at each of their meetings, and these discussions may relate to either an ACD or a FAD, the arrangements for a meeting at which a FAD is agreed are the same as those described for a meeting at which an ACD is agreed (see sections 3.5.6–3.5.8).

Minutes

3.5.42 NICE publishes unconfirmed minutes of the Appraisal Committee meeting on its website within 15 working days of the meeting. When the Appraisal Committee has approved them, NICE publishes the confirmed minutes on its website normally within 6 weeks of the meeting. The minutes of an Appraisal Committee meeting provide a record of the proceedings and a list of the issues discussed.

Distribution of the FAD

3.5.43 After the Appraisal Committee meeting in which the content of the FAD is agreed, NICE contacts consultees and commentators by email to let them know when they can expect to receive a copy of the FAD.

3.5.44 The FAD contains the Appraisal Committee's recommendations and:

- A description of the technology, including its licensed indication and dosage, mode of action, and cost.
- A summary of the evidence submission from the manufacturer or sponsor (plus responses to clarification if appropriate).
- A summary of the key issues raised by the ERG.
- A description of how the Appraisal Committee has interpreted the evidence submission from the manufacturer or sponsor together with the key issues raised by clinical specialists, NHS commissioning experts and patient experts.
- Recommendations for further research, if appropriate.
- A list of related NICE guidance.
- A date for review of the guidance.

3.5.45 The NICE project team undertakes a final review of the FAD, signs it off, and submits a report to NICE's Guidance Executive (made up of NICE's Executive Directors and Centre Directors). The Guidance Executive checks that the Appraisal Committee has appraised the technology in accordance with the terms of the Secretary of State for Health's referral and the scope. If satisfied, the Guidance Executive approves the FAD for publication on behalf of the NICE Board.

3.5.46 NICE issues the FAD to consultees, along with the consultation response to the ACD if produced, so that they can consider whether to appeal (see section 4). They can also highlight any factual errors. Commentators receive the FAD for information only.

3.5.47 NICE distributes new, non-confidential evidence submitted by manufacturers or sponsors, and further analysis undertaken by NICE or the ERG during development of the FAD, to consultees and commentators, as well as publishing the evidence on its website with the FAD. When NICE sends the FAD to consultees and commentators, it also sends the comments received from consultees and commentators on the ACD (if produced), together with NICE's responses to them, and the comments received from the public via the website. NICE publishes all this information on its website 5 working days after sending it to consultees and commentators.

3.5.48 NICE usually circulates the FAD within 30 working days of the Appraisal Committee meeting. NICE notifies consultees and commentators if a delay is expected.

3.5.49 In exceptional circumstances, for example, if relevant information is published while the FAD is being developed or because of comments from consultees or commentators, NICE may undertake further analysis. The ERG or Decision Support Unit normally carry out this further analysis before NICE circulates the FAD. The Centre Director takes this decision in discussion with the Chair of the Appraisal Committee and the NICE project team. The decision is not taken lightly and is made to make sure NICE is able to provide robust guidance to the NHS. If further analysis is undertaken, NICE will inform consultees and commentators. NICE will distribute any such analysis to consultees and commentators and publish it on the website at the same time as the FAD.

Publication of the guidance

3.5.50 Subject to any appeal by consultees, the FAD forms NICE's guidance on the use of the technology.

3.5.51 After receiving the FAD, any consultee (whether or not they are submitting an appeal) can request correction of factual errors. Some examples of what might constitute factual errors are:

- wrong names or misspelling of technologies, manufacturers or sponsors
- errors in figures presented in the FAD
- incorrect or incomplete quotes from marketing authorisations
- text to be changed to ensure that the facts are described appropriately in the FAD.

3.5.52 The Guidance Executive considers all requests for correction of factual errors and decides whether to make changes to the FAD. This decision is made after all appeal proceedings have concluded. NICE then publishes the FAD as STA guidance on its website. NICE also

publishes a lay version for patients and carers (known as 'Understanding NICE guidance') and a 'quick reference guide' for healthcare professionals on its website.

3.5.53 The ERG will further develop its report for subsequent publication as a supplement in 'Health technology assessment' (www.hta.ac.uk/project/htapubs.asp).

3.5.54 NICE invites the manufacturer or sponsor of the technology appraised to attend a debriefing meeting within 2 weeks of the guidance being published. Up to five individuals involved in the development of the manufacturer or sponsor's submission can attend. The aim of the meeting is to examine the manufacturer or sponsor's evidence submission in the context of the Appraisal Committee's recommendations.

Table 4 Expected timelines for the STA process if an ACD is produced*

		Weeks (approx.) since process began
Step 8	Appraisal Committee meeting to develop an ACD attended by clinical specialists, NHS commissioning experts and patient experts	21
Step 9	The ACD is produced. NICE distributes the ACD and publishes it on the website 5 working days later	24
Step 10	Fixed 4-week consultation period on the ACD	24–28
Step 11	Appraisal Committee meeting to consider comments on the ACD from consultees and commentators, and comments received through the consultation on the NICE website. Appraisal Committee agrees the content of the FAD	29
Step 12	The FAD is produced. NICE distributes the FAD and publishes it on the website 5 working days later	34

*Timelines may change in response to individual appraisal requirements.

Table 5 Expected timelines for the STA process if an ACD is not produced*

		Weeks (approx.) since process began
Step 8	Appraisal Committee meeting to develop a FAD, attended by clinical specialists, NHS commissioning experts and patient experts	21
Step 9	The FAD is produced. NICE distributes the FAD and publishes it on the website 5 working days later	26

*Timelines may change in response to individual appraisal requirements.

4 Appeal

Full details of NICE's appeals process are set out in a separate document on NICE's website ('Technology appraisal process: guidance for appellants') and only a brief summary is given here (see table 6 for expected stages in the appeals process).

4.1 For appeals to be considered, NICE must receive them, in writing, within 15 working days of sending the FAD. Appeals must be submitted in the manner described in 'Technology appraisal process: guidance for appellants'. An Appeal Panel appointed by NICE's Board considers appeals.

4.2 Appellants cannot submit appeals because they do not agree with the recommendations. An appeal is not an opportunity to reopen arguments and issues that the Appraisal Committee has decided on. An Appeal Panel will not substitute its own judgement for that of the Appraisal Committee or look afresh at the evidence submitted for the STA. It will not accept new evidence.

4.3 An Appeal Panel will not consider an appeal unless the grounds for appeal are appropriate. Please see 'Technology appraisal process: guidance for appellants' for details of the grounds for appeal.

4.4 After considering the appeal (either at a verbal hearing or through a written appeal), the Appeal Panel usually sends its decision to NICE within 21 days of the hearing, but sometimes more time may be needed. NICE's Guidance Executive then considers the decision. The time between the appeal decision and its consideration by the Guidance Executive depends on the time needed to prepare all the final documents, and so will vary.

4.5 If the Appraisal Committee has to reconsider the FAD, NICE informs consultees and commentators of the appeal decision, and arrangements for further consideration of the FAD. If the Appraisal Committee has to reconsider the FAD, the STA process will resume at an appropriate point as specified in the decision of the Appeal Panel.

4.6 If the Appeal Panel asks the Guidance Executive to make changes to the FAD that do not require further consideration by the Appraisal Committee, NICE publishes the Appeal Panel's decision and the final guidance. NICE informs the consultees and commentators of the publication date, and sends them the Appeal Panel's decision and a copy of the final guidance 2 working days before they are published on the website.

4.7 If the appeal is dismissed and the Appeal Panel does not recommend changes to the FAD, the Appeal Panel informs the Guidance Executive of this decision. NICE publishes the Appeal Panel's decision and the final guidance. NICE informs the consultees and commentators of the publication date, and sends them the Appeal Panel's decision and a copy of the final guidance 2 working days before they are published on the website.

Table 6 Expected stages in the appeals process

Step 13/10	Any appeals lodged (fixed 15-working-day period)
Step 14/11	If necessary, NICE convenes the Appeal Panel
Step 15/12	NICE notifies appellants and other consultees of the appeal
Step 16/13	NICE advises consultees and commentators of the appeal decision
Step 17/14	NICE publishes the decision on its website

5 Patient access and flexible pricing schemes

5.1 The Association of the British Pharmaceutical Industry (ABPI) and the Department of Health published their agreement on a new Pharmaceutical Price Regulation Scheme (PPRS) in January 2009 (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS). The 2009 PPRS allows manufacturers to submit proposals for patient access and flexible pricing schemes as part of an ongoing or published NICE technology appraisal.

Definitions

5.2 Patient access schemes are proposed by a pharmaceutical company and agreed between the Department of Health (with input from NICE) and the pharmaceutical company. They improve the cost effectiveness of a drug and enable patients to receive access to cost-effective innovative medicines (see below for further information on the types of scheme).

5.3 Flexible pricing recognises that the initial launch indication of a medicine may not fully reflect its longer-term value to patients in the NHS. It therefore allows a company to propose an initial price for a medicine that reflects its value at launch. However, companies retain the freedom to increase or decrease this original list price in the light of new evidence or when new indications for the medicine emerge and the effective value that the medicine offers to NHS patients changes.

5.4 NICE can only consider patient access (see figure 3) and flexible pricing schemes (see figure 4) after formal referral by the Department of Health.

Patient access schemes

5.5 The Department of Health asked NICE to establish a Patient Access Scheme Liaison Unit (PASLU) to assess whether patient access schemes are feasible and to produce final advice on this to the Department of Health. When assessing whether a patient access scheme is feasible the PASLU considers the key principles for implementing patient access schemes in the NHS in England and Wales as outlined in the PPRS 2009. The PASLU assesses the feasibility of schemes using its own process. This is not part of the STA process. The ERG, Appraisal Committee and Appeal Panel are not bound by any decision of the PASLU.

5.6 The process for reviewing the impact of a patient access scheme on the clinical and cost effectiveness of a technology depends on when the scheme is submitted to NICE. Manufacturers and sponsors should use the template for submission to the PASLU

to submit information to NICE for assessing the feasibility of implementing a patient access scheme. Changes to a scheme after ministers have approved it require additional ministerial approval.

Patient access schemes submitted during an appraisal

5.7 When a manufacturer or sponsor submits a patient access scheme with the evidence submission as part of an appraisal this will be incorporated into the technology appraisal process (see section 3.4).

5.8 NICE considers the effect of the patient access scheme on the clinical and cost effectiveness of the technology and clarifies relevant points with the manufacturer (see section 3.4). The ERG assesses the impact of the scheme and submits an independent review to the Appraisal Committee.

5.9 Exceptionally ministers may approve schemes for consideration after the release of an ACD. The impact of the scheme on the clinical and cost effectiveness of the technology may lead the Appraisal Committee to revise their recommendations. If the recommendations become or remain positive or largely positive, a FAD will be issued for appeal (see section 3.5.43 onwards). In any other case NICE will issue a further ACD for consultation (see section 3.5.22 onwards). Information will be released so that the scheme and its impact on the clinical effectiveness, cost effectiveness and the recommendations can be understood. Subject to any appeal by consultees, the FAD forms the basis of NICE guidance on the technology.

5.10 If the Appraisal Committee recommends a technology after reviewing the impact of an outcomes-based patient access scheme, it is important that the outcomes of the scheme are formally considered in the future. The Appraisal Committee therefore meets at the time point outlined in the patient access scheme and agreed by the Committee and NICE. If the actual outcomes differ sufficiently from those assumed during the original appraisal, the Appraisal Committee may decide to bring forward a review of the recommendations.

Patient access schemes submitted after guidance publication

5.11 Patient access schemes are designed to maximise the opportunity for access to a new technology. Therefore, within 16 weeks of guidance publication, a rapid review facility is available to consider new patient access schemes. NICE can only consider these schemes after ministerial approval and confirmation by the Department of Health. After approval, the rapid review of the guidance is planned, as a priority, into the work programme. The Appraisal Committee will usually consider the scheme within 6 months of referral of the scheme. The manufacturer or sponsor must use the patient access

scheme submission template to provide details of the scheme, a revised economic model incorporating the patient access scheme, and an updated version of the checklist of confidential information, if necessary. Although NICE will include rapid review patient access schemes under consideration on the relevant Committee meeting agenda, NICE makes no public announcement about the specific topics. NICE considers it essential that such schemes can be received and considered in confidence. NICE also understands that manufacturers and sponsors may suffer commercial and other harm if information on the proposed schemes were to be made public at this point. Therefore, NICE treats all proposed patient access schemes for rapid review as confidential and will not release any information relating to these schemes under the Freedom of Information Act, or for any other purpose (including during the public part of Appraisal Committee meetings), unless the manufacturer or sponsor has agreed to this.

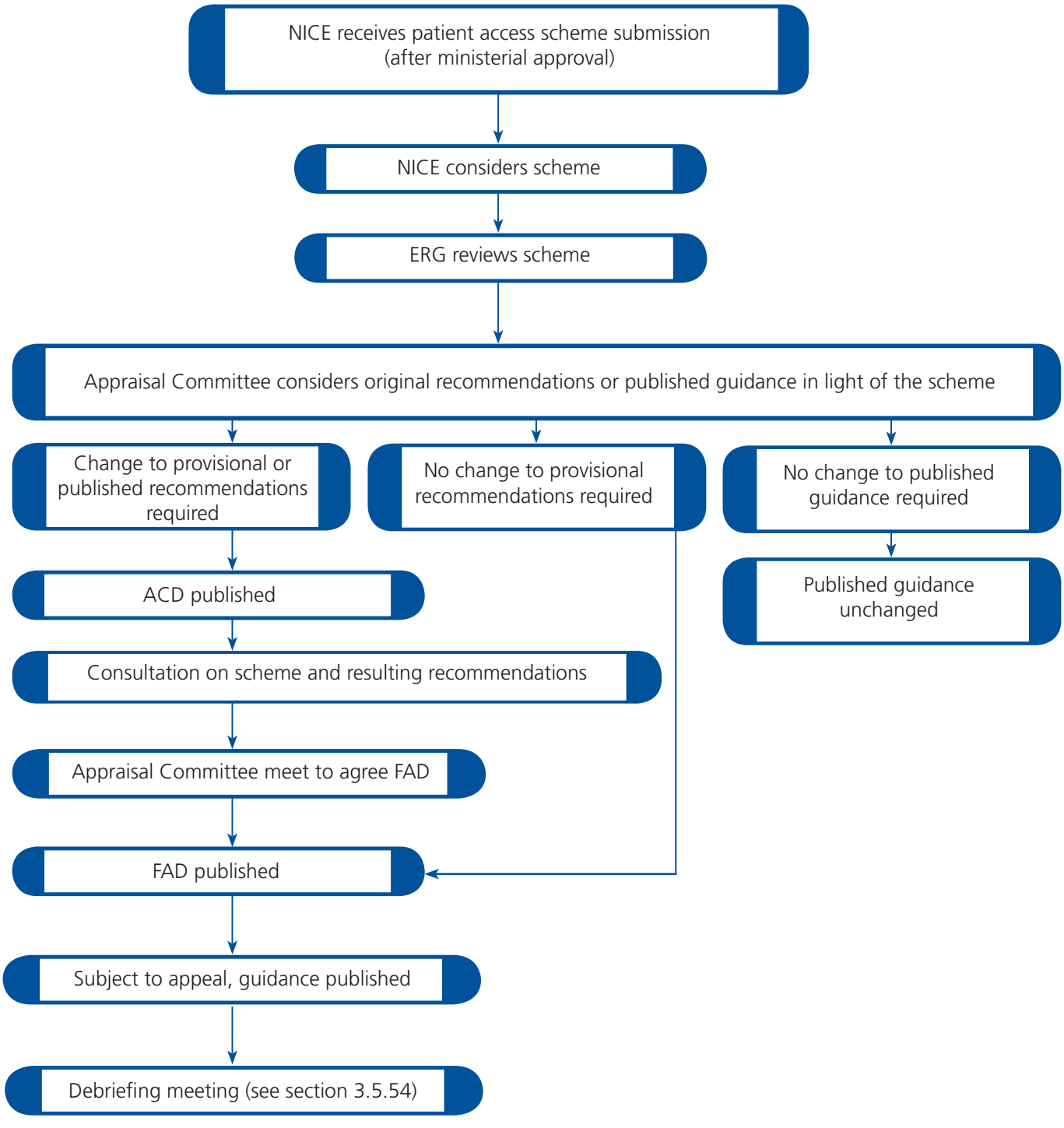
5.12 Schemes submitted through the rapid review facility are considered 'commercial in confidence' and all matters relating to the scheme (except the existence of the scheme proposal) will remain confidential unless consideration by the Appraisal Committee results in a change to guidance recommendations. In this situation, NICE will issue an ACD for consultation (see section 3.5.22 onwards). NICE releases information during the ACD consultation so that the scheme and its impact on the clinical effectiveness, cost effectiveness and the recommendations can be understood.

5.13 If the Appraisal Committee recommends a technology after reviewing the impact of an outcomes-based patient access scheme, it is important that the outcomes of the scheme are formally considered in the future. The Appraisal Committee therefore meets at the time point outlined in the patient access scheme and agreed by the Committee and NICE. If the actual outcomes differ sufficiently from those assumed during the original appraisal, the Appraisal Committee may decide to bring forward a review of the recommendations.

5.14 Appeals following the rapid review of guidance, when consideration of the impact of patient access scheme proposals on current guidance has resulted in a change to the guidance, will only be accepted on points relating to the new patient access scheme. The Appeal Panel will not consider points previously raised or points that could have been raised at earlier appeals. Subject to any appeal by consultees, the FAD forms the basis of NICE guidance on the use of the technology.

5.15 NICE will consider proposals for patient access schemes approved by ministers more than 16 weeks after guidance publication via the standard review process (see section 6).

Figure 3 Process for considering a patient access scheme



Flexible pricing schemes

5.16 Requests to consider a flexible pricing scheme for an existing indication of a technology must be linked to the emergence of new evidence. The manufacturer or sponsor therefore needs time to gather the additional evidence necessary to justify a price change. NICE will consider reviewing the guidance only in the light of significant new evidence that is likely to have an impact on the clinical or cost effectiveness of the technology. This could include: new clinical trial evidence, new evidence on identified subgroups of patients, or significant new evidence supporting additional benefits previously unaccounted for (for example, long-term outcomes). New evidence does not include new analyses of existing data. Schemes that are not supported by new evidence will not be considered.

5.17 For technologies launched after 1 January 2009, if NICE receives a flexible pricing scheme proposal for an existing indication within 12 months of guidance publication, NICE will consider the impact of new evidence and the flexible pricing scheme on the clinical and cost effectiveness of the technology. NICE will clarify relevant points with the manufacturer or sponsor before the ERG reviews the proposal. The Appraisal Committee will then consider the proposal together with the independent review from the ERG.

5.18 NICE considers flexible pricing schemes for an existing indication submitted more than 12 months after guidance publication via the standard review process (see section 6).

5.19 All flexible pricing schemes for technologies launched before 1 January 2009 are considered via the standard review process (see section 6).

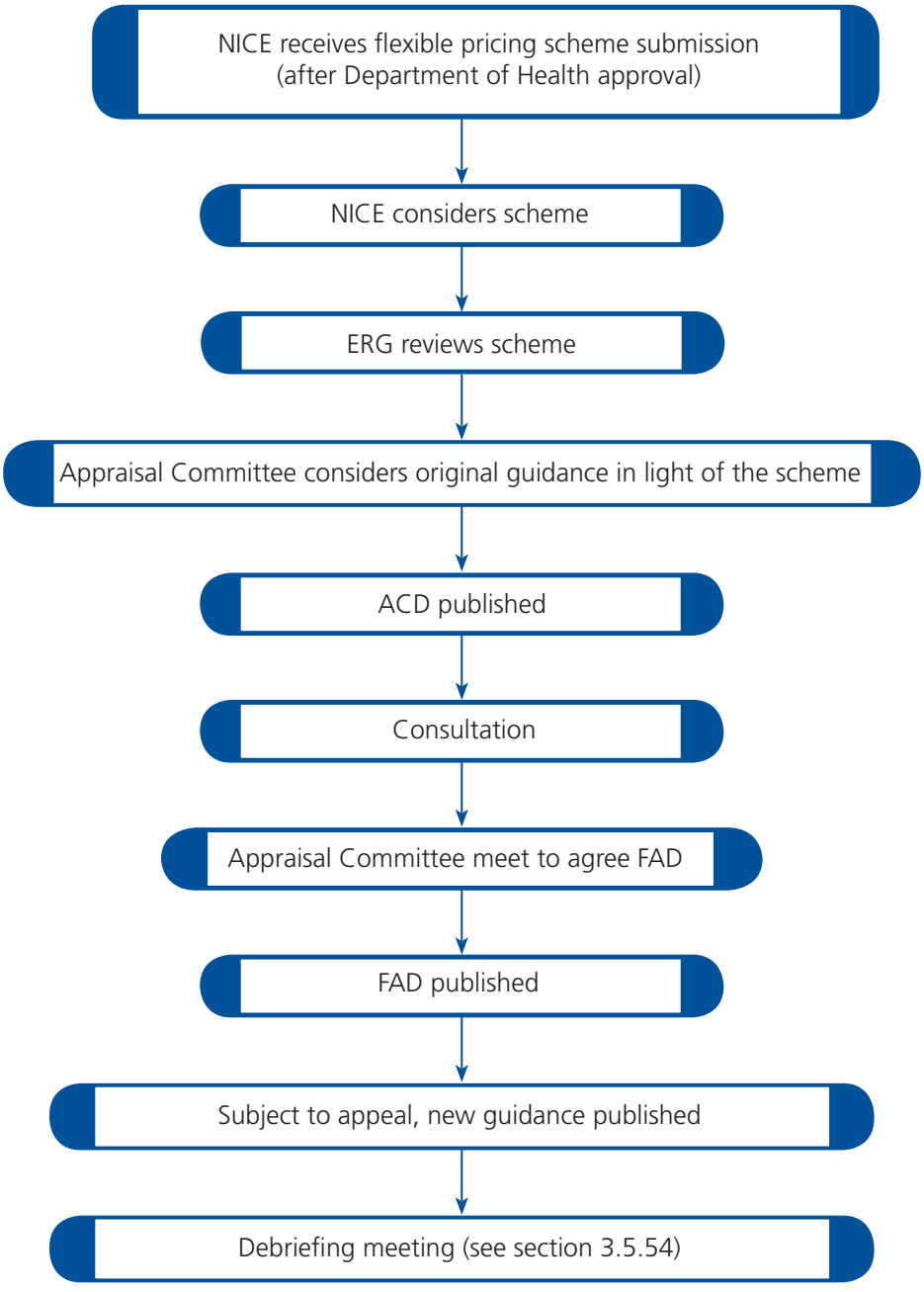
5.20 When the Appraisal Committee considers a flexible pricing scheme for an existing indication, the Committee will review the original guidance in light of the new evidence and the proposed new price. The Committee's assessment of cost effectiveness will be based on the assessment used in the original appraisal.

5.21 Although NICE includes flexible pricing schemes under consideration on the relevant Committee Meeting agenda, NICE makes no public announcement about the specific topics. NICE considers it essential that such schemes can be received and considered in confidence. NICE also understands that manufacturers and sponsors may suffer commercial and other harm if information on the proposed schemes were to be made public at this point. Therefore, NICE treats all proposed flexible pricing schemes for existing indications as confidential and will not release any information relating to these schemes under the Freedom of Information Act, or for any other purpose (including during the public part of Appraisal Committee meetings), unless the manufacturer has agreed to this.

5.22 When the Appraisal Committee has reviewed the existing guidance on the technology in the light of the new evidence and flexible pricing proposal, an ACD will be published for consultation (see section 3.5.22 onwards). Detailed information will be released as part of the ACD consultation so that the scheme and its impact on the clinical effectiveness, cost effectiveness and the recommendations can be understood. As with the normal appraisal process, the Appraisal Committee will review consultation responses on the ACD and develop a FAD. NICE will issue the FAD to consultees, along with the consultation response to the ACD, for appeal. Appeals will be accepted only on points relating to the flexible pricing scheme proposals. The Appeal Panel will not consider points previously raised or points that could have been raised at an earlier appeal. Subject to any appeal by consultees, the FAD forms NICE's updated guidance on the use of the technology.

5.23 Flexible pricing schemes for new indications of existing technologies are also covered in the 2009 PPRS. New indications are potential new appraisals. Consideration of their suitability for technology appraisal is therefore covered under topic selection (see section 2 onwards for further details).

Figure 4 Process for considering a flexible pricing scheme



6 Reviews

6.1 When NICE publishes STA guidance, a review date is given. This is the month and year when NICE will consult with relevant organisations on a review proposal to decide whether or not the guidance needs to be updated, and if so, how to update the guidance. The length of time between guidance publication and the review date will vary depending on the available evidence for the technology, and knowledge of when ongoing research will be reported.

6.2 Guidance may be reviewed before the review date when there is significant new evidence that is likely to change the recommendations. NICE is keen to hear about any new evidence that becomes available before the review date (please send information to nice@nice.org.uk). NICE will assess the likely impact of the new evidence on the recommendations and will propose an update to the published guidance if required.

6.3 NICE develops the review proposal after gathering relevant information and undertaking a literature search. NICE identifies new indications for the appraised technology, searches for new related technologies, assesses the progress of ongoing trials, and gathers new available evidence. NICE also asks manufacturers and sponsors to provide information relating to marketing authorisation (or equivalent) or any extensions to the marketing authorisations.

6.4 NICE's Guidance Executive uses this information to consider the review proposal and decides if and how the published guidance should be updated.

6.5 The Guidance Executive decides on one of the following options if the published guidance needs updating:

- Plan an appraisal to update the published guidance.
- Plan an appraisal that combines the published guidance with one or more related pieces of published guidance (including terminated appraisals) or ongoing appraisals.
- Update the published guidance within another guidance producing centre (for example in a clinical guideline).

6.6 The Guidance Executive decides on one of the following options if the published guidance does not require updating:

- The guidance is valid and does not require an update because the evidence base is not likely to change substantially. It is therefore designated as static guidance.
- Defer the decision on if and how to update the published guidance to a future date.
- Incorporate the published guidance into a clinical guideline and withdraw the appraisal when the guideline is published.

6.7 When the Guidance Executive has agreed the review proposal, NICE asks consultees and commentators to comment on the proposal and to identify any other interested parties that NICE needs to consult with.

6.8 NICE publishes the review proposal, together with the list of consultees and commentators, on its website 5 working days after sending it to consultees and commentators.

6.9 NICE must receive comments from consultees and commentators within 20 working days of the date of sending for them to be considered.

6.10 The Guidance Executive considers the review proposal in light of the consultation comments and reaches a final decision on the most appropriate option for the published guidance. NICE writes to consultees and commentators informing them of the final decision and attaches a table of responses to the comments on the review proposal for information.

6.11 NICE publishes the final decision and the table of comments on its website 5 working days after contacting consultees and commentators.

6.12 If a piece of guidance needs updating within the appraisal programme, the update is timetabled and follows either the STA or MTA process.

Appendix A: Steering Group and Process Working Party

A Steering Group and Process Working Party, as set out below, developed this document.

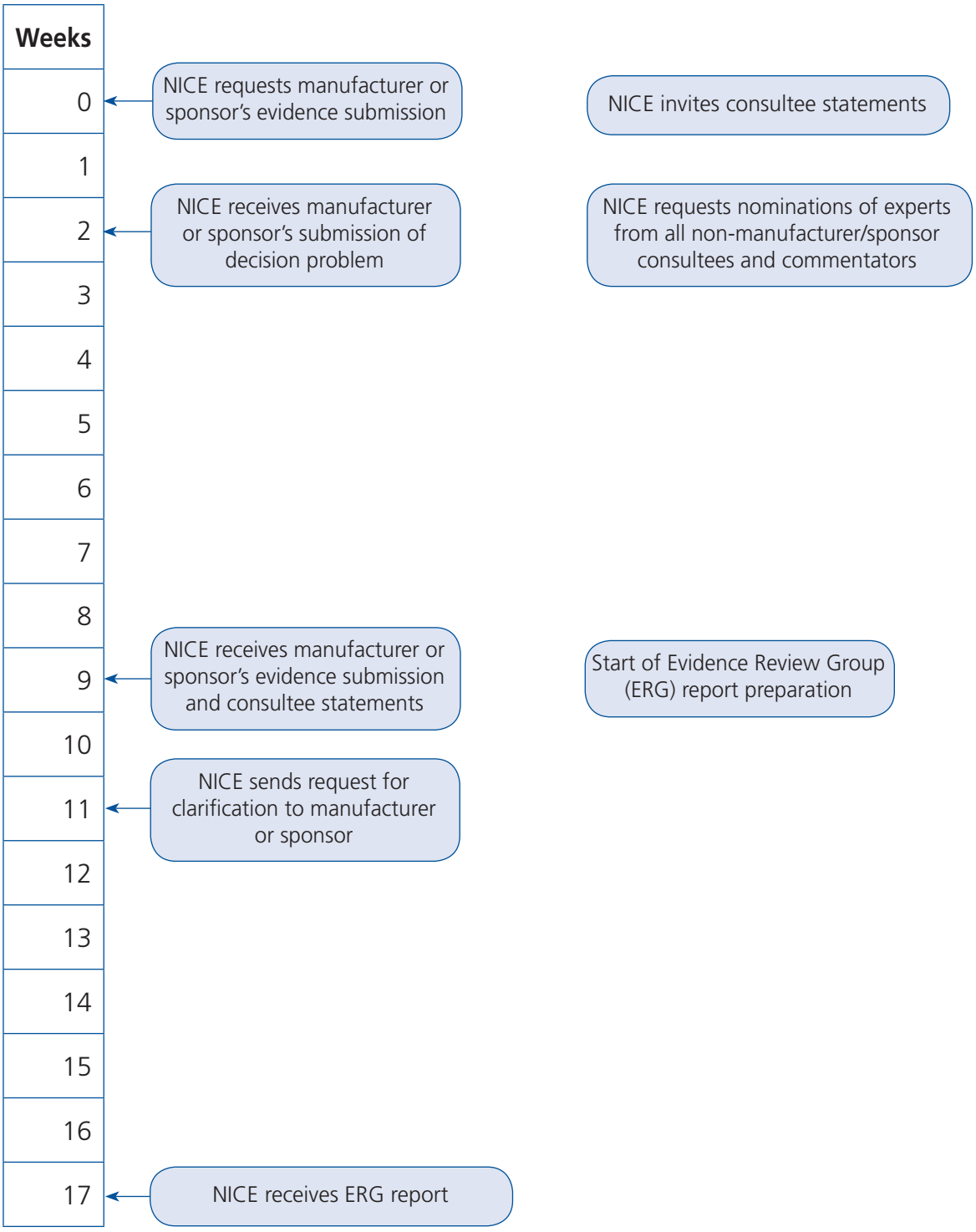
Steering Group

Andrew Dillon	Chief Executive, NICE
David Barnett	Chair (retired), Appraisals Committee
Andrew Stevens	Chair, Appraisals Committee
Carole Longson	Centre Director, NICE
Nina Pinwill	Associate Director, CHTE, NICE
Meindert Boysen	Associate Director, CHTE, NICE

Process Working Party

Nina Pinwill (Chair)	Associate Director, CHTE, NICE
Meindert Boysen	Associate Director, CHTE, NICE
Elisabeth George	Associate Director, CHTE, NICE
Kim Turner	Project Manager, CHTE, NICE
Christopher Feinmann	Project Manager, CHTE, NICE
Shaun Minehan	Project Manager, CHTE, NICE
Natalie Bemrose	Project Manager, CHTE, NICE
Bijal Chandarana	Project Manager, CHTE, NICE
Jenniffer Alty	Project Manager, CHTE, NICE
Joanna Richardson	Technical Adviser, CHTE, NICE
Zoe Charles	Technical Adviser, CHTE, NICE

Appendix B: STA process timelines



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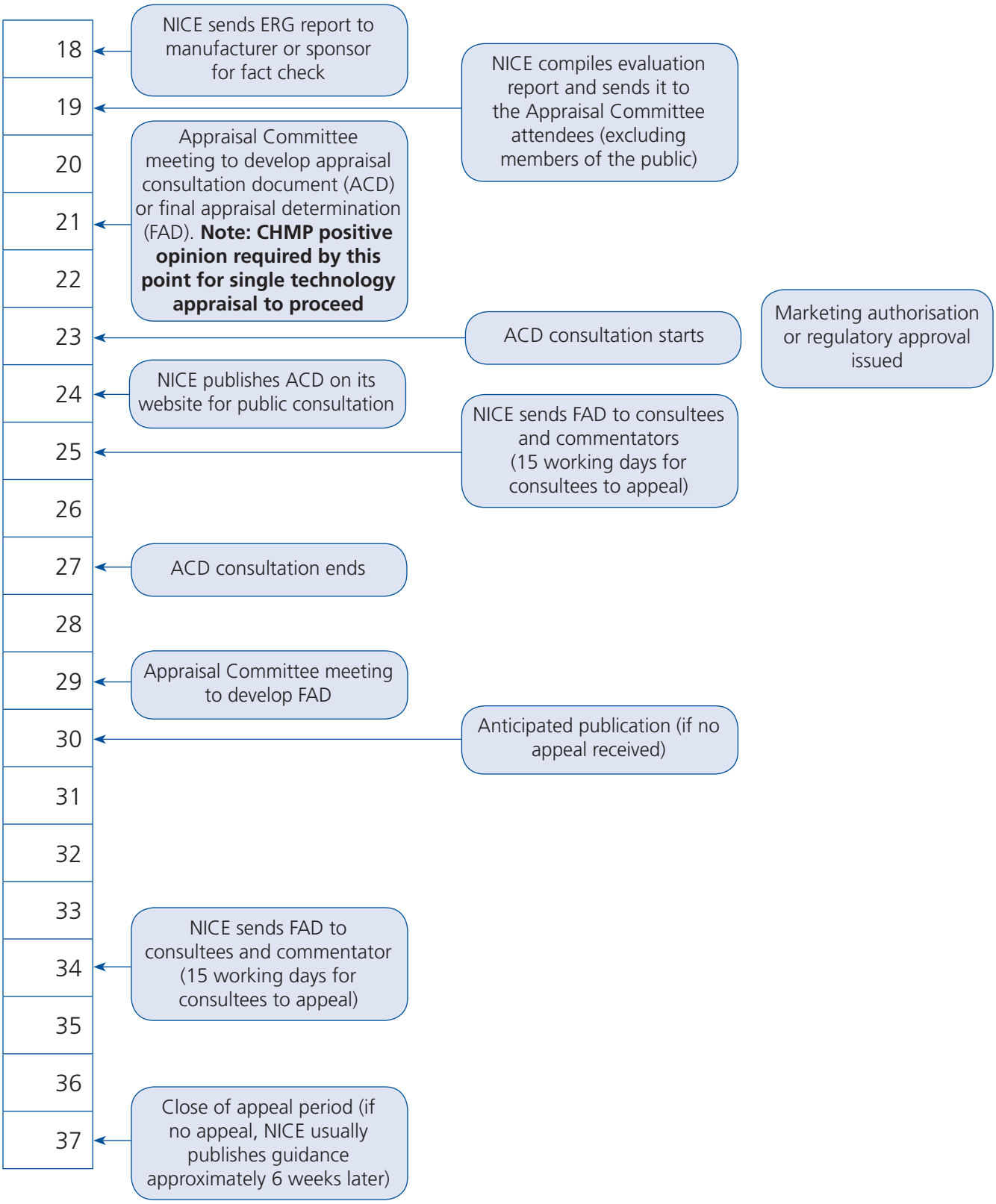
18
NICE sends ERG report to manufacturer or sponsor for fact check
19
NICE compiles evaluation report and sends it to the Appraisal Committee attendees (excluding members of the public)
20
21
Appraisal Committee meeting to develop appraisal consultation document (ACD) or final appraisal determination (FAD). Note: CHMP positive opinion required by this point for single technology appraisal to proceed
22
23
ACD consultation starts
Marketing authorisation or regulatory approval issued
24
NICE publishes ACD on its website for public consultation
25
NICE sends FAD to consultees and commentators (15 working days for consultees to appeal)
26
27
ACD consultation ends
28
29
Appraisal Committee meeting to develop FAD
30
Anticipated publication (if no appeal received)
31
32
33
34
NICE sends FAD to consultees and commentator (15 working days for consultees to appeal)
35
36
37
Close of appeal period (if no appeal, NICE usually publishes guidance approximately 6 weeks later)

Appendix C: Glossary

The Association of the British Pharmaceutical Industry (ABPI) The trade association for more than 90 companies in the UK producing prescription medicines for human use.

Abstract Summary of a study, which may be published alone or as an introduction to a full scientific paper.

Academic in confidence See 'In confidence material'.

Appraisal See 'Technology appraisal (single and multiple)'.

Appraisal Committee An independent advisory committee to NICE. The members are from a variety of backgrounds, including doctors, nurses, pharmacists, health economists, statisticians and lay representatives.

Appraisal consultation document (ACD) Sets out the Appraisal Committee's provisional recommendations to NICE.

Carer A close family member, relation or other person other than a healthcare professional who is involved in caring for a person with a medical condition providing either physical and/or emotional care.

CE mark(ing) The CE mark is a mandatory conformity mark on medical device products placed on the single market in the European Economic Area. The CE mark certifies that a product has met EU consumer safety, health or environmental requirements.

Centre Director The Director of the Centre for Health Technology Evaluation is responsible for the delivery of the technology appraisal programme. The Director is also responsible for ensuring that appraisals are conducted in accordance with the published appraisal process and methodology.

Citizens Council The Citizens Council represents the views of the public when NICE is formulating guidance on the promotion of good health and the prevention and treatment of ill health. The Citizens Council consists of a group of 30 people drawn from all walks of life. It tackles challenging questions about values such as fairness and need.

Clinical effectiveness How well a technology works in routine clinical practice.

Clinical specialist Clinical specialists act as expert witnesses to the Appraisal Committee. They have specialist expertise and personal knowledge of the use of the technology and other treatments for the condition. They often have insights not typically available in the published literature.

Commentator Commentators are invited by NICE to take part in the appraisal process and comment on the various documents produced during the process. Commentators cannot appeal against the final appraisal determination.

Commercial in confidence See 'In confidence material'.

Comparator A technology that is competing with the one under appraisal. The comparator can be no intervention, for example, best supportive care.

CONSORT statement (consolidated reporting of clinical trials) Recommendations for improving the reporting of randomised controlled trials in journals. A flow diagram and checklist allow readers to understand how to conduct a study and assess the validity of the results.

Consultation The process that allows stakeholders and individuals to comment on draft versions of NICE guidance and other documents (for example, the draft scope) so that their views can be taken into account when the final version is being produced.

Consultee NICE invites consultees to take part in the appraisal process. This involves commenting on the various documents produced and writing a submission. Consultee organisations (with the exception of manufacturers) are also asked to nominate patient experts or clinical specialists. Manufacturer or sponsor consultees can nominate clinical specialists. Only consultees can appeal against the final appraisal determination.

Cost effectiveness How well a technology works in relation to how much it costs.

Decision problem The decision problem describes the approach taken by the manufacturer or sponsor in its evidence submission to answering the question in the final scope.

Decision Support Unit The Decision Support Unit helps the technical team at NICE to meet the information needs of the Appraisal Committee. This is achieved by providing support, as required, to the technical team and the Evidence Review Group. The objective of the Decision Support Unit is to enhance the delivery of robust information to support Appraisal Committee decision-making. The Decision Support Unit is a multidisciplinary team, expert in methods of health technology assessment and capable of providing advice and high-quality analyses to decision-makers within very tight deadlines.

Department of Health The Department of Health is responsible for standards of healthcare in the UK, including the NHS. The Department sets the strategic framework for adult social care and influences local authority spending on social care. The Department is also responsible for promoting and protecting the public's health, taking the lead on issues like environmental hazards to health, infectious diseases, health promotion and education, the safety of medicines, and ethical issues.

Economic evaluation An economic study design that allows the consequences of different interventions to be measured against a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.

Economic model An explicit mathematical framework that is used to represent clinical decision problems. It incorporates evidence from a variety of sources so that the costs and health outcomes can be estimated.

Evaluation report This includes all of the evidence seen by the Appraisal Committee. It is made up of the ERG report, written submissions, and the personal statements of patient experts and clinical specialists, as well as comments received on the ERG report.

Evidence Information on which a decision or guidance is based. Evidence is obtained from a range of sources, including randomised controlled trials, observational studies and expert opinion (of clinical professionals, NHS commissioners and/or patient groups).

Evidence Review Group (ERG) An independent academic group commissioned by the NHS Research and Development Health Technology Assessment Programme (HTA Programme) to compile the ERG report.

Evidence Review Group report During the single technology appraisal process, the ERG reviews the manufacturer or sponsor's evidence submission and submits its findings to NICE in the ERG report.

Final appraisal determination (FAD) The FAD sets out the Appraisal Committee's final recommendations to NICE on how the technology should be used in the NHS in England and Wales.

Guidance Executive A team comprising the Executive Directors and Centre Directors at NICE who are responsible for approving the final appraisal determination before publication.

Health-related quality of life A combination of an individual's physical, mental and social wellbeing, not merely the absence of disease.

Health technology Any method used by those working in health services to promote health, prevent and treat disease, and improve rehabilitation and long-term care. Technologies in this context are not confined to new drugs or items of sophisticated equipment.

In confidence material Information (for example, the findings of a research project) defined as 'confidential' because its public disclosure could have an impact on the commercial interests of a particular company or the academic interests of a research or professional organisation, or the policy interests of government.

Incremental cost-effectiveness ratio (ICER) The ratio of the change in costs of a therapeutic intervention (compared with the alternative, such as doing nothing or using the best available alternative treatment) to the change in effects of the intervention.

Indication The defined use of a technology as licensed by the Medicines and Healthcare Products Regulatory Agency (MHRA) or the European Commission.

Lead team Members of the Appraisal Committee asked to introduce individual appraisals at Committee meetings.

Licence An authorisation from the regulatory authorities in the UK or Europe to market a medicinal product in the UK.

Medicines and Healthcare Products Regulatory Agency The Executive Agency of the Department of Health. It protects and promotes public health and patient safety by ensuring that medicines, healthcare products and medical equipment meet appropriate standards of safety, quality, performance and effectiveness, and are used safely.

National Health Service (NHS) The NHS is the name commonly used to refer to the publicly funded healthcare systems of the UK.

National Institute for Health Research – Health Technology Assessment Programme (NIHR HTA Programme) The National Institute for Health Research – Health Technology Assessment (NIHR HTA) is part of the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) based at the University of Southampton. The NIHR HTA coordinates the Health Technology Assessment (HTA) Programme on behalf of the NIHR. The aim of the HTA Programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way.

Outcome A measure of the possible results of a preventive or therapeutic intervention. Outcome measures may be intermediate or final end points.

Palliative therapy To relieve the pain and treat a disease as far as possible, but not cure it completely.

Patient and Public Involvement Programme (PPIP) The PPIP is the team at NICE that supports and develops patient and public involvement across NICE's work programme. A PPIP project manager is assigned to each appraisal and supports patient and carer consultee organisations, their representatives, and individual patients or carers throughout the appraisal. The PPIP project manager also supports the lay members of the Appraisal Committees and supplies the patient and carer group information for the 'Understanding NICE guidance'.

Patient experts Act as expert witnesses to the Appraisal Committee. They have experience of the use of the technology either personally or as part of a representative group. They provide an individual view on the risks and benefits of the technology from personal experience as a patient or carer, and an understanding of the wider range of patient/carer views. They often have insights not typically available in the published literature.

Pharmaceutical Price Regulation Scheme (PPRS) The PPRS is a non-contractual scheme, effective from 1 January 2009. The parties to this agreement are the Department of Health, acting on behalf of the health departments of England, Wales, Scotland and Northern Ireland, and the Association of the British Pharmaceutical Industry (ABPI).

The purpose of the scheme is to ensure that safe and cost-effective medicines are available on the NHS in England and Wales (see www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/DH_494 for the agreement in full).

Remit This is the brief the Department of Health gives to NICE when it formally refers a technology for appraisal. Typically, the remit outlines the disease, the patients and the technologies that will be covered by the appraisal.

Scope Provides a detailed framework for the appraisal and defines the disease, the patients and the technologies that will be covered by the appraisal. The questions the appraisal aims to address are also part of the scope.

Summary of product characteristics (SPC) The SPC provides information for healthcare professionals on how to use medicines safely and effectively. The SPC does not give general advice on the treatment of particular medical conditions.

Technology appraisal (single and multiple) The process of developing recommendations on the use of new and existing health technologies within the NHS in England and Wales. A multiple technology appraisal will normally cover more than one technology, or one technology for more than one indication. A single technology appraisal covers a single technology for a single indication.

Technology assessment The process of evaluating the clinical, economic and other evidence relating to the use of a technology and to formulate guidance on its use.

Terminated appraisal The single technology appraisal process relies on manufacturers or sponsors submitting evidence, in line with NICE's specification. Occasionally, they do not make a submission or the submission does not meet the specification. The appraisal is therefore terminated and NICE asks NHS organisations to take into account the reasons why the manufacturer or sponsor did not make an evidence submission when making local decisions on whether to offer the treatment.

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