NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guide to the processes of technology appraisal

April 2018

Acknowledgements

NICE is very grateful to everyone who contributed to the development of this guide (see section 7).

Foreword

The National Institute for Health and Care Excellence (NICE) provides guidance to the NHS in England on the clinical and cost effectiveness of selected new and established technologies. NICE carries out appraisals of health technologies at the request of the Department of Health and Social Care. Guidance produced by NICE on health technologies is also applied selectively in Northern Ireland and Wales.

This document is one of a series describing the processes and methods that NICE uses to carry out technology appraisals. It focuses on the technology appraisal processes (and provides an overview for organisations invited to contribute to an appraisal).

The documents in the series are:

- Guide to the processes of technology appraisal (this document).
- Guide to the methods of technology appraisal.
- Cancer Drugs Fund technology appraisal process and methods (addendum).
- Guide to the technology appraisal and highly specialised technologies appeal process.

Organisations invited to contribute to NICE technology appraisals (consultees and commentators) should read this guide with the other documents listed above. All documents are available on the NICE website.

1 Introduction

1.1 This guide describes the processes, including expected timescales, that NICE follows when carrying out a technology appraisal. The processes are designed to produce robust guidance for the NHS with appropriate contribution from stakeholders. This guide should be read with NICE's guide to the methods of technology appraisal.

1.2 Technology appraisals are developed by the Centre for Health Technology Evaluation in NICE.

1.3 The National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 indicate that NICE may make a technology recommendation:

- in relation to a health technology identified in a direction by the Secretary of State
- that relevant health bodies provide funding within a specified period to ensure that the health technology be made available for the purposes of treatment of patients.

1.4 The Health and Social Care Act 2012 describes NICE's general duties as follows: In exercising its functions, NICE must have regard to:

- the broad balance between the benefits and costs of providing health services or of social care in England
- the degree of need of people for health services or social care in England and
- the desirability of promoting innovation in providing health services or of social care in England.

1.5 The Regulations require clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities, to comply with NICE technology appraisal guidance that recommends the relevant health service body provides funding within the period specified. When NICE recommends that a treatment be funded by the NHS, the Regulations require that the period

within which the health service must comply will be stated in the recommendations as 3 months, except when particular barriers to implementation within that period are identified (see section 5 on varying the funding requirement). NICE provides advice and tools to support the local implementation of its guidance. This includes resource impact tools or statements for most technology appraisals and additional tools for some technology appraisals.

1.6 The technology appraisal processes are designed to provide recommendations, in the form of NICE guidance, on the use of new and existing medicines, products and treatments in the NHS. Health technologies referred to NICE's Technology Appraisal Programme include:

- medicinal products
- medical devices
- diagnostic techniques
- surgical procedures or other therapeutic techniques
- therapeutic technologies other than medicinal products
- systems of care
- screening tools.

Some of these technologies will also be considered by other programmes within NICE, such as NICE guidelines, the Medical Technologies Evaluation Programme, the Diagnostics Assessment Programme or the Interventional Procedures Programme, or will have medicines and prescribing support from the Medicines and Technologies Programme at NICE. This process guide relates only to technologies appraised through the Technology Appraisal Programme.

1.7 The technology appraisal process is specifically designed to appraise a product, device or other technology, for a single indication. The process normally covers new technologies (typically, new pharmaceutical products or new 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 company submits the principal evidence. The evidence review group (ERG), an

external academic organisation independent of NICE, produces a review of the evidence submission (see sections 3.3.8 and 3.3.9). Consultees provide information (see table 1) and selected clinical experts, NHS commissioning experts and patient experts also give evidence (see section 3.4).

1.8 Companies can ask to fast track an appraisal using the fast track process. The aim of this option is to provide an equally robust but less resource-intensive appraisal process than the standard appraisal process. NHS England and commissioners have committed to provide funding for the highly cost-effective technologies recommended in fast track guidance within 30 calendar days of publication.

1.9 NICE makes the decision on whether the standard or fast track process will be used to appraise a technology. Once published, NICE technology appraisal guidance has the same status, regardless of whether it was produced by the standard or the fast track process. Any health technologies that are referred to NICE for technology appraisal, such as pharmaceuticals or medical devices, can be fast tracked as long as they fulfil the criteria (see section 2.4.31 – 2.4.32).

1.10 An appraisal is based on a review of clinical and economic evidence, mainly provided by the company, supported by testimonies from patients, healthcare professionals and commissioners. Clinical evidence shows how well the technology works – the health benefits. The evidence includes the impact on quality of life (for example, pain and disability), and the likely effects on mortality. Economic evidence shows how well the technology works in relation to how much it costs the NHS and whether it represents value for money.

1.11 The appraisal committee (see table 1) considers the evidence and decides whether or not the technology should be recommended as a clinically effective and cost-effective use of NHS resources, or whether it should only be recommended for specific groups of people.

1.12 The appraisal committee provides its recommendations to NICE in either an appraisal consultation document (ACD) or a final appraisal document (FAD). Normally, the committee produces an ACD only if its preliminary

recommendations are substantially more restrictive than the terms of the marketing authorisation (or equivalent, for example, CE marking for devices) for the technology being appraised or do not recommend use of the technology. If the committee produces an ACD, then NICE invites consultees, commentators and the public to comment on it. After considering these comments, the committee finalises its recommendations and provides them to NICE in the form of a FAD. The FAD forms the basis of the guidance that NICE issues to the NHS in England.

1.13 The NICE technology appraisal process complies with the principles underpinning the UK government's Review of quality assurance of government models (the Macpherson recommendations). The Director of the Centre for Health Technology Evaluation is the senior responsible owner with overall responsibility for assuring the quality of models developed in their areas of responsibility. The quality of models is assured through the requirements for the development of evidence submissions (see NICE's guide to the methods of technology appraisal) and the process used to involve stakeholders in testing the reliability of models (see section 3.2.11).

1.14 NICE is committed to advancing equality of opportunity, eliminating unlawful discrimination and fostering good relations between people who share a protected characteristic and society as a whole, and to complying fully with its legal obligations on equality and human rights. NICE's equality scheme describes how NICE meets these commitments and obligations.

1.15 In formulating its recommendations, the appraisal committee will have regard to the provisions and regulations of the Health and Social Care Act 2012 relating to NICE. The committee will also take into account NICE's Social value judgements: principles for the development of NICE guidance. This document, developed by NICE's Board, describes the principles NICE should follow when designing the processes used to develop its guidance. In particular, it outlines the social value judgements that NICE and its advisory bodies, including appraisal committees, should apply when making decisions about the effectiveness and cost effectiveness of interventions.

1.16 Service level agreements are in place to help disseminate NICE technology appraisal guidance within the devolved administrations in Wales and Northern Ireland.

Table 1 Participants in the technology appraisal processes

Appraisal committee	The appraisal committee considers and discusses the evidence for a technology. The appraisal committee is an independent standing committee that produces recommendations. NICE recruits committee members through open, competitive 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 in the recruitment and selection procedure for advisory bodies. NICE allocates members to 1 of 4 standing committees. Members will normally remain in the same committee for the duration of their membership. Sometimes members may be needed to join another committee to ensure that the meeting is quorate and that business can be done in line with the committee standing orders and terms of reference. Although the committee seeks the views of organisations representing healthcare professionals, patients, carers, companies and government, its advice is independent. Names of committee members are posted on NICE's website. See the appraisal committee's standing orders and terms of reference.

Lead team	A lead team, selected from the committee members at the start of each appraisal, helps the NICE team prepare a technical report to brief the committee. The lead team normally consists of 3 committee members; 1 focuses on clinical effectiveness; 1 on cost effectiveness and 1 on patient and carer evidence (called the lay lead).
The technical team	The technical team consists of the chair or vice chair of the committee along with the NICE team, which normally comprises of the following: the associate director, the technical adviser and the technical lead. The technical team will be responsible for considering the company evidence submission, ERG critique and submissions from other consultees and commentators. It aims to identify and explore issues, come to preliminary scientific judgements, and advise the appraisal committee in its discussion of the evidence. The technical team will seek input from the lead team, the ERG and experts where appropriate.
Consultees	NICE invites consultees to take part in the appraisal. They include: • national groups representing patients and carers • organisations representing healthcare professionals • the company that holds, or is expected to hold, the marketing authorisation for medicinal products, or the equivalent for other technologies • the Department of Health and Social Care • the Welsh government • NHS England as the commissioner for specialised services • clinical commissioning groups (2 are randomly selected).

	As part of the scoping process, NICE invites consultees to comment on draft remits and draft scopes. Consultees can submit evidence and take part in the consultation on the appraisal consultation document (ACD; if produced). All non-company consultees can nominate clinical experts and patient experts to take part in the appraisal. Company consultees can only nominate clinical experts. Representatives from NHS England and clinical commissioning groups invited to take part in the appraisal may also nominate NHS commissioning experts to attend appraisal committee meetings. All consultees have the opportunity to appeal against the final recommendations, or report any factual errors, in the final appraisal document (FAD). Consultees can also comment on the proposal for reviewing the guidance (see section 6).
Commentators	NICE invites commentator organisations with an interest in the technology to take part in the appraisal. They include, but are not restricted to: • relevant comparator technology companies • any relevant National Collaborating Centres (groups commissioned by NICE to develop clinical and social care guidelines) and/or the relevant 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 Commercial Medicines Unit, the Scottish Medicines Consortium, the Medicines and Healthcare products Regulatory Agency, the Department of Health and Social Care, Social

	Services and Public Safety for Northern Ireland and the Academic Health Science Networks). As part of the scoping process, NICE invites commentators to comment on draft remits and draft scopes. Commentators can take part in the consultation on the ACD (if produced), but NICE does not ask them to submit evidence for the appraisal. Non-company commentator organisations can nominate clinical experts and patient experts to take part in the appraisal. Commentator organisations can only nominate clinical experts. These organisations receive the FAD and have the opportunity to report any factual errors. Commentators can also comment on the proposal for reviewing the guidance (see section 6).
Clinical experts and patient experts	The chair of the appraisal committee selects clinical experts and patient experts from those nominated by consultees and commentators; taking into account the NICE policy on declaring and managing interests for NICE advisory committees. Experts are invited to help clarify issues about the submitted evidence and attend committee meetings. They may be asked to provide advice before, during and after committee meetings.
NHS commissioning experts	NICE invites 2 NHS commissioning experts from those nominated by NHS England and the clinical commissioning groups to help clarify issues about the submitted evidence. They may be asked to provide advice before, during and after committee meetings about their views and experiences of the technology and the condition from an NHS perspective.
Cancer Drugs Fund clinical lead	For appraisals of pharmaceutical products for cancer indications, the clinical lead for the Cancer Drugs Fund, or a nominated deputy, is invited to submit a statement and attend both the public and private parts of appraisal committee meetings.

Evidence review group (ERG)	The ERG is an independent (academic) group that reviews the company's evidence submission and may also prepare some additional analyses. The ERG is normally commissioned by the National Institute for Health Research's Health Technology Assessment Programme.
Decision support unit (DSU)	The DSU is commissioned by NICE to provide a research and training resource to support NICE's Technology Appraisal Programme.
NICE staff	
Centre director	The centre director is responsible for delivering all outputs of the Centre for Health Technology Evaluation. The centre director must also ensure that appraisals are carried out in line with the published appraisal process and methods.
Programme director	The programme director is responsible for all aspects of managing and delivering the appraisal work programme. The programme director interacts with the NICE sponsor branch at the Department of Health and Social Care 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 carried out in line 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 approving documentation for consultation 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.
Administrator	The administrator is responsible for supporting the project manager in the planning and management of individual appraisals, including ensuring the timelines and process are followed, and liaising with consultees, commentators and other individuals and organisations.
Technical lead	The technical lead is the analyst responsible for the technical aspects of the appraisal, including liaising with the ERG, scoping the appraisal, preparing drafts of guidance and advising the appraisal committee. There may be more than 1 technical lead for an appraisal.
Technical adviser	The technical adviser is responsible for the technical quality of the appraisal. This involves providing advice on technical issues, and if appropriate, reviewing and quality assuring the work of the technical lead. The technical adviser also ensures a consistent approach is taken across the appraisal programme.
Communications lead	The communications lead is responsible for circulating and communicating the guidance to appropriate groups within the NHS in England, and to patients and the public.
Guidance Information services lead	The guidance 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 guidance documents are accurate, clear and consistent. The editorial lead prepares the final versions of the guidance and information for the public.
Public Involvement Programme (PIP) public involvement adviser	The PIP is the team at NICE that supports and develops public involvement across NICE's work programme. A PIP public involvement adviser 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 and statements, consultation responses or other documentation, and nominating experts. The PIP public involvement adviser also supports the lay members of the appraisal committees and supplies the patient and carer organisations for the 'Information for the public' tab of the guidance page of the NICE website.
Commercial and Managed Access Programme (CMAP)	The CMAP will be responsible for managed access activities, including the Cancer Drugs Fund and Patient Access Schemes Liaison Unit. This team will support commercial engagement between companies and NHS England when a commercial access agreement or patient access scheme is needed to address specific uncertainties within a topic.
Resource impact lead	The resource impact lead works with the technical lead and clinical experts to produce guidance-related costing tools. The tools consist of a resource impact report and template to help organisations assess the financial impact of implementing NICE guidance. They are published at the same time as the guidance and are subject to a limited consultation. The resource impact lead also provides input at the topic selection stage, assessing the potential financial impact of each topic scoped.

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.
Pathways lead	The pathways lead is responsible for ensuring there is a process in place for making guidance accessible through NICE Pathways. This includes ensuring that new guidance is included in new or existing NICE Pathways with agreement from the Centre for Health Technology Evaluation management team.
Adoption lead	The medicines and technologies programme adoption team lead will work with the NHS to provide a systematic approach to the adoption of new technologies such as pharmaceuticals, diagnostic and monitoring devices, surgical implants and other technologies that improve the care given to patients.

2 Selecting technologies

2.1 *Overview*

2.1.1 Topic selection is the process for deciding which topics NICE will produce technology appraisal guidance on. NICE aims to consider all new significant drugs and indications. Health technologies referred to NICE's Technology Appraisal Programme include:

- medicinal products
- medical devices
- diagnostic techniques
- surgical procedures or other therapeutic techniques
- therapeutic technologies other than medicinal products
- systems of care
- screening tools.

2.1.2 The topic selection process has been designed to support the technology appraisal process so that topics chosen will add value and support healthcare professionals and others to provide care of the best possible quality, which offers the best value for money. The steps involved are shown in figures 1 and 2.

2.1.3 NICE manages this process on behalf of the Department of Health and Social Care. NICE can only begin to appraise a technology when it has been formally referred by the Secretary of State for Health.

2.1.4 The aims of the topic selection process are to:

- ensure NICE addresses topics of importance to patients, carers, healthcare professionals, commissioners, providers and public health
- help make the best use of NHS resources
- coordinate the selection of topics using a standard selection process
- make topic selection as rapid as possible to minimise the period of uncertainty before guidance is issued
- ensure that all topic selection activities are inclusive, open, transparent and consistently applied
- ensure that all stages of the process are well documented with clear operating procedures and responsibilities and that throughout there is clear and visible progress tracking for all topics considered
- ensure there are appropriate governance structures and arrangements in place with all relevant parties.

2.1.5 Most topics are identified by the National Institute for Health Research Innovation Observatory at the University of Newcastle. This centre notifies NICE about key new and emerging healthcare technologies that might be suitable for NICE technology appraisal. It aims to notify NICE of new drugs in development about 20 months before marketing authorisation and of new indications about 15 months before marketing authorisation. These time frames are to enable NICE to publish guidance as close as possible to product launch. They may vary depending on whether the topic is a cancer or non-cancer indication. Suggestions for technology appraisal guidance on a

new medicinal product (that has not yet received a marketing authorisation) should be made by the relevant company through UKPharmaScan. Healthcare professionals, researchers and patients can also suggest potential technologies for NICE to appraise by contacting the National Institute for Health Research Innovation Observatory.

2.2 *Elimination, filtering and prioritisation*

2.2.1 Topic selection decisions are based on considering each potential topic against elimination and prioritisation criteria. The elimination criteria filter out topics unsuitable for guidance development through the Technology Appraisal Programme. A topic will not be considered if the technology has not been granted a marketing authorisation (or equivalent) or if there are no plans for it to receive a marketing authorisation (or equivalent) or if it is identical to:

- a topic for which there is published NICE guidance
- a topic for which NICE guidance is in development
- a topic currently in the topic selection process
- a topic that has been considered and eliminated from the topic selection process
- a topic that has been considered in the last 3 years and not been prioritised
- a topic widely accepted and implemented on the basis of existing published guidance from the Department of Health and Social Care, Arm's Length Body or other government departments (excluding national service frameworks, white papers and planning priorities guidance).

2.2.2 The following topic areas are outside the remit of technology appraisal guidance development at NICE:

- Population screening – falls under the remit of the UK National Screening Committee.

- Vaccination – generally falls under the remit of the Joint Committee on Vaccination and Immunisation. However, NICE does consider therapeutic vaccines.
- HIV technology or therapy – falls under the remit of the British HIV Association. However, there may be situations when the Department of Health and Social Care considers that a NICE appraisal of an HIV technology or therapy would be helpful to the NHS and these will be dealt with on a case-by-case basis.
- Haemophilia – for technologies that are considered suitable for existing national procurement processes.

2.2.3 Topics are not considered unless:

- there is appropriate evidence, either available or anticipated to be available in the near future, to support the appraisal (refer to section 3.3 of the guide to the methods of technology appraisal) and
- the relevant clinical question(s) can be addressed by applying the technology appraisal methodology. This may mean excluding topics for which technology appraisal guidance would not add value without broader guidelines on the clinical pathway.

2.2.4 The importance of each topic is considered against prioritisation criteria that help the Secretary of State for Health and Social Care decide which topics should be referred to NICE for guidance development through the Technology Appraisal Programme. This includes consideration of the population size, disease severity, resource impact and the value that NICE could add in carrying out a technology appraisal. The prioritisation criteria are:

- Is the technology likely to result in a significant health benefit, taken across the NHS as a whole, if given to all patients for whom it is indicated?
- Is the technology likely to result in a significant impact on other health-related government policies?

- Is the technology likely to have a significant impact on NHS resources if given to all patients for whom it is indicated?
- Is there significant inappropriate variation in the use of the technology across the country?
- Is NICE likely to be able to add value by issuing national guidance? For example, without such guidance is there likely to be significant controversy over the interpretation or significance of the available evidence on clinical and cost effectiveness?

2.2.5 Elimination, filtering and prioritisation is done by the consultant clinical adviser in the topic selection team. It includes seeking expert opinion and engaging with the relevant commissioners, clinical reference group chairs or members and national clinical directors when appropriate. The filtering recommendations are considered by an internal group at NICE and by NHS England.

2.2.6 Summary information on topic progress is published on the NICE website. The list of potential topics is handed over to the technology appraisal scoping team to develop the draft scopes.

2.2.7 The National Institute for Health Research Innovation Observatory at the University of Newcastle develops technology briefings for potential appraisal topics. The briefings, prioritisation recommendations and draft scopes are considered by a joint decision-making group made up of NICE, the Department of Health and Social Care and NHS England. This group meets (known as decision point 3 [DP3]) to decide the next steps for each topic being considered, to ensure the timely production of guidance. The group considers each topic and decides whether it is potentially suitable for NICE appraisal and as a result, whether the scope should be sent out for consultation.

2.2.8 Medicinal products marketed in England that do not meet the criteria for referral into the Technology Appraisal Programme can be considered for the Highly Specialised Technologies Programme, for an evidence summary to

help inform local decision-making or for the Commissioning Support Programme.

2.2.9 As part of the arrangements for managing the Cancer Drugs Fund from 2016, all new cancer drugs and significant new licensed indications for cancer drugs will be referred automatically to NICE for appraisal. As a result, referral for all cancer drugs is sought early in the selection process and will be received before the draft scope consultation.

2.2.10 Technologies can be routed to the technology appraisal topic selection process from the Medical Technologies Evaluation Programme (MTEP) following consideration at the Medical Technologies Topic Oversight Group. These technologies go straight to the pre-scoping stage, DP3. For further details on the MTEP programme and its routing options please see the process guide.

2.3 *Process*

Figure 1 Overview of the topic selection stages for non-cancer topics

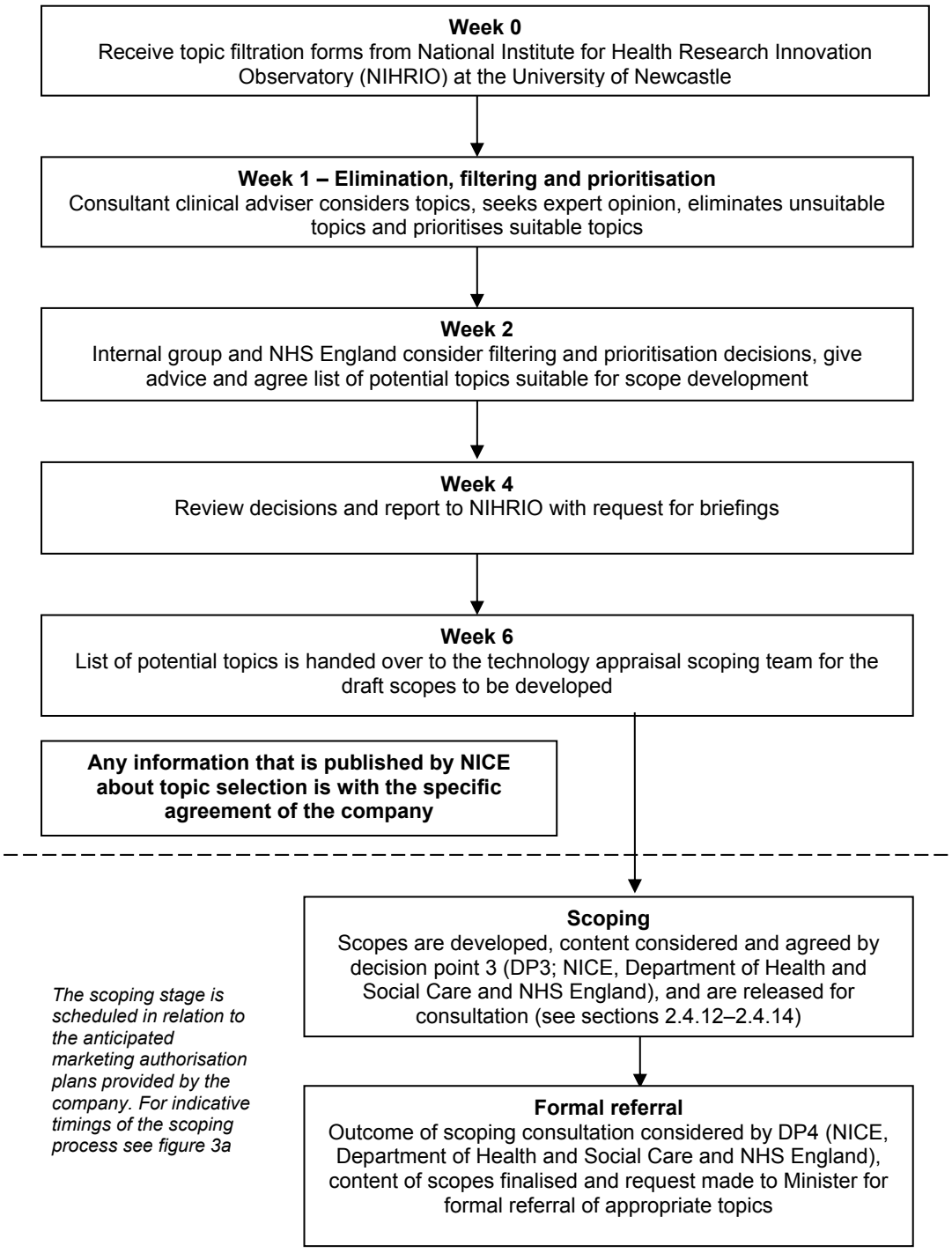
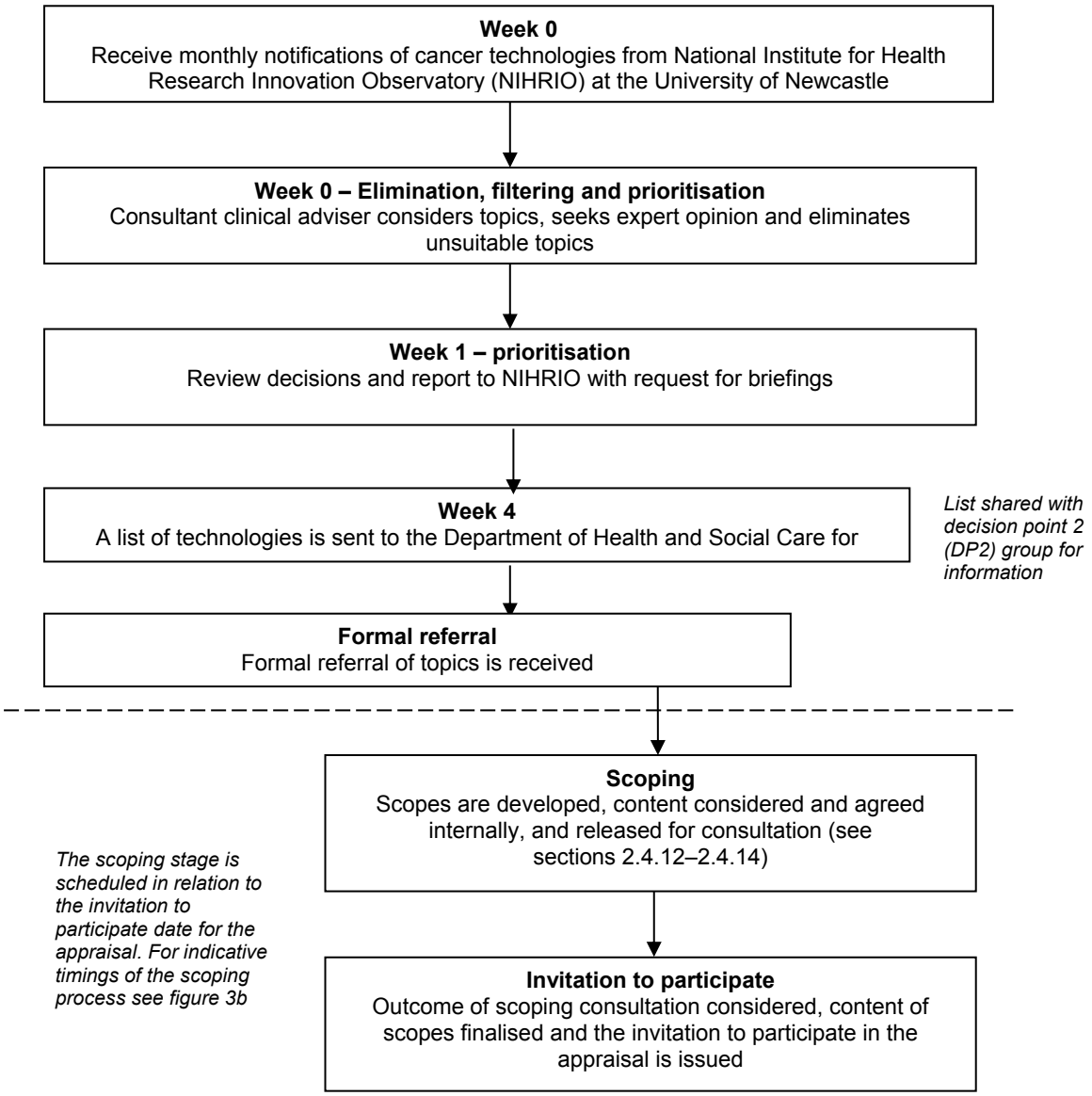


Figure 2 Overview of the topic selection stages for cancer topics



2.4 *Developing the remit and scope*

Developing the draft scope

2.4.1 After identifying topics through the topic selection process, NICE seeks the views of interested parties. At this stage, NICE develops a draft remit and draft scope for each potential appraisal. The steps involved are shown in figures 3a and 3b.

2.4.2 The draft scope sets out what questions the potential appraisal will address. It will steer and focus the appraisal.

2.4.3 The first step in the scoping process is to identify information about the technology. NICE's information specialists work with the technical leads to carry out literature searches, check the availability of relevant evidence, and contact the company. NICE uses this information, along with the technology briefing prepared by the National Institute for Health Research Innovation Observatory, to prepare a draft scope.

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

- the population, for whom treatment with, or use of, the technology would be appraised
- the potential comparators
- the potential subgroups
- the health outcome measures
- any other special considerations and issues that are likely to affect the potential appraisal, including equality and diversity issues.

For further information on how scopes are developed, see NICE's guide to the methods of technology appraisal.

2.4.5 For appraisals that are identified as potentially suitable for the fast track appraisal process, consultees and commentators are invited to comment during the scope consultation on whether the technology is suitable for this process.

2.4.6 Unless the Department of Health and Social Care specifically indicates otherwise, NICE will not publish guidance on the use of a technology for indications that have not been given regulatory approval in the UK (that is, for unlicensed or 'off-label' use outside the terms of the technology's marketing authorisation).

Identifying interested parties

2.4.7 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.

2.4.8 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 the company and specialised commissioning groups; NHS England and 2 clinical commissioning groups. The 2 clinical commissioning groups are selected at random from the clinical commissioning groups operating in the NHS in England.

2.4.9 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 organisations covering Northern Ireland or Scotland or Wales only, and relevant comparator and companion diagnostic test companies. Other organisations may be included as commentators when appropriate.

2.4.10 During the scoping phase, NICE aims to identify the widest possible range 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 or learning disabilities.

2.4.11 Any organisation meeting the criteria in sections 2.4.8–2.4.9 that wishes to become a consultee or commentator for a proposed appraisal can contact the relevant project manager (see the NICE website for details). A request to join the appraisal as a consultee or commentator can be made at any point during the scoping and appraisal phases of the process (up to final appraisal document [FAD] stage).

Consultation on the draft stakeholder list and draft scope

2.4.12 NICE sends the draft remit and draft scope to the identified provisional consultees and commentators, together with the list of consultees and commentators (known as the 'stakeholder list'), for comment. The aim of this consultation is to gather views on whether NICE should appraise the

technology (non-cancer topics only), as well as ensuring all the relevant areas and issues are covered in the potential appraisal. NICE asks identified provisional consultees and commentators if there are other organisations that need to be included in the consultation. Consultees and commentators have 28 calendar days from the date of sending to submit comments.

2.4.13 NICE asks the company to confirm the expected timing and details of marketing authorisation or CE marking in the UK.

2.4.14 NICE publishes the draft remit, draft scope and list of consultees and commentators on its website, for information, 7 calendar days after it sends these documents to the provisional consultees and commentators.

The scoping workshop

2.4.15 After the provisional consultees and commentators have submitted their comments on the draft remit, draft scope and list of consultees and commentators, NICE may hold a scoping workshop meeting. A scoping workshop may be held if the topic covers a new disease area that the Technology Appraisal Programme has not appraised before, or a workshop for the disease area in question has not been held for a while, or there are uncertainties with the topic that a workshop could address. The workshop can be a face-to-face or a teleconference meeting. NICE invites all provisional consultees and commentators to send up to 2 representatives to this meeting.

2.4.16 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
- discuss the appropriateness of completing an appraisal and the appropriate appraisal process
- identify important evidence and any other issues relevant to the potential appraisal.

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

2.4.18 At the scoping workshop, NICE encourages the company to provide preliminary details of the evidence it would submit if NICE were 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 company can discuss commercially sensitive information and technical issues about the proposed appraisal with NICE, in confidence.

Final scope

2.4.19 NICE updates 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 and Social Care.

2.4.20 For non-cancer topics only, NICE submits a report to the Department of Health and Social Care summarising the results of the consultation and scoping workshop discussions (known as the block scoping report). This information helps the Minister to decide whether or not the technology should be formally referred to NICE for appraisal. If the Minister decides to refer a technology, it is formally referred to NICE for appraisal along with the final remit.

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

2.4.22 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 carry out further consultation with consultees and commentators. An additional scoping workshop is not routinely held.

2.4.23 NICE may need to refine the remit and scope further at the request of the Minister.

Figure 3a Steps in developing the scope (non-cancer topics)

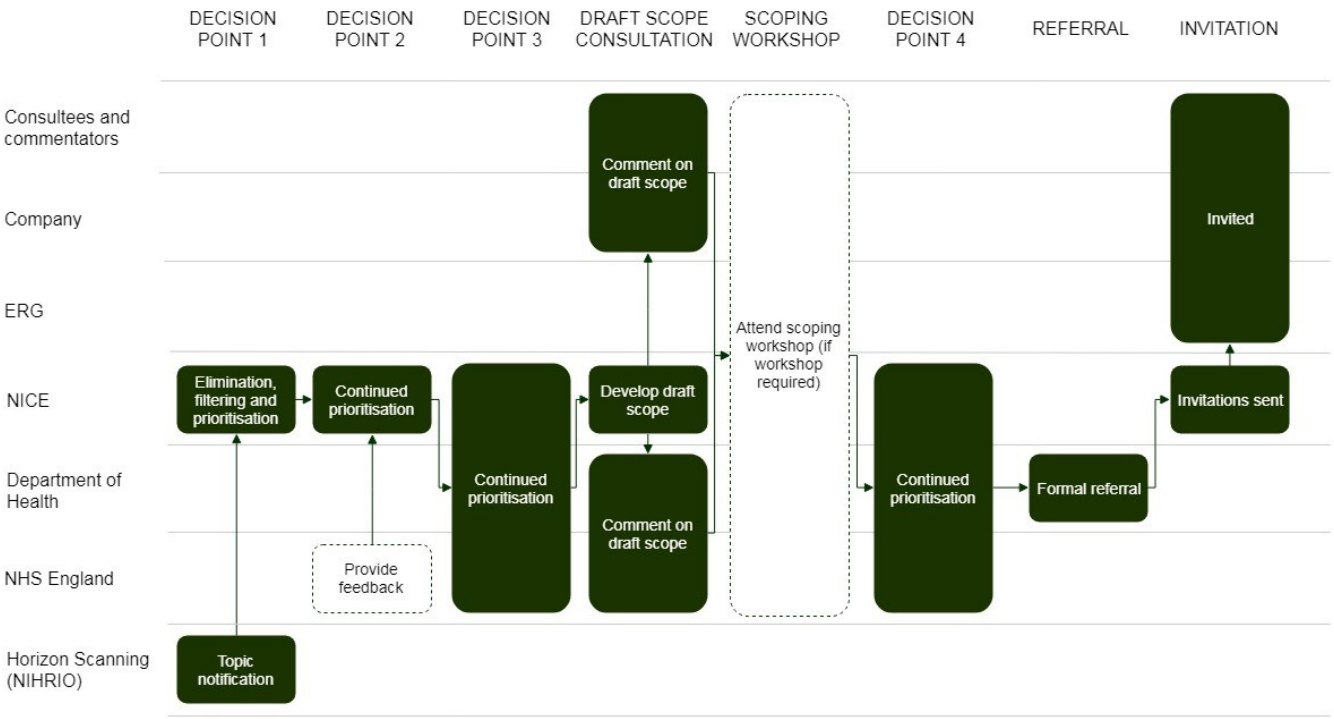
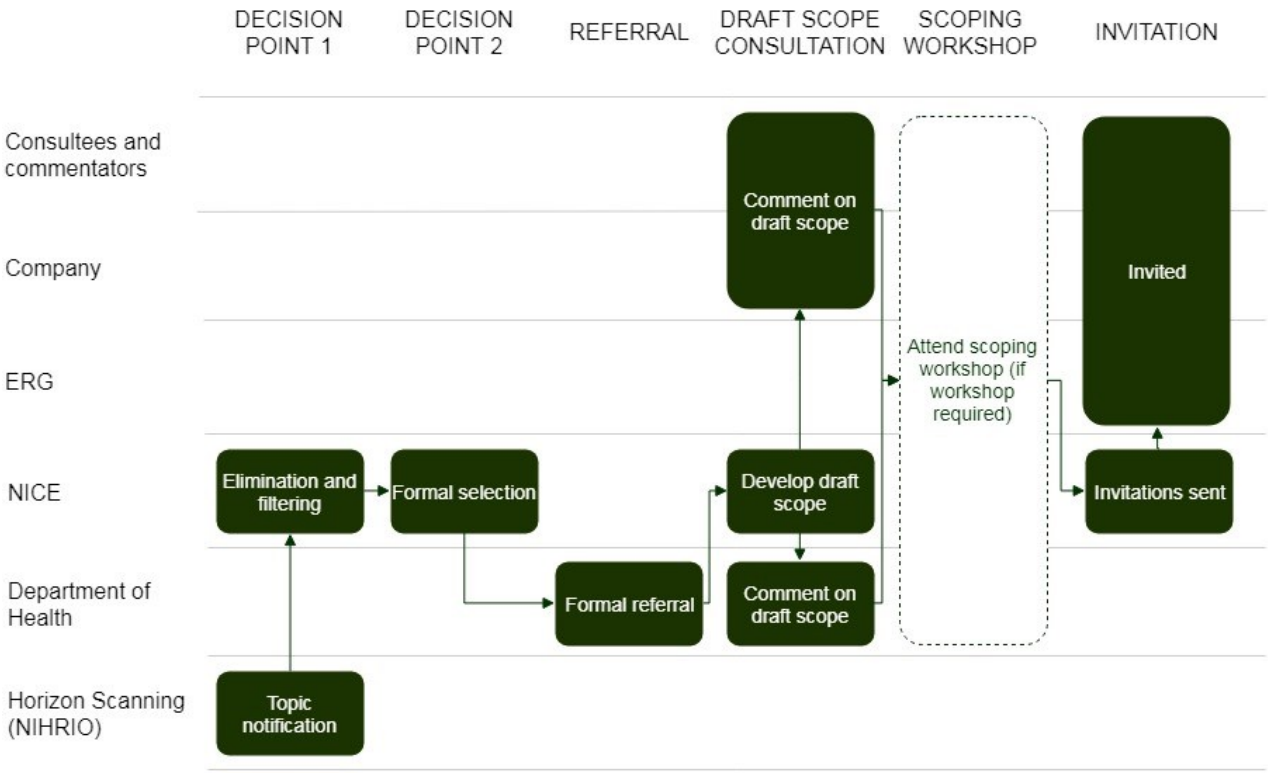


Figure 3b Steps in developing the scope (cancer topics)



Planning the referred appraisals into the work programme

2.4.24 After formal referral, NICE plans the topic into the work programme, and normally publishes the detailed timelines on its website within 6 weeks. NICE will also liaise with the company to confirm the timing of the appraisal. If the company requests a delay, NICE will consider this on a case-by-case basis. If a delay is agreed, NICE works with the company to release as much information as possible to interested parties. Information will also be published on the topic webpage on the NICE website.

2.4.25 Occasionally, timelines may have to change, either before or during the appraisal. NICE will inform consultees and commentators about these changes and, if possible (subject to any confidentiality restrictions), explain the reasons for the changes.

2.4.26 An appraisal is expected to begin before UK regulatory approval for the technology has been granted.

2.4.27 If the timelines of the appraisal are following the anticipated time frame for regulatory approval, the company must notify NICE when it sends a letter of intent to the regulator for the technology being appraised. The notification should also specify when an opinion is expected from the Committee for Medicinal Products for Human Use (or equivalent), when it expects to receive regulatory approval, and the expected wording of the marketing authorisation. The company should also state whether it expects the launch date for its technology in the UK to differ from the regulatory approval date. Companies must inform NICE immediately if there are changes in the regulatory approval process that will affect the time frame or have implications for the wording of the marketing authorisation or CE mark.

2.4.28 For medicinal products, NICE aims to hold the first appraisal committee meeting as soon as possible after the technology gains a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency, or equivalent from the Medicines and Healthcare products Regulatory Agency. It is therefore essential that the company 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 the company receives the marketing authorisation and introduces the technology in the UK. For medical devices and diagnostics, the committee meeting will be planned early enough to allow timely access, subject to NICE guidance.

2.4.29 During the referral process, NICE asks the National Institute for Health Research's Health Technology Assessment Programme to formally commission the evidence review group (ERG) to produce a report.

2.4.30 The process timings described in this guide are in calendar days. Process timings will be extended where they are affected by public holidays.

Selecting technologies for the fast track appraisal process

2.4.31 A technology can be considered for the fast track appraisal process if:

- The company's base-case incremental cost-effectiveness ratio (ICER) is less than £10,000 per quality-adjusted life year (QALY) gained.
- It is likely that the most plausible ICER is less than £20,000 per QALY gained, and it is highly unlikely that it is greater than £30,000 per QALY gained.

  or

- A cost comparison case can be made that shows it is likely to provide similar or greater health benefits at similar or lower cost than technologies already recommended in technology appraisal guidance for the same indication.

2.4.32 Judgements about the technology's suitability for the fast track appraisal process, considering the criteria outlined in section 2.4.31, will be based on:

- the robustness of the clinical effectiveness evidence and its generalisability to the population under consideration
- the consistency of the submission with the scope of the appraisal
- the consistency of approach to modelling with models accepted in previous appraisals in the same, or similar indications
- the size of the population
- the budget impact of implementing the technology
- the uncertainties in the evidence and
- the consequences of decision error.

2.4.33 Topics will not be appraised through the fast track appraisal process if NICE considers that the uncertainty is too great for a recommendation to be made without the appropriate level of scrutiny required by the committee. For example, if there is a very high degree of uncertainty in the cost-effectiveness estimates then the topic will be appraised through the standard process.

2.4.34 Companies who want their technology to be appraised through the fast track appraisal process are encouraged to get in touch with NICE as early as possible, for example during the scoping stage.

2.4.35 The scheduling of any fast track appraisal will initially follow the timing of a standard appraisal until NICE confirms that the technology is suitable for fast tracking.

2.4.36 The final decision about using the fast track appraisal process is the responsibility of NICE, informed by stakeholder input during scoping. It is based on NICE's review of the evidence supported by an ERG, and is normally made 6 to 8 weeks after the company submission is received.

3 The appraisal process

Although there are many similarities between the standard technology appraisal and fast track appraisal processes, they differ in process steps and timelines between the start of the appraisal and the first appraisal committee meeting. Differences between the processes are described in sections 3.2.8 and 3.3.23–3.3.27.

3.1 *General points*

3.1.1 NICE sends the name and contact details of the project manager assigned to an individual appraisal to all consultees and commentators. Consultees and commentators should send all correspondence, including consultation responses about an individual appraisal, to the project manager.

3.1.2 NICE sends correspondence for an appraisal electronically (or in other formats on request) to key contacts 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, during the appraisal process.

Process timelines

3.1.3 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 to 5 indicate the minimum number of weeks for each stage of the appraisal process. Additional time may be given to particular stages if they coincide with public holidays.

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

3.1.5 If possible, NICE informs consultees and commentators about timeline changes during an appraisal and the reasons for these changes. Sometimes, however, if the reasons are commercially sensitive, NICE cannot disclose the details. NICE works with the company to release as much information as possible to consultees and commentators, and on the NICE website.

Information handling – general considerations

3.1.6 NICE adheres to the principles and requirements of data protection legislation, including the General Data Protection Regulation and the Freedom of Information Act when dealing with information received during an appraisal.

3.1.7 Organisations who want to be involved in an appraisal must sign a confidentiality agreement first (formally known as the confidentiality acknowledgement and undertaking) to be considered a participating consultee or commentator. After this, NICE can release appraisal documents to them.

3.1.8 NICE is required to meet the requirements of copyright legislation. If a company cites journal articles in its submission, it must include the full articles in its submission and have copyright clearance to do so.

3.1.9 If NICE requires journal articles for its own use within the process, NICE will obtain the article, paying a copyright fee when necessary.

3.1.10 NICE requires the medical director of the company to sign a statement confirming that all clinical trial data necessary to address the remit and scope of the technology appraisal as issued by the Department of Health and Social Care and NICE, within the company's or any of its associated companies'[1]

[1] within the meaning of s.256 of the Companies Act.

possession, custody, or control in the UK or elsewhere in the world, have been disclosed to NICE or its authorised agents.

3.1.11 NICE requires companies to consent to NICE being provided directly by European Economic Area regulatory authorities all clinical trial data necessary to address the remit and scope of the technology appraisal as issued by the Department of Health and Social Care and NICE. This includes all data that have been submitted to the regulatory authorities by the company or any of its associated companies and that were relevant to the granting of a marketing authorisation, and for NICE to use those data in carrying out the technology appraisal. NICE will only ask regulatory authorities directly after having first approached the company for the information and the company is unable or unwilling to provide the information in a timely manner.

3.1.12 Care should be taken when submitting information about individual people. Personal and sensitive information, for example, the name of a person's clinician, should be removed from submissions.

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

3.1.14 NICE may comment publicly on the content of an appraisal during the process and when draft or final guidance has been produced. The following circumstances may also apply:

- NICE reserves the right to comment publicly if there has been an unauthorised disclosure from a confidential NICE document before it has been published on the NICE website. NICE's chief executive will take this decision. 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 appraisal consultation document (ACD) or final appraisal document (FAD) that could mislead or misinform.

3.1.15 Consultees and commentators, including any other party that has signed a confidentiality agreement for the appraisal, are responsible for treating appraisal documents that are not in the public domain as confidential until NICE makes those documents, or the data within them, public. NICE considers individuals in 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.

3.1.16 Any organisation or individual not directly employed by the consultee or commentator organisation is a third party. Consultees and commentators may release 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 NICE confidentiality agreement.

3.1.17 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 agreement to NICE.

3.1.18 In the technical report, committee papers (see section 3.5.3), ACD and FAD, NICE reserves the right to use any material submitted during the appraisal process that is not marked as confidential by the consultee, or which ceases to be so under section 3.1.16. All confidential information should be clearly signposted and marked as such in the committee papers.

3.1.19 If changes are made to the expected marketing authorisation or CE mark during the regulatory approval process, NICE will discuss the implications with the evidence review group (ERG) and the company and agree how to incorporate the changes into the submission, the ERG report and the technical report.

3.1.20 NICE will not make public any final guidance documents on a technology until UK regulatory approval has been granted and the technology's price is

known. NICE may share documents with participating consultees and commentators who have signed and returned a confidentiality agreement to NICE.

Information handling – confidential information

3.1.21 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 made available to stakeholders and is publicly available. In some circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes commercial in confidence information (for example, the findings of a research project considered confidential because public disclosure could have a significant impact on the commercial interests of a particular company) and academic in confidence information (because public disclosure would seriously jeopardise the ability of the data owner to publish the information in a scientific paper).

3.1.22 NICE has the following principles for handling confidential information:

- Information marked as confidential should be kept to an absolute minimum. Data that are likely to be fundamental to the appraisal committee's decision-making cannot be marked as confidential (for example, the list price of a technology after launch and incremental cost-effectiveness ratio [ICER] estimates).
- Reasons for confidentiality must be stated clearly, including the date of expected release into the public domain by the data owner, with specific consideration to be given to release of data by regulators as part of granting of the marketing authorisation for a medicinal product.
- When a NICE document quoting evidence from a clinical trial is released before the results are published in a journal, or released through the European Medicines Agency's transparency policy, 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. An equivalent approach is needed for all data and studies that underpin, and are included in, economic analyses and models.

- 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.
- Executable economic models used by companies in their submission will be made available (on request) to consultees and commentators who have signed a confidentiality agreement.
- If NICE wishes to publish or publicly share data regarded by the data owner as academic or commercial in confidence, both NICE and the data owner will negotiate to find a mutually acceptable solution, recognising the need for NICE to support its recommendations with evidence and the data owner's right to confidentiality. However, the data owner retains the right to make a final decision about the release of confidential information into the public domain.
- Details of a patient access scheme or commercial access agreement, once referred to NICE for consideration in a technology appraisal, are not confidential except when NHS England has agreed that a simple scheme discount is confidential. In this case the discount and any data that could lead to back-calculation of the discount will not be shared with consultees and commentators or released into the public domain.
- When the details of the patient access scheme or commercial access agreement are not published in final NICE guidance, the NHS must have access to the details, so that providers and commissioners are able to properly account for the patient access scheme.
- NICE will not share confidential details of a simple discount in a patient access scheme for a comparator technology with the company for a new technology being appraised. For each technology with a comparator that has a confidential patient access scheme, the company must include a 'discount' field in its economic model. This should allow the user to input any value between 0 and 100%, which is then applied as a discount to the list price of the technology. By providing this feature in its model, the company will be responsible for the initial programming, which the ERG will check. All parties should then be confident that the discount is programmed correctly. The ERG will be

authorised to know the exact level of discount for all patient access schemes in the appraisal.

- The ERG will use the list price of the comparator in its main report when reproducing the company's analyses and for any exploratory analyses. To allow the committee to explore the impact of using the actual cost of the comparator in the analyses, the ERG will also create a confidential appendix to its report, which will reproduce all analyses from the main ERG report using the exact level of discount for the comparator. Although the results of these analyses are classed as commercial in confidence, NICE will have to publish an ICER range that informs the recommendation(s), after taking into account the exact level of the discount provided in the commercial arrangement for the comparator.
- If NICE is challenged that confidential information it has received should be publicly released in the interests of fairness during an appraisal, at appeal, through judicial review or otherwise, data owners must, on request, promptly reconsider whether it is necessary to maintain confidentiality. If disclosure is not possible, the data owner must be prepared to assert publicly that the information is confidential, and must submit evidence justifying why NICE should maintain that confidentiality. Without such assertion and evidence, NICE is entitled to conclude that the information is no longer confidential.

3.1.23 Appraisal committee members and ERG members, and in the case of a cancer drug appraisal the Cancer Drugs Fund clinical lead, attending the appraisal committee meeting will be provided with all confidential information submitted.

3.1.24 The clinical experts, NHS commissioning experts and patient experts who attend the appraisal committee meeting will be provided with all confidential information submitted, except confidential patient access schemes and commercial access agreements.

3.1.25 In the event that the technical engagement phase (see sections 3.3.14–3.3.22) occurs before regulatory approval of a technology, all information

marked as confidential will not be released to consultees and commentators even though they have signed a confidentiality agreement.

3.1.26 In the event that the technical engagement phase (see sections 3.3.14–3.3.22) happens after regulatory approval of a technology, all information marked as confidential, except confidential patient access schemes and commercial access agreements, will be released to consultees and commentators who have signed a confidentiality agreement.

3.1.27 If a company's evidence submission, or a statement from a non-company consultee contains confidential information, it is the responsibility of the submitting organisation to provide 3 versions:

- A version for NICE, the appraisal committee and the ERG with all the confidential information marked.
- A version for experts and consultees and commentators with all the confidential information marked, and with information about the patient access scheme and commercial access agreement redacted.
- A version for public release after the committee has met, in which all the confidential information is redacted.

3.1.28 A checklist will be provided that must be completed by the consultee at the time of submission, listing all confidential information included in the submission or statement, the reason for its confidentiality, and the date at which it will no longer be considered confidential. If NICE does not receive a completed checklist with a document, none of the information will be considered confidential.

3.1.29 Data owners will be asked to check that confidential information is correctly marked in documents created by others in the technology appraisal process before release; for example, the technical report and ERG report.

3.1.30 NICE releases the documents listed in table 2 to consultees and commentators during the appraisal process. NICE publishes these documents on its website at least 7 calendar days after they have been sent

to consultees and commentators. After NICE has published these documents on its website, they are no longer confidential.

Table 2 Documents NICE publishes during the appraisal process

Document (confidential information redacted in public documents; see sections 3.1.26 to 3.1.27)
List of consultees and commentators
Final scope and remit for the appraisal
Company's evidence submission(s)
Statements/submissions from non-company consultees and experts
Evidence review group (ERG) report
Clarification questions and responses
Technical report
Comments from consultees, commentators and experts on the technical report, and responses from NICE
If produced, the appraisal consultation document (ACD)
Comments from consultees and commentators and members of the public on the ACD, and responses from NICE
Final appraisal document (FAD)

3.2 *Start of the appraisal and evidence submission*

See figures 4 and 5 for an overview of the process and timelines.

3.2.1 The process consists of 3 distinct phases: start of the appraisal and evidence submission, evidence review (including initial clarification and technical consideration), and appraisal. The first phase can only begin after the scoping phase has been completed and NICE has received formal referral from the Secretary of State for Health and Social Care.

3.2.2 It is the responsibility of the company to inform NICE as soon as possible of any potential regulatory developments or delays. This should be done by contacting the project manager.

3.2.3 Before the start of the appraisal, the company has the opportunity to discuss the decision problem that follows from the draft scope with the NICE team and ERG representatives. The company must submit an outline of how it intends to approach the decision problem when preparing the evidence submission. This outline is to include, but is not limited to, evidence sources to be used, evidence likely to become available during the appraisal and how this might be managed, the planned approach to disease and economic modelling, potential challenges in interpreting the evidence, and the proposed approach to handling of uncertainty. The meeting will also allow companies to discuss potential handling of patient access schemes or commercial access agreements and proposals for access to the fast track appraisal process. The meeting is not an opportunity to discuss or request changes to the scope.

3.2.4 NICE will publish the final remit and final scope (see section 2.4), the name of the ERG and the list of consultees and commentators on its website at the start of an appraisal. Each appraisal is assigned to a project team. The roles of key members of the project team are summarised in table 1.

3.2.5 The appraisal starts when NICE sends consultees and commentators the invitation to participate, together with a list of key dates.

Figure 4 Summary of the appraisal process

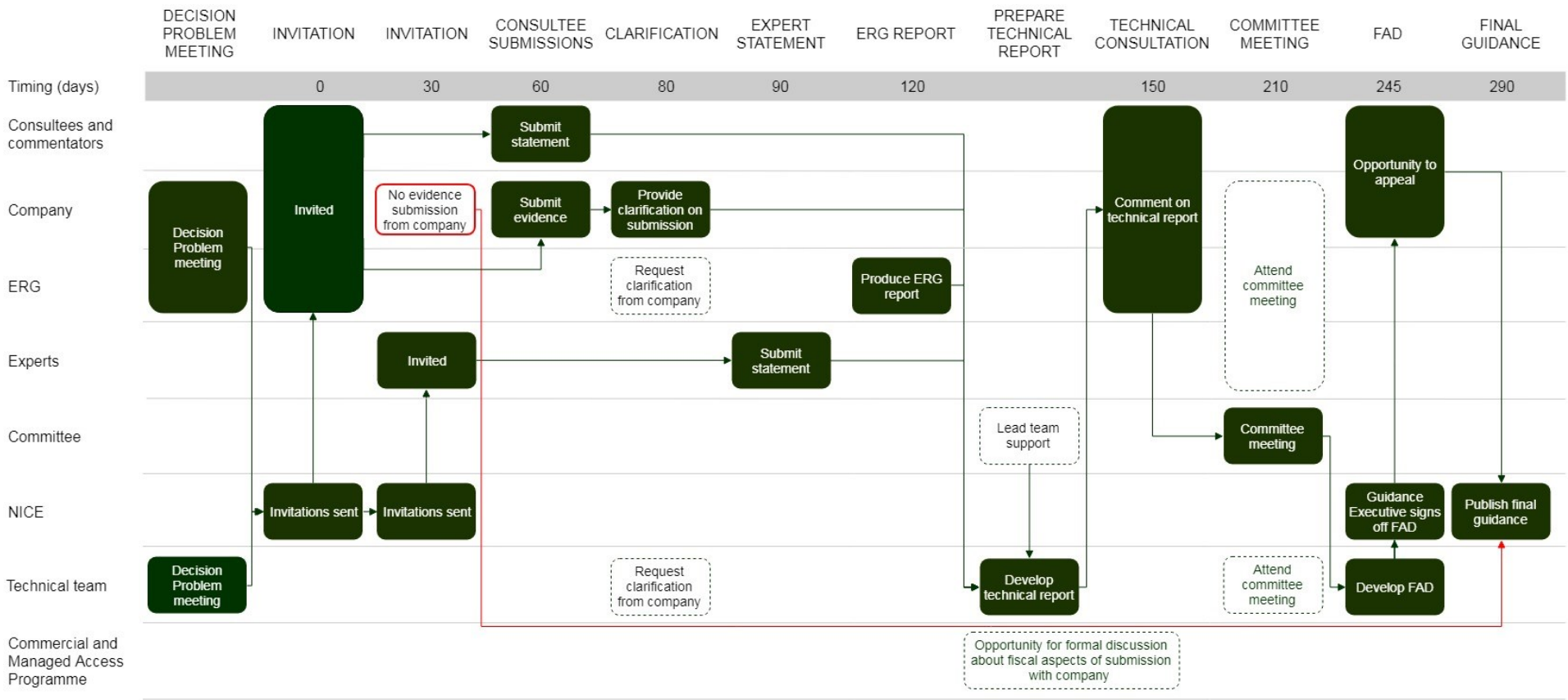
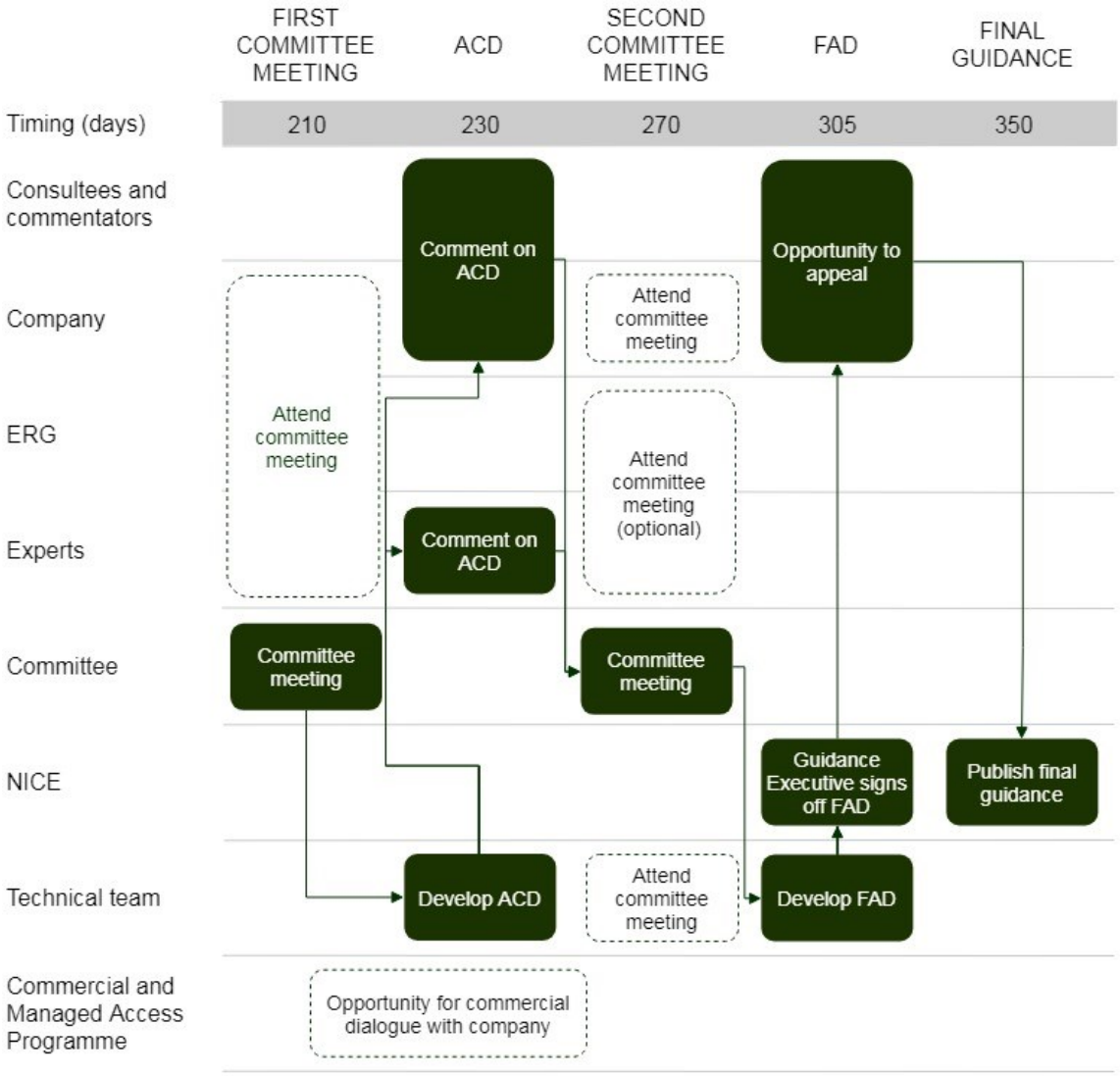


Figure 5 Summary of the appraisal process when an ACD is produced



Evidence submission from the company

3.2.6 NICE invites the company to provide an evidence submission using a detailed submission template. The deadline for receipt of the evidence submission is 60 calendar days from invitation. After receiving this NICE sends it to the ERG for review.

3.2.7 The information needed for the evidence submission is derived from the approach NICE uses to evaluate the clinical and cost effectiveness of health technologies. This approach is outlined in NICE's guide to the methods of technology appraisal.

3.2.8 For fast track appraisals the evidence must be submitted in the standard submission template or, if it is a cost comparison case, in the cost-comparison template.

3.2.9 During the 60-day submission preparation stage there will be at least 1 opportunity for the company to discuss key issues with NICE and, if needed, the ERG. NICE will ask the company to provide an update on their submission before the meeting. This engagement will also allow companies to discuss potential regulatory developments during the appraisal and the potential inclusion and handling of commercial arrangement proposals. During the 60-day submission preparation stage companies can request additional engagement with NICE. Engagement will depend on availability of the NICE team at the time of request.

3.2.10 If the company plans to submit an economic model, it should inform NICE which software will be used. NICE accepts fully executable economic models using standard software, that is, Excel, DATA/Treeage, R or WinBUGs. If the company plans to submit a model in a different software package, it should tell NICE in advance. NICE, in association with the ERG, will then investigate whether the requested software is acceptable. When the company submits a fully executable electronic copy of the model, it 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.

3.2.11 NICE offers to send the economic model (in its executable form) to consultees and commentators during engagement on the technical report. If the model contains confidential material that the data owner is unwilling to share with consultees and commentators, despite the assurances provided through the signed confidentiality agreements, NICE will ask the company to redact the model 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 provides 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 relevant company. It cannot be used for any purpose other than to inform the recipient's understanding of the committee papers.
- The economic model cannot be published by consultees or commentators (except by the company who owns the model), in whole or in part, or be used to inform the development of other economic models.
- The model must not be run for purposes other than to test its reliability.

3.2.12 If the company wishes to include a patient access scheme or commercial access agreement proposal as part of its submission, specific requirements apply (see section 4 for more information).

Submissions from non-company consultees

3.2.13 NICE invites all non-company consultees to make a submission providing information on the potential clinical and cost effectiveness of a treatment using the appropriate templates available on the NICE website. The submission should reflect the experience of patients, healthcare professionals and commissioners of current standard treatment in the NHS in England 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 60 calendar days to provide their submission to NICE. After receiving the evidence submissions, NICE sends them to the ERG and technical team for information.

3.3 *Evidence review*

Initial clarification and additional analysis

3.3.1 After receiving the company's evidence submission, the NICE technical lead and the ERG assess whether the submission is complete and whether the decision problem is specified appropriately with reference to the final scope.

3.3.2 If the evidence submission is incomplete or the decision problem is not specified appropriately, the technical lead consults with the ERG and sends a letter of clarification and any requests for additional analyses to the company within 21 calendar days of receiving the submission. The company has 14 calendar days from the date of the correspondence to respond. When the company provides additional analyses, it should include full descriptions of the analyses as appendices to the original submission. If necessary NICE will organise a clarification meeting between the NICE team, the company and the ERG to resolve any issues.

3.3.3 If requests for clarification and any additional analyses delay the published timelines, NICE will inform consultees and commentators and publish the reason for the delay on its website.

3.3.4 At the same time as the response to the clarification request the company should review the confidential status of information in its evidence submission before the appraisal committee meeting (see sections 3.1.21–3.1.30 for details on submission of confidential information).

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

Terminating an appraisal

3.3.6 NICE aims to ensure that the company prepares the best possible evidence submission for the appraisal committee. NICE will not validate the submission but it will 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 if no evidence submission has been received, the centre director or programme director will

recommend to NICE's guidance executive that the appraisal should be terminated. NICE will inform the company that an inadequate evidence submission has been received. NICE will subsequently advise the NHS that the appraisal has been terminated and that NICE is unable to make a recommendation about the use in the NHS of the technology because no evidence submission was received from the company. NICE will also provide an explanation to help the NHS make local decisions on making the technology available.

3.3.7 A terminated appraisal can be restarted if the company indicates that it wishes to make a full evidence submission.

Evidence review group report

3.3.8 The ERG prepares a report on the clinical and cost effectiveness of the technology in line with NICE's guide to the methods of technology appraisal. The report is based on a review of the company's evidence submission and advice from the ERG's clinical advisers. The ERG prepares the report in line with the National Institute for Health Research Health Technology Assessment Programme's quality criteria, the scope of work as identified in the service level agreement between the Department of Health and Social Care, the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) and NICE, and will use an agreed report template. The ERG is responsible for the content and quality of the report.

3.3.9 The ERG critically evaluates the evidence submission. If the ERG, as part of exploratory analyses, amends the company's model, NICE will make the analyses available to the company at the technical engagement stage. All other consultees and commentators may request, in writing, the ERG analyses during technical engagement.

3.3.10 Following receipt of the ERG report, NICE will share a copy with the company, for information only. This will allow the company time to prepare for the technical engagement stage of the process.

Technical report

3.3.11 After receiving the ERG report the technical team will create a technical report. NICE may also seek advice from the selected experts at this stage, if additional clarification on the submitted individual expert statement is needed.

3.3.12 The technical report will include:

- a commentary on the evidence received
- a commentary on the written statement
- technical judgements of the evidence by the technical team
- reflections on the NICE structured decision-making framework.

3.3.13 The technical report will be accompanied by:

- the company submission (and model when appropriate)
- the ERG's critique of the company submission
- statements from stakeholder organisations and clinical and patient experts
- the overview of the discussions with the company about the technical aspects of the case
- preliminary scientific judgements of the technical team.

Technical engagement

3.3.14 The technical report is usually sent to consultees and commentators for comment within 30 calendar days of NICE receiving the ERG report. NICE notifies consultees and commentators if a delay is expected.

3.3.15 The technical report is also sent to the clinical experts, NHS commissioning experts, patient experts and, in the case of a cancer drug appraisal the Cancer Drugs Fund clinical lead, for comment.

3.3.16 The purpose of the technical engagement is to seek views on the judgements made by the technical team and to allow the company to consider how it could mitigate the remaining uncertainties in the case for clinical and cost effectiveness in the evidence base.

3.3.17 Consultees, commentators and the experts have 28 calendar days to submit comments on the technical report. Comments must be submitted electronically. Approximately half way through the engagement period, NICE will hold a teleconference meeting with the company. When considered necessary by the technical team, experts will also be invited.

3.3.18 NICE will ask the company to re-confirm the expected timing of marketing authorisation or CE mark in the UK.

3.3.19 If a comment contains confidential information, it is the responsibility of the organisation or person who submitted the comment to provide 2 versions; one with all the confidential information marked and another with the confidential information redacted (to be published on NICE's website), together with a checklist of the confidential information. Detailed instructions on sending NICE confidential information are available from the project manager.

3.3.20 During technical engagement, new evidence and analyses can only be accepted if the technical team agrees that this information is likely to affect the appraisal committee's judgements. The new evidence must be presented in a separate appendix to the comments on the draft technical report. NICE may need to extend timelines and reschedule the subsequent committee meeting to allow the new evidence to be considered. The company must inform NICE, in writing, of its intention to submit new evidence and analyses, as early as possible.

3.3.21 Any ERG review of new evidence will not normally be sent out for additional technical engagement before the committee meeting.

3.3.22 If comments received on the economic model need a company or ERG response, NICE sends those comments to the company or ERG. Their responses will be tabled at the next appraisal committee discussion.

Table 3 Expected timelines for the appraisal process: starting the process, preparing the ERG report and technical engagement*

		Calendar days (approx.)
Step 1	NICE invites organisations to participate in the appraisal as consultees or commentators	0
Step 2	NICE invites selected clinical experts, NHS commissioning experts and patient experts to attend the appraisal committee meeting and asks them to submit a written statement	30
Step 3	NICE receives evidence submissions from consultees	60
Step 4	NICE requests clarification on the evidence submission	80
Step 5	Selected clinical experts, NHS commissioning experts and patient experts submit written statements	90
Step 6	NICE receives the ERG report	120
Step 7	The technical team prepare the technical report and send it out for engagement	150
Step 8	NICE compiles the supporting documentation (see section 3.5.3) and sends it to the appraisal committee	195

*Timelines may change in response to individual appraisal requirements.

Fast track appraisal process: evidence review, confirming the process and developing the technical report

3.3.23 When NICE receives a company evidence submission for a fast track appraisal, the NICE team, supported by the ERG, will confirm whether the selection criteria (see section 2.4.31) are met, and that the appraisal can follow the fast track process.

3.3.24 If the selection criteria are not met, the appraisal will follow the standard process. If this is the case and a company has made a case for the fast track process based on cost comparison, the company will be asked to make a submission using the full cost-utility template used for the standard process and the topic will be rescheduled into the work programme at the earliest opportunity.

3.3.25 If an appraisal is not selected for the fast track process, NICE will provide the company with the rationale for this decision. If the company does not agree with this, it must contact NICE within 2 days of receiving the decision stating reasons for its objections. The centre director will then review the routing decision rationale and the company's objections and make a final decision on the appropriate route for the appraisal.

3.3.26 If NICE confirms that an appraisal can follow the fast track process NICE will establish a technical team, who will produce a technical report.

3.3.27 The company will have an opportunity to consider the report before the appraisal committee meets. NICE will not issue the report for technical engagement before the appraisal committee meeting.

3.4 *External participation in the appraisal process*

Participation of experts

3.4.1 NICE encourages consultees and commentators to nominate clinical experts and patient experts. This is so that the experts can provide their views and experience throughout the appraisal process, help to clarify issues that the technical team has identified, respond to the technical engagement and attend the appraisal committee meeting. NICE asks NHS England and the

2 clinical commissioning groups selected at random to nominate NHS commissioning experts to respond to the technical engagement and attend the appraisal committee meeting.

3.4.2 Experts identified during the scoping process may be invited to take part in the appraisal.

3.4.3 The PIP public involvement adviser gives advice and information to the patient and carer organisations nominating experts and to people interested in becoming patient experts. Patient organisations may nominate both patient and clinical experts.

3.4.4 The nominating organisation and the experts (clinical, patient or NHS commissioning) jointly complete a nomination form. The form includes a section asking the expert to provide a 50-word summary describing their experience and knowledge of the condition, any experience of the technology, and any previous involvement with NICE. The form also asks for any conflicts of interest as per the NICE declarations of interest policy.

3.4.5 The chair of the appraisal committee, with input from the NICE team and PIP teams, selects experts from the nominations received and from those identified during scoping. The choice of clinical experts and patient experts is based on the nominees' experience of the technology and the condition(s) that the technology is designed to treat. Selection also takes into account the NICE Policy on declaring and managing interests for NICE advisory committees. If possible, the clinical experts and patient experts will have complementary rather than similar backgrounds and experiences. NICE uses the following criteria to select clinical experts, NHS commissioning experts and patient experts for appraisal committee meetings:

- 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 FAD.
- They have knowledge or experience of the condition or the technology under appraisal or the way it is used in the NHS.

- They are willing and able to discuss the condition and the technology at a committee meeting where there may be members of the public and press observing.
- They are familiar with the purpose and processes of NICE (the PIP public involvement adviser at NICE can give patient experts an overview that enables them to contribute to the technical engagement and discussions at appraisal committee meetings).
- They are prepared to declare any interests they have in the technology under appraisal at committee meetings.

3.4.6 Additionally, the following criteria are used to select clinical experts:

- They are in active clinical practice and have specialist expertise in the subject area of the appraisal.
- Their principal place of work is in the NHS.
- If they have acted as a clinical expert for the company, or 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 technology company or any relevant comparator technology companies. However, there is discretion to invite an expert who holds official office when the work of the committee would be seriously compromised without their testimony.

3.4.7 Usually, 2 clinical experts, 2 patient experts and 2 NHS commissioning experts are selected. NICE asks them to submit a short written personal statement on the technology and the way it should be used in the NHS in England. If the clinical experts and patient experts support the submission made by their nominating organisation they do not need to submit a separate statement. NICE gives the written statements to the appraisal committee and publishes them as part of the committee papers. The experts are expected to engage fully in the technical engagement phase of the process ahead of the appraisal committee meeting. Further advice about the contribution of clinical

experts, NHS commissioning experts and patient experts is available from the NICE project manager.

3.4.8 Clinical experts, 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 people from the nominations received for clinical experts and patient experts, taking into account potential conflicts of interest. For example, for patient experts, NICE would select a person with direct personal experience of the condition and, if possible, the technology, and a member of a patient, carer or professional organisation.

3.4.9 For all cancer drug appraisals the clinical lead for the Cancer Drugs Fund, or a nominated deputy, is invited to submit a statement and attend the appraisal committee meeting to:

- receive, consider and interpret evidence on the clinical and cost effectiveness of health technologies for treating cancer that are being appraised by NICE, particularly when these are potentially eligible for funding from the Cancer Drugs Fund
- provide the appraisal committee with expert insight into how the Cancer Drugs Fund operates to help its decision-making.

3.4.10 For fast track appraisals all selected experts will not be routinely invited to take part in the appraisal committee meeting. In exceptional circumstances, the technical team may agree to invite clinical, patient or NHS commissioning experts to the meeting to help address specific uncertainties that cannot be resolved in writing.

3.4.11 NICE includes the names and affiliations of the selected clinical experts, NHS commissioning experts, patient experts and the Cancer Drugs Fund clinical lead in the minutes of appraisal committee meetings.

3.4.12 It is important that sufficient expertise feeds into all stages of the technology appraisal. NICE welcomes and values the input from patient experts, NHS commissioning experts and clinical experts. Experts will be able to opt out of

attending the appraisal committee meeting if they feel that their views are adequately reflected in the technical report, key areas of uncertainty have been addressed, and their attendance would not add to the committee discussion.

Participation of company representatives

3.4.13 Two representatives from the company (normally 1 with health economics expertise and 1 with medical expertise) for the technology being appraised can attend part 1 of the appraisal committee meeting discussions. The chair will ask them to respond to questions from the appraisal committee. The chair will also 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 committee meeting, specifically to respond to questions from the committee about confidential information in the company's submission. Each representative must:

- be an employee of the company or have been involved in developing the company's 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 or 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.

3.4.14 Company representatives will not receive the confidential appendix that the ERG may create for an appraisal with a comparator that has a confidential patient access scheme or commercial access agreement.

3.4.15 The ACD, FAD and the minutes of appraisal committee meetings will include the industry representation at the appraisal committee meetings but not name the representatives who attended.

3.5 *Appraisal*

3.5.1 The appraisal phase of the process has 4 possible stages:

- consideration of the evidence at an appraisal committee meeting to discuss the content of either the ACD or FAD
- development of, and consultation on, the ACD (if needed)
- review of the ACD (if produced) after comments from consultation at a second appraisal committee meeting
- development of the FAD.

Preparing for the appraisal committee meeting

3.5.2 The technical team and the ERG meet to discuss the results of the technical engagement step, if held, and prepare the presentation for the committee meeting.

3.5.3 The committee papers are usually circulated to all attendees (except members of the public) 2 weeks before the meeting, and consist of:

- a link to the final scope of the appraisal and the list of consultees and commentators
- the technical report, including comments from technical engagement (if held) and the technical team's summary of them.

3.5.4 Appraisal committee meetings are usually 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, the meetings in public team at NICE publish a notice and draft agenda on the website at least 28 calendar days before the appraisal committee meeting. Members of the public who wish to attend can

register on NICE's website. Up to 20 places will be available, depending on the size of the venue. If any meeting is oversubscribed, NICE may need to limit the number of places offered. To allow wide public access, NICE reserves the right to limit attendees to 1 representative per organisation. The closing date for registration is 14 calendar days before the meeting. NICE will contact applicants to let them know whether they have a place at the meeting. NICE publishes the final agenda on its website 7 calendar days before the meeting.

Appraisal committee meeting

3.5.6 When the appraisal committee meets for the first time to discuss an appraisal, it is intended that a FAD will be developed. Sometimes it may develop an ACD (see section 3.5.26). The committee papers include the written evidence submitted by consultees and commentators. The verbal evidence is drawn from discussions with invited clinical experts, NHS commissioning experts, patient experts, ERG representatives and in the case of a cancer drug appraisal, the Cancer Drugs Fund clinical lead.

3.5.7 Committee decisions are normally based on consensus. If a vote is taken, it will be noted in the minutes. More information on how appraisal committees consider the evidence and make decisions is available in NICE's guide to the methods of technology appraisal.

3.5.8 The committee can conclude that the technology is:

- recommended for routine commissioning or
- not recommended for routine commissioning or
- not recommended for routine commissioning, but recommended for inclusion in the Cancer Drugs Fund, or in some other form of managed access arrangement or
- not recommended for routine commissioning, but invites the company to submit a proposal for inclusion in the Cancer Drugs Fund, or in some other form of managed access arrangement.

3.5.9 For fast track appraisals a FAD will be developed after the meeting. In exceptional circumstances, the committee may find it is unable to develop recommendations for the technology without further scrutiny, or further submission of evidence. If this is the case, NICE will publish a statement indicating that the committee is unable to make a recommendation.

3.5.10 For fast track appraisals, if a company wishes to resubmit after the committee has stated that it is unable to make a recommendation, the topic will be rescheduled into the committee work programme although it will not always be possible to prioritise the topic for immediate review.

Part 1 (public session)

3.5.11 Part 1 of NICE appraisal committee meetings is usually 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 business without referring to confidential information, or without discussions being commercially sensitive.

3.5.12 Members of the committee and people having direct input into the discussions declare their interests, which are recorded in the minutes. For further information on how NICE deals with conflicts of interest, please see the NICE Policy on declaring and managing interests for NICE advisory committees

3.5.13 The lead or technical team presents the appraisal topic to the other appraisal committee members and attendees, using the technical report as the basis for the introduction. The lay lead's role is to include the patient evidence in the topic introduction. This introduction does not pre-empt the committee's debate or drafting of the guidance.

3.5.14 Clinical experts, NHS commissioning experts and patient experts will be encouraged to help clarify issues about the submitted evidence, including responding to and raising questions, but they do not make a presentation to the committee.

3.5.15 Company representatives respond to questions from the appraisal committee and comment on any matters of factual accuracy.

3.5.16 The appraisal committee considers the evidence during the public session. However, it will not discuss commercial in confidence information, or information contained in a statement from a clinical expert, NHS commissioning expert or patient expert that has been marked as confidential during this part of the meeting. See section 3.1.233.1.23 for further details on how academic in confidence information is handled at appraisal committee meetings.

3.5.17 The ERG representatives answer questions from the appraisal committee and provide clarification on the ERG report.

3.5.18 Representatives from other guidance-producing teams (for example, guidelines and public health) at NICE who are responsible for developing NICE guidance in areas related to the appraisal 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 (see section 3.5.12).

3.5.19 NICE staff may present additional evidence, provide advice on NICE policies and procedures, and respond to questions from the appraisal committee.

Part 2 (closed session)

3.5.20 During the closed session, the appraisal committee considers commercial in confidence information and agrees the recommendations. Members of the public and press along with the clinical experts, NHS commissioning experts, patient experts, company representatives and the ERG representatives are asked to leave the meeting promptly before this discussion takes place.

3.5.21 The chair may ask clinical experts, NHS commissioning experts, patient experts, company representatives and ERG representatives to remain when confidential information is discussed, but the chair will ask them to leave before the committee agrees the recommendations in the ACD or FAD.

3.5.22 A patient expert can ask to have any personal, sensitive or confidential information heard by the committee in private. The patient expert should formally request this through the project team at NICE and it must be agreed with the chair of the committee before the meeting.

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

3.5.24 The appraisal committee concludes the discussions and agrees the content of either the ACD (see section 3.5.28), which sets out its preliminary recommendations, or the FAD (see section 3.5.44), which sets out its final recommendations. After the meeting, the ACD or the FAD is drafted based on the discussions at the meeting, including the preliminary or final recommendations agreed by the appraisal committee. NICE may issue an ACD or FAD on a technology before that technology receives final UK regulatory approval (see section 3.1.20 for further information).

3.5.25 The outcome of the appraisal committee meeting will be shared with participating consultees and commentators within 7 calendar days of the committee meeting. This will be a brief statement of the committee decision.

Consultation on the ACD (if produced)

3.5.26 Normally, formal consultation (when an ACD is produced) takes place only if the preliminary recommendations from the appraisal committee do not recommend use of the technology, limit the use of the technology further than the marketing authorisation (or instructions for use) for the indication being appraised, or if the company is asked to provide further clarification on the commercial arrangements in their evidence submission.

3.5.27 NICE usually circulates the ACD to consultees and commentators within 21 calendar days of the appraisal committee meeting. NICE alerts consultees and commentators if a delay is expected.

3.5.28 The ACD summarises the evidence and views that have been considered by the appraisal committee and sets out preliminary recommendations. The ACD is not NICE's final guidance on a technology. The recommendations may change after consultation. The ACD usually contains:

- the appraisal committee's preliminary recommendations to the NHS on the technology and how it should be used
- a description of the technology, including its licensed indication and dosage and cost
- a description of how the appraisal committee has interpreted the evidence together with the key issues raised by clinical experts, NHS commissioning experts and patient experts
- the appraisal committee's preferred assumptions and maximum acceptable ICER, if appropriate
- expectations about implementation of the recommendations, if appropriate
- proposed recommendations for further research, if appropriate
- the proposed date for considering a review of the guidance.

3.5.29 When a cancer drug has the potential to be recommended for use within the Cancer Drugs Fund, the appraisal committee will state the conditions for its use in the ACD and will identify the nature of the clinical uncertainty that should be addressed through data collection. Details of data collection, including a protocol and analysis plan (when applicable), will be set out in a managed access agreement.

3.5.30 The data collection arrangements for drugs being recommended through the Cancer Drugs Fund will be developed by the company, NHS England, Public Health England, NICE and the Cancer Drugs Fund clinical lead. Input from experts taking part in the appraisal will be requested when needed. The data collection arrangements will be completed before the final guidance is published. Further details can be found in the data collection specification.

3.5.31 The ACD and any committee papers are sent to consultees, commentators, the clinical experts, NHS commissioning experts and patient experts for

consultation. These documents are confidential until NICE publishes them on its website 7 calendar days after circulation. Information designated as commercial in confidence will be redacted from the public documentation. No clinical confidential information will be shared with consultees and commentators at this stage unless marketing authorisation (or the CE mark) has been received.

3.5.32 The purpose of the consultation is to seek views on the appraisal committee's preliminary 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 preliminary recommendations are sound and constitute a suitable basis for guidance to the NHS
- there are any equality issues that need special consideration that are not covered in the ACD.

3.5.33 Consultees and commentators (and the clinical experts, NHS commissioning experts and patient experts) have 28 calendar days from the date of sending to submit comments on the ACD. They must submit their comments in writing, preferably electronically.

3.5.34 NICE publishes the ACD on its website with an electronic comment facility and any additional committee papers not already shared on the NICE website (with confidential material redacted for public consultation) 7 calendar days after circulation to consultees and commentators.

3.5.35 If a comment contains confidential information, it is the responsibility of the organisation or person who submitted the comment to provide 2 versions, a complete version and another with the confidential information redacted (to be published on NICE's website), together with a checklist of the confidential information. Detailed instructions on sending NICE confidential information

about an appraisal are available from the project manager (see section 3.1.22).

3.5.36 After the ACD has been developed, new evidence will not be accepted unless specifically requested by the appraisal committee (see section 3.5.37). The opportunity to provide additional evidence is offered at the technical report engagement stage.

3.5.37 The appraisal committee may find it is unable to develop recommendations for the technology without further scrutiny, or further submission of evidence. If this is the case, there is the possibility for a pause in the appraisal. NICE will ask the company to submit specific information and if relevant, further analyses. If the company has carried out new analyses, it must submit an updated version of the economic model. When the appraisal committee seeks such clarification, NICE will inform consultees and commentators within 7 calendar days of the committee meeting. After this pause, the committee will be required to make a recommendation, as set out in section 3.5.8.

3.5.38 When consultees and commentators submit comments that lead to a substantial revision of the committee's previous decision, involving a significant change in the recommendations, considerations or the evidence base, the centre director or programme 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 committee papers with the second ACD, together with consultation comments and any new evidence not circulated with the previous ACD.

Appraisal committee meeting to develop the FAD

3.5.39 If an ACD is produced, the appraisal committee usually meets again, with members of the public and press observing, to consider the preliminary recommendations in 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 people or organisations.

3.5.40 Representatives from the company, the ERG and from other guidance-producing teams at NICE (for example, guidelines and public health) who are responsible for developing NICE guidance in areas related to the appraisal, may attend the meeting. In exceptional circumstances, if clarification of issues raised during the consultation period is needed, the chair of the appraisal committee can, at their discretion, invite 1 or more of the clinical experts, NHS commissioning experts or patient experts to attend.

3.5.41 The appraisal committee discusses the responses to the ACD consultation in part 1 of the meeting (see section 3.5.11) and moves to a closed session (part 2, see section 3.5.20) to consider any confidential information and to agree the content of the FAD, which sets out the final recommendations. After the meeting, the FAD is drafted based on the discussions at the meeting and the final recommendations agreed by the appraisal committee.

3.5.42 If the company responds to the consultation by making an updated commercial offer and the revised ICER is below the maximum acceptable ICER specified by the appraisal committee in the ACD (see section 3.5.32), the chair can decide, on behalf of the appraisal committee, whether the company's proposal is likely to result in positive guidance. In these circumstances, the chair may decide that another committee meeting is not needed. A FAD is drafted and the final recommendations are agreed by the appraisal committee electronically. The final recommendations will be shared with participating consultees and commentators within 7 calendar days of sign-off. This will be a brief statement of the committee's decision.

3.5.43 If the committee has requested new analyses and the company has carried these out using the appraisal committee's preferred assumptions, if the revised ICER is below the maximum acceptable ICER specified by the appraisal committee in the ACD (see section 3.5.32), the chair may decide that another committee meeting is not needed. A FAD is drafted and the final recommendations are agreed by the appraisal committee electronically.

3.5.44 The FAD contains:

- the appraisal committee's final recommendations to the NHS on the technology and how it should be used
- a description of the technology, including its licensed indication and dosage and cost
- a description of how the appraisal committee has interpreted the evidence together with the key issues raised by clinical experts, NHS commissioning experts and patient experts
- the appraisal committee's preferred assumptions and maximum acceptable ICER, if appropriate
- expectations about implementation of the recommendations, if appropriate
- proposed recommendations for further research, if appropriate
- the date for considering a review of the guidance.

3.5.45 The centre director or programme director signs off the final FAD and submits a report to NICE's guidance executive. The guidance executive checks that the appraisal committee has appraised the technology in accordance with the terms of the Secretary of State for Health and Social Care'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 so that they can consider whether to appeal against the final recommendations. They can also highlight any factual errors. Commentators and the experts receive the FAD for information and can also highlight any factual errors. Details of the appeal process are set out in NICE's guide to the technology appraisal and highly specialised technologies appeal process.

3.5.47 Any further analysis done by the company, NICE or the ERG during development of the FAD will be made available to consultees and commentators. When NICE sends the FAD to consultees and commentators, it also sends the comments received from consultees, commentators and

experts on the ACD (if produced), together with NICE's responses to them, and the comments received from the public through the website.

3.5.48 NICE usually sends the FAD within 35 calendar days of the appraisal committee meeting to consultees and commentators. NICE notifies consultees and commentators if a delay is expected. NICE publishes the FAD and the committee papers, with confidential material redacted, on its website 7 calendar days after circulation to consultees and commentators.

3.5.49 In highly exceptional circumstances NICE may carry out further analysis. The ERG or Decision Support Unit (DSU) normally does this further analysis before NICE circulates the FAD. The centre director or programme director decides whether this should be done, with the chair of the appraisal committee and the NICE team. The decision is not taken lightly and is made to make sure that NICE is able to provide robust guidance to the NHS. If further analysis is done, 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.

Minutes

3.5.50 NICE publishes unconfirmed minutes of the appraisal committee meeting on its website within 28 calendar 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.

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

		Calendar days (approx.) since process began
Step 8/10	Appraisal committee meeting to develop an ACD attended by clinical experts, NHS commissioning experts and patient experts.	210

Step 9/11	The ACD is produced. NICE distributes the ACD and publishes it on the website 7 calendar days later.	221
Step 10/12	Fixed 28-calendar day consultation period on the ACD.	259
Step 11/13	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.	270
Step 12/13	The FAD is produced. NICE distributes the FAD and publishes it on the website 7 calendar days later.	305

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

		Calendar days (approx.) since process began
Step 8/10	Appraisal committee meeting to develop a FAD, attended by clinical experts, NHS commissioning experts and patient experts.	210
Step 9/11	The FAD is produced. NICE distributes the FAD and publishes it on the website 7 calendar days later.	245

Publication of the guidance

3.5.51 Unless there are any appeals by consultees, the FAD forms NICE's guidance on the use of the technology.

3.5.52 After receiving the FAD, any consultee (whether or not they are submitting an appeal) or commentator can ask for factual errors to be corrected. Some examples of factual errors are:

- wrong names or misspelling of technologies or companies
- errors in figures presented in the FAD
- incorrect or incomplete quotes from a marketing authorisation or CE mark
- text describing the facts incorrectly in the FAD.

3.5.53 The guidance executive considers all significant requests for correcting factual errors and decides whether to make changes to the FAD. This decision is made after any appeal proceedings have concluded. NICE then publishes the FAD as technology appraisal guidance on its website. NICE also publishes a lay version for patients and carers (known as 'Information for the public').

4 Patient access schemes, commercial access agreements and flexible pricing

4.1 The Pharmaceutical Price Regulation Scheme (PPRS) 2014 allows companies who are members of the scheme to submit proposals for patient access schemes and flexible pricing proposals as part of an ongoing or published NICE technology appraisal.

4.2 In the context of the Cancer Drugs Fund, companies can also agree commercial access agreements with NHS England. Such arrangements will be considered in the NICE technology appraisal.

Definitions

4.3 A patient access scheme is a scheme proposed by a company that is a member of the 2014 PPRS. Up to January 2018, these were approved by the Department of Health and Social Care, but from January 2018 onwards they are approved by NHS England. Patient access schemes allow patients to have a technology when NICE's assessment of value, on the current evidence base, is unlikely to support the list price.

4.4 Flexible pricing recognises that the initial launch price of a technology 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 technology that reflects value that can be demonstrated at launch, while retaining the freedom to apply to increase or decrease this original list price either as further evidence or as new indications emerge and change the effective value that the technology offers to NHS patients.

4.5 A commercial access agreement between a company and NHS England supports use of a technology for which at least 1 indication is currently, or has been, considered as part of the Cancer Drugs Fund.

4.6 NICE can only consider patient access scheme proposals, flexible pricing proposals and commercial access agreements after NHS England has formally approved them (see figure 6).

4.7 The Commercial and Managed Access Programme at NICE will provide companies with opportunities to engage in commercial and managed access conversations with both NICE and NHS England. The relevant stages for commercial dialogue are:

- before formal invitation to participate in the appraisal (for example during scoping)
- at the decision problem meeting
- on receipt of the evidence submission
- at clarification
- during technical report consultation
- during consultation on the ACD.

Patient access schemes and commercial access agreements

4.8 The 2014 PPRS identifies 2 types of patient access scheme (see chapter 5 of the 2014 PPRS for more details):

- simple discount schemes and
- complex schemes.

4.9 The Patient Access Scheme Liaison Unit (PASLU) at NICE advises NHS England on the feasibility of implementing patient access scheme proposals.

When assessing a patient access scheme proposal, the PASLU considers the key principles for implementing patient access schemes in England as outlined in the 2014 PPRS. The PASLU process is not part of the appraisal process. Changes could be made to a patient access scheme proposal after NHS England has referred it to NICE, however, these must be discussed and agreed with NHS England.

4.10 The appraisal committee considers the effect of a patient access scheme proposal on the clinical and cost effectiveness of the technology and clarifies relevant points with the company (see section 3.3). The ERG or the NICE team assesses the impact of the proposed scheme on clinical and cost effectiveness.

4.11 The process for reviewing the impact of a patient access scheme proposal on the cost effectiveness of a technology depends on when the proposal is submitted to NICE. When companies wish to propose a patient access scheme in the context of a NICE technology appraisal, they should follow these rules:

- As a general rule, companies should include a patient access scheme when making their initial evidence submission to NICE. This means that any patient access scheme proposal should be sent to NHS England long before the evidence submission for the NICE appraisal. This allows sufficient time for the patient access scheme to be approved before the first appraisal committee meeting.
- In exceptional circumstances, a simple discount patient access scheme may be accepted at other times in the NICE process. A simple discount scheme can be proposed:
  - in response to the technical engagement step
  - in response to the ACD
  - at the end of the appraisal process, once any appeals have been heard and NICE's final guidance has been issued to the NHS, in a rapid review of the guidance.

The appraisal process could accommodate approval of a complex patient access scheme, particularly when introduced in response to technical engagement or the ACD. It is the company's responsibility to ensure that

NHS England has sufficient time to complete its consideration of the proposed patient access scheme in time for the appraisal committee meeting.

4.12 If the appraisal committee recommends a technology with an outcomes-based patient access scheme or commercial access agreement, it is essential that arrangements are in place to collect and analyse the relevant outcomes. If the actual outcomes differ significantly from those assumed during the original appraisal, NICE may decide to bring forward a review of the recommendations.

4.13 For fast track appraisals (this is an exception to the statement in section 4.11) a patient access scheme proposal must be included in the company evidence submission.

4.14 Any significant new proposals for, or structural changes to, a patient access scheme or commercial access agreement after release of the final appraisal document (FAD) will not be accepted, but minor changes to an agreed commercial arrangement, such as a change in the level of discount could be accepted. At this point an update to the guidance will only be considered in a rapid review of the guidance. See sections 4.21–4.18 for further details.

Patient access scheme proposals submitted during an appraisal

4.15 The appraisal committee can consider a patient access scheme or commercial access agreement proposal before formal approval from NHS England when the risk of non-approval is considered low (for example when the PASLU advice to NHS England supports the proposal). NICE must not release an ACD or FAD until approval of the patient access scheme is received from NHS England.

4.16 If, in exceptional circumstances, the company wants to submit a proposal for a simple discount patient access scheme at a different time in the appraisal process, that is, after their evidence submission, the following conditions apply:

- The company must inform the NICE Technology Appraisal Programme in writing of its intention to submit a simple discount proposal, as early as possible.

- The simple discount proposal must be submitted to NHS England in sufficient time for it to complete its consideration of the proposed scheme and notify NICE at least 14 calendar days before the next committee meeting, to allow sufficient time for ERG or NICE review.
- The company must provide information about the simple discount proposal in a separate submission, using NICE's patient access scheme submission template.
- The patient access scheme submission must be submitted to NICE by either the technical report or the ACD consultation closing date, and if possible earlier.

4.17 When a simple discount patient access scheme proposal is submitted after the ACD is released, NICE may choose to reschedule the subsequent committee meeting to allow sufficient time to consider and review the proposed scheme.

4.18 When NHS England approves a simple discount patient access scheme proposal after the release of an ACD, the impact of the proposed scheme on the cost effectiveness of the technology may lead the appraisal committee to revise its recommendations. If the technology is recommended, a FAD will be issued for appeal (see section 3.5.44 onwards). Information will be released so that the proposed scheme and its impact on the cost effectiveness and the recommendations can be understood. Unless there are any appeals by consultees, the FAD forms the basis of NICE guidance on the technology. In certain circumstances, the centre director or programme director and the chair of the appraisal committee may decide that it is necessary to produce another ACD. If so, the consultation process will be repeated. The decision to produce another ACD will extend the timelines for the appraisal.

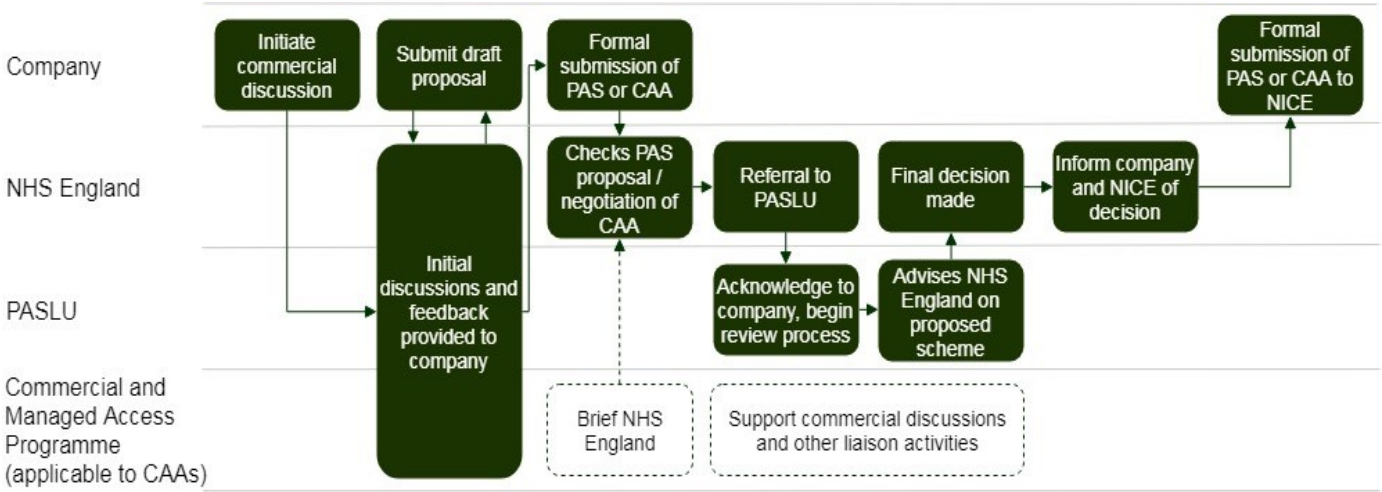
Cancer Drugs Fund commercial access agreements

4.19 When the appraisal committee decides to recommend a technology for use within the Cancer Drugs Fund, the company will be invited to propose a commercial access agreement, or vary an existing agreement.

4.20 For a cancer drug to be recommended for use through the Cancer Drugs Fund, it must display plausible potential for satisfying the criteria for routine use, taking

into account the application of the end-of-life criteria when appropriate. Companies should work with NICE and ask for advice about the assumptions used in the appraisal committee's consideration of clinical and cost effectiveness, which must form the basis of their proposal for a commercial access agreement.

Figure 6 Process for considering a proposal for a patient access scheme or commercial access agreement



Patient access schemes submitted after guidance publication

4.21 Patient access schemes are designed to maximise the opportunity for cost-effective access to a new technology. Therefore, within 12 weeks of publication of the final guidance, companies can request a rapid review to consider new patient access scheme proposals. The rapid review of the guidance is planned, as a priority, into the work programme after final guidance publication. NICE can only consider a new proposal with NHS England's agreement. The appraisal committee will usually consider the proposal within 6 months of the company request.

4.22 The rapid review of guidance will be used for the consideration of a new patient access scheme proposal only. If the company wishes to submit additional new evidence other than for a patient access scheme proposal, NICE will consider whether this would be acceptable in the context of a rapid review or whether it would trigger a full review proposal (see section 6).

4.23 The company must use the patient access scheme submission template to provide details of the proposed scheme, a revised economic model incorporating the patient access scheme proposal, and an updated checklist of confidential information, if necessary. This is in addition to the information that must be submitted to NHS England as part of a submission for a patient access scheme proposal.

4.24 Although NICE will include patient access scheme proposals submitted for rapid review on the relevant committee meeting agenda, NICE makes no public announcement about the specific topics. Scheme proposals submitted as a rapid review are treated by NICE as commercial in confidence and all matters about the proposed scheme (except the existence of the scheme proposal) will usually remain confidential unless consideration by the appraisal committee results in a change to guidance recommendations. In this situation, NICE will issue a FAD for appeal (see section 3.5.44 onwards). NICE releases information during the FAD appeal stage so that the proposed scheme and its impact on the clinical effectiveness, cost effectiveness and the recommendations can be understood.

4.25 If, in exceptional circumstances, NHS England were to approve a patient access scheme proposal more than 16 weeks after guidance publication, the topic could be considered under the rapid review arrangements but it would not be prioritised in the schedule and NICE would need to be assured that the principles of rapid review apply.

Flexible pricing

4.26 The 2014 PPRS identifies 2 circumstances in which flexible pricing may be relevant:

- when significant new evidence is generated that changes the value of an existing indication and
- when a significant new indication is proposed.

4.27 Requests to consider a flexible pricing proposal for an existing indication of a technology must be linked to new evidence emerging. The company 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. Flexible pricing proposals that are not supported by new evidence will not be considered.

4.28 For technologies launched after 1 January 2009, if NICE receives a flexible pricing proposal for an existing indication within 12 months of guidance publication, NICE will consider the impact of the new evidence and the flexible pricing proposal on the clinical and cost effectiveness of the technology. NICE will clarify relevant points with the company before the ERG reviews the proposal. The appraisal committee will then consider the proposal together with the ERG's independent review.

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

4.30 All flexible pricing proposals for technologies launched before 1 January 2009 are considered through the standard review process (see section 6).

4.31 When the appraisal committee considers a flexible pricing proposal 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 consistent with that used in the original appraisal.

4.32 Although NICE includes flexible pricing proposals under consideration on the relevant committee meeting agenda, NICE makes no public announcement about the specific topics. NICE considers it essential that such proposals can be received and considered in confidence. NICE also understands that companies may suffer commercial and other harm if information on the proposals were to be made public at this point. Therefore, NICE treats all flexible pricing proposals

for existing indications as confidential and will not normally release any information about these schemes under the Freedom of Information Act, or for any other purpose at this stage (including during the public part of appraisal committee meetings), unless the company has agreed to this.

4.33 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 3.5.26 onwards). Detailed information will be released as part of the ACD consultation so that the proposed new price 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 proposal. They 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.

4.34 Flexible pricing proposals for new indications of existing technologies are also covered in the 2014 PPRS. New indications are potential new appraisals. Consideration of their suitability for technology appraisal is therefore covered under topic selection (see section 2).

5 Varying the funding requirement to take account of net budget impact

Policy context

5.1 As referred to in sections 1.3–1.5, the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013, (the 'Regulations'), expect NICE to:

- ‘recommend […] that relevant health bodies provide funding within a specified period to ensure that the health technology be made available for the purposes of treatment of patients’ and
- ‘specify in a technology appraisal recommendation the period within which the recommendation […] should be complied with’, which ‘must be a period that begins on the date the recommendation is published by NICE and ends on the date 3 months from that date’.

5.2 The Regulations state that if NICE considers it appropriate, NICE must specify a longer period, when:

- the health technology cannot be appropriately administered until:
  - training is,
  - certain health service infrastructure requirements including goods, materials or other facilities are, or
  - other appropriate health services resources, including staff, are, in place; or
- the health technology is not yet available in England.

5.3 The Regulations require NICE, when it is minded to specify a longer period, to consult with ‘such persons with an interest in the appraisal of a health technology…about the appropriate period that may be specified in a technology appraisal recommendation’, and that this consultation must include ‘the Secretary of State and the [Commissioning] Board [now referred to as NHS England]’.

5.4 NHS England has indicated that it may request consideration of a longer time to implement the statutory funding requirements for technologies funded through its specialised commissioning budgets, when the potential net budget impact is expected to exceed £20 million per year in any of the first 3 financial years of its use in the NHS. NHS England has indicated that it will also do this on behalf of clinical commissioning groups, for locally commissioned technologies that NICE has appraised.

5.5 If the potential net budget impact is expected to exceed £20 million per year in any of the first 3 financial years of a technology's use in the NHS, NHS England will offer to engage in commercial discussions with companies whose technologies are being appraised by NICE before requesting a variation to the funding requirement.

5.6 A commercial discussion may not result in a budget impact of less than £20 million per year in each of the first 3 financial years of the technology's use in the NHS in England. In such cases, and when NHS England requests a variation to the funding requirement, NICE will take into account any relevant aspects of the commercial discussion in responding to the variation request.

Evidence submission

See figure 7 for an overview of the process and timelines.

5.7 After receiving the company submission, NICE will assess the potential budget impact of the technology by estimating the net annual cost to the NHS (see the assessing resource impact process manual for further details).

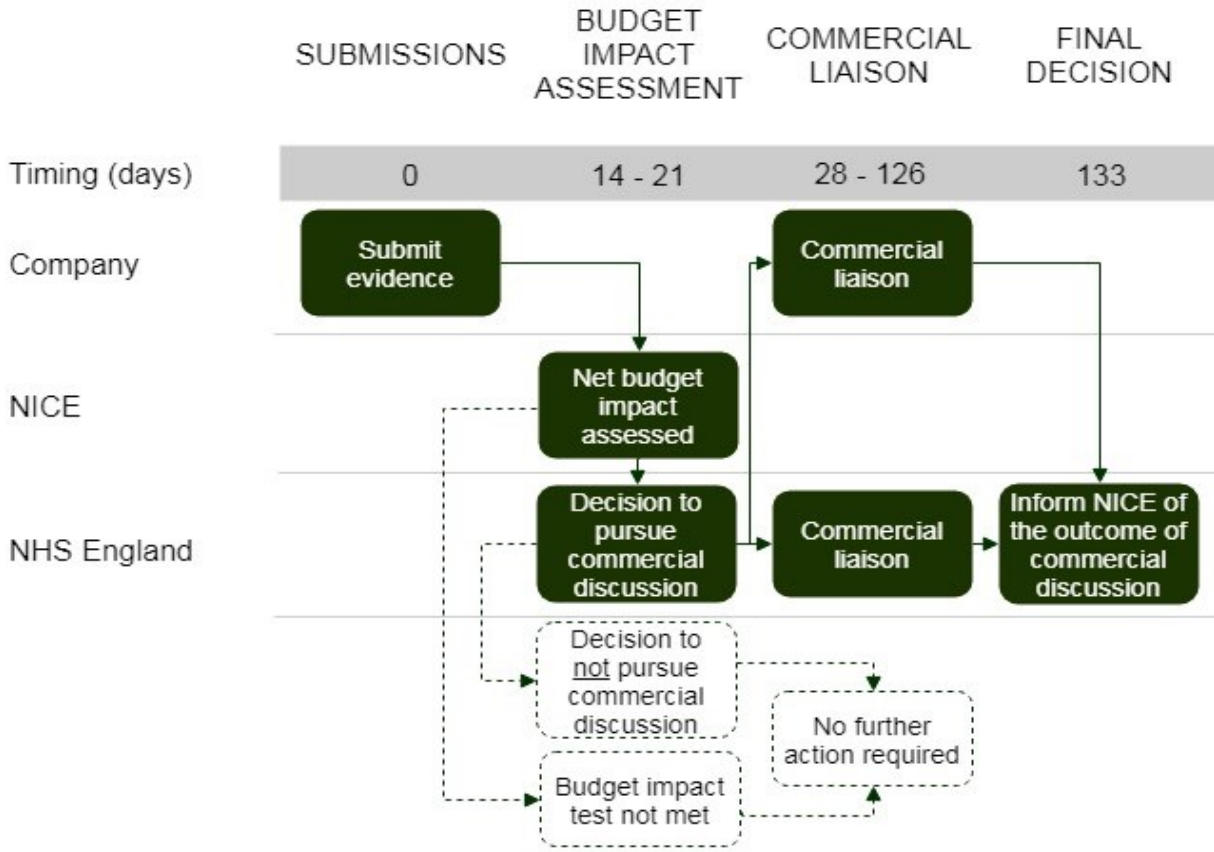
5.8 NICE will inform the company and NHS England of any technology which is likely to exceed a net budget impact of £20 million in each of the first 3 financial years of its use, normally within 17 calendar days after receiving the company submission.

5.9 Within 7 calendar days after receiving the net budget impact estimate, NHS England must inform NICE whether it intends to have a commercial discussion with the company. This will allow NICE to plan for potential changes to the timelines of a technology appraisal.

5.10 The budget impact commercial discussion between the company and NHS England will be carried out in parallel with the appraisal timescales. NHS England must provide a progress update to NICE at least 7 calendar days before the first appraisal committee meeting. Any budget impact commercial agreements confirmed at this point will be to specifically manage the net budget impact of the technology, and will not be reviewed by the appraisal committee.

5.11 For a rapid review or Cancer Drugs Fund review topic, the time frame for the budget impact commercial discussion between the company and NHS England will be readjusted accordingly.

Figure 7 Steps in budget impact assessment (before the first appraisal committee meeting)



First appraisal committee meeting

See figures 8 and 9 for an overview of the process and timelines.

5.12 If the appraisal committee recommends the technology as an option or makes a recommendation that optimises use of the technology, NICE will update its budget impact assessment of the technology.

5.13 NICE will inform the company and NHS England of the (new) estimate for budget impact, at the same time the appraisal consultation document (ACD) or final appraisal document (FAD) is published.

5.14 If NHS England and the company intend to pursue a commercial access agreement after the first appraisal committee meeting, and they anticipate that it will need more time than the next phase of the NICE process provides, NHS England must formally notify NICE 7 calendar days after receiving details of the potential budget impact of the committee's recommendations. NICE will suspend the appraisal process for a maximum of 12 weeks, to allow a second opportunity for commercial engagement and will inform consultees and commentators. NICE will decide when the appraisal will restart. The subsequent appraisal committee meeting will be rescheduled in line with the time needed for concluding the commercial engagement.

5.15 If NHS England intends to apply for a variation to the funding requirement after the first appraisal committee meeting, it must do so at the earliest opportunity, and no later than the end of the suspension period.

5.16 When a FAD is issued for appeal after the first appraisal committee meeting (the topic has gone straight to FAD), NICE will not offer to formally suspend the process to allow the company and NHS England to re-enter a commercial engagement period. NHS England and the company will be informed of the net budget impact before the release of the FAD and will have an opportunity for commercial engagement before FAD publication.

Figure 8 Steps in budget impact assessment (after the first appraisal committee) when an ACD is released

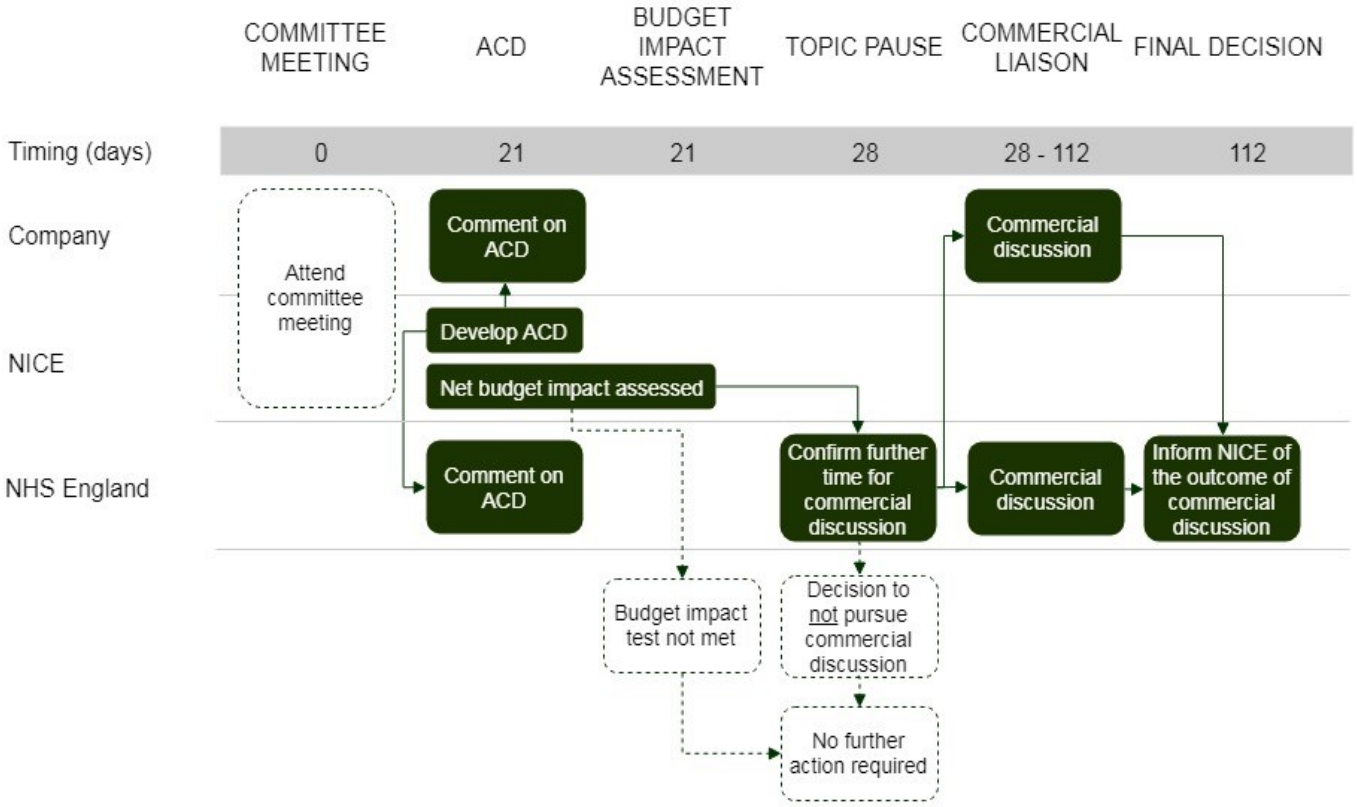
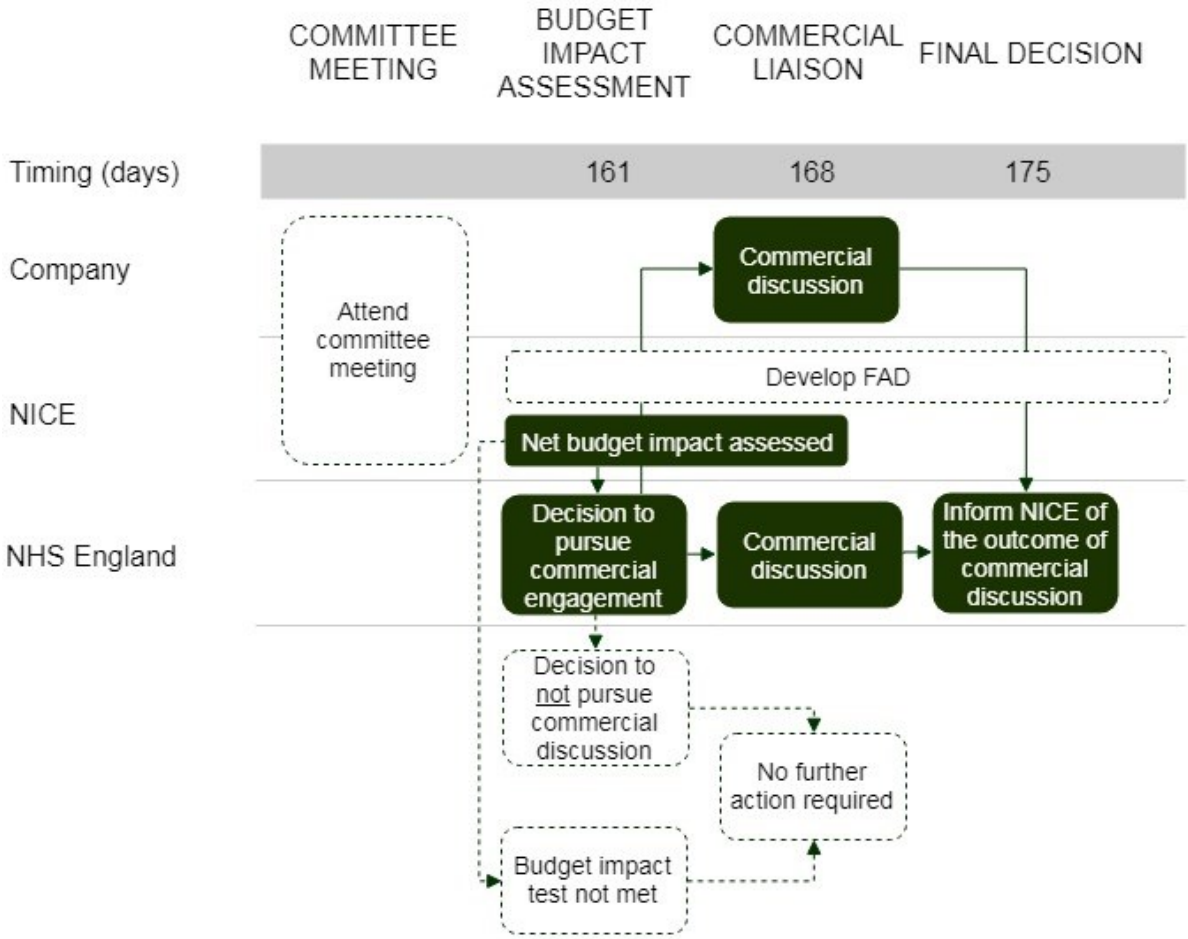


Figure 9 Steps in budget impact assessment (after the first appraisal committee) when a FAD is released



Subsequent technology appraisal committee meeting

5.17 If the appraisal committee chooses to alter the draft recommendations, NICE will update its assessment of the budget impact of the technology, when appropriate (see NICE's assessing resource impact process manual). NICE will inform the company and NHS England of the updated budget impact when the FAD is published. No further pause will be offered to the company and NHS England to re-enter a commercial engagement period.

5.18 In the event that NHS England intends to apply for a variation to the funding requirement, it must do so at the earliest opportunity, and no later than the end of the period for consideration and lodging an appeal.

Guidance executive and applying to vary the funding requirement

5.19 NHS England can advise NICE that it may need to apply to vary the funding requirement directly after receiving the estimate of the net budget impact at the evidence submission stage or at later stages in the technology appraisal.

5.20 When requesting a variation to the funding requirement, NHS England should provide:

- The duration of, and the justification for, the proposed variation.
- The relevant provisions of any commercial arrangement reached with the company.
- In the case of a technology funded from the national specialised commissioning budgets, the amount and phasing of funding that will be made available and how it is intended that this should be applied to patients eligible for treatment.
- In the case of technologies funded by clinical commissioning groups, the direction it intends to give about the phasing of funding during the deferred funding period.
- An assessment of the impact on patients, eligible for treatment under the guidance, but whose treatments will be delayed because of the funding variation, taking into account NHS England's and NICE's responsibilities under equalities legislation.
- Details of the interim commissioning policy that would be applied to phase in funding and to manage access to the technology during the extended funding variation period.

5.21 The NICE appraisal project team will present the application for a variation to the funding requirement to NICE's guidance executive at the earliest opportunity.

5.22 This can be at the stage of developing the ACD (to allow for consultation on guidance executive's decision to vary the timescale for the funding requirement at the same time as consultation on draft recommendations), with a FAD, or during the FAD appeal period.

5.23 At each of these stages, guidance executive will decide whether it will vary the timescale for the funding requirement taking into account whether:

- the budget impact test has been met
- all reasonable opportunities for reaching a commercial arrangement have been pursued
- the request is in proportion to the size of the budget impact
- the request takes account of the severity and acuity of the condition to which the guidance relates
- NHS England's and NICE's duties under equalities legislation have been considered
- an interim commissioning policy has been developed to provide phased funding for, and access to, the technology during the extended funding period.

5.24 Regardless of the duration of the variation requested, all applications will need to contain proposals for a phased allocation of funding.

5.25 For technologies for which the budget impact test is met, guidance executive will consider applications to vary the funding requirement, normally for up to a maximum of 3 years. In exceptional circumstances, a longer period may be considered.

5.26 Applications to vary the funding requirement are specific to each appraisal. However, when considering technologies with indications for which a treatment has already been recommended and a funding variation is in place, NICE will take into account the combined budget impact for both technologies, when considering an application for a funding variation for the second (and subsequent) technologies.

5.27 When guidance executive decides to vary the timescale for the funding requirement, this decision will be shared with consultees and commentators, including NHS England and the Secretary of State for Health and Social Care, for a 21 calendar day consultation period. The provisional decision will be

published for information on the NICE website 7 calendar days later (see figure 10).

5.28 Comments received during consultation from consultees and commentators will be presented to guidance executive to reach a final decision on the timescale for the funding requirement. The decision and comments received will be published on the NICE website at the next appropriate step in the process.

5.29 The final guidance will refer to the variation to the funding requirement (when appropriate).

5.30 In line with the Regulations, consultees, including NHS England, can lodge an appeal against this decision.

5.31 As the decision to vary the timescale for the funding requirement is made by guidance executive, and not the appraisal committee, a representative of guidance executive will attend any appeal hearing on behalf of NICE.

Figure 10 Steps in the assessment of the application to vary the funding requirement

Tools and resources

5.32 The implementation of the budget impact assessment within the appraisal process will not affect publication of the advice and tools to support the local implementation of NICE guidance. This includes resource impact tools or statements for most technology appraisals and additional tools for some technology appraisals.

6 Reviews

Standard review considerations

6.1 When NICE publishes guidance, a suggested time for its review is given. This is the length of time after publication when NICE will consult with relevant organisations on a proposal about 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 review consideration varies 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 suggested review time 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 time of review (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 needed. The steps involved are shown in figure 11.

6.3 NICE develops the review proposal after gathering relevant information and doing 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 evidence. NICE also asks companies to provide information about the existing marketing authorisation (or equivalent) or any extensions to the marketing authorisation.

6.4 When guidance includes a patient access scheme or commercial access agreement, the (possible) review provides a useful opportunity to review how the scheme or agreement is operating and consider whether it would be appropriate to make any changes to simplify and improve its operation. Any changes to a patient access scheme or commercial access agreement are subject to discussion with, and agreement by, NHS England.

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

6.6 NICE proposes to update the published guidance if there is new evidence available that is likely to change the existing recommendations. Evidence that may lead to a change in the clinical or cost effectiveness of the technology, or an extension or revision to the marketing authorisation or CE mark for the technology could lead NICE to propose that the guidance should be updated.

6.7 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 1 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). See NICE's document on updating technology appraisals within clinical guidelines.

6.8 The guidance executive decides on one of the following options if the published guidance does not need updating:

- The guidance is valid and does not need an update because the evidence base is not likely to change substantially. It is therefore designated as static guidance.
- Incorporate the published guidance into guidance from another guidance-producing centre. The technology appraisal is then designated as static guidance and remains in force.

6.9 When the guidance executive decides that guidance can be designated as static, it may also decide that a consultation with consultees and commentators is not needed. NICE will notify consultees and commentators of the decision to designate the guidance as static guidance and will share the paper considered by the guidance executive. NICE publishes the review decision on its website 7 calendar days after notifying consultees and commentators.

6.10 If the guidance executive has agreed to consult with consultees and commentators on 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. NICE publishes the review proposal, together with the list of consultees and commentators, on its website 7 calendar days after sending for consultation.

6.11 Consultees and commentators must send comments to NICE within 28 calendar days of the date of sending for the comments to be considered.

6.12 After considering the comments received during consultation, the NICE Technology Appraisal Programme agrees a review decision. If the review decision differs from the original proposal, the guidance executive will agree the most appropriate option, taking consultation comments into account.

6.13 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. NICE publishes the final decision and the table of comments on its website 7 calendar days after contacting consultees and commentators.

6.14 If guidance needs updating within the Technology Appraisal Programme, the update is scheduled.

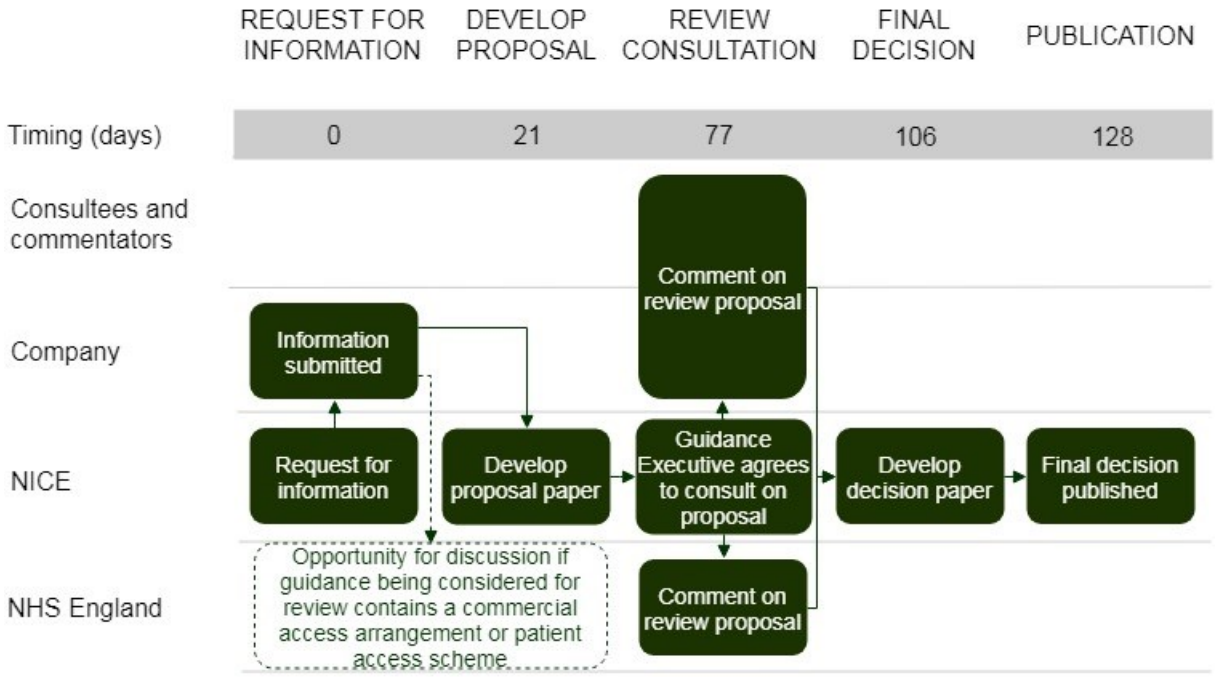
6.15 For guidance designated as static guidance, NICE considers whether a review is needed 5 years after the guidance is added to the static list. This is called a 'static list review'. NICE does a literature search to see if there is any new evidence to update the existing recommendations.

6.16 If it is decided that the evidence base has changed significantly, then a full review proposal is developed to assess whether an update of the guidance is needed. If a review of the static guidance uncovers no new evidence that is likely to change the existing recommendations, it remains on the static list.

6.17 NICE notifies consultees and commentators of the outcome of the static list review, and publishes this information on the NICE website 7 calendar days after sending it to consultees and commentators.

6.18 At any point during the development of a review proposal, NICE may decide that the consideration of a review is not appropriate. This may be because evidence not yet available is considered likely to change the existing recommendations. In this instance, NICE notifies stakeholders of the decision to defer the review proposal. The decision is also published on the NICE website. NICE also identifies the likely time for the next consideration of a review. This is usually within 6 months of the availability of the required evidence.

Figure 11 Summary of the review proposal process



Updating technology appraisal guidance for technologies included in the Cancer Drugs Fund

6.19 NICE will normally review its guidance for a drug funded through the Cancer Drugs Fund within 24 months of publishing it. The aim of the Cancer Drugs Fund guidance review is to decide whether or not the drug can be recommended for routine use. The drug (or indication) may not remain in the Cancer Drugs Fund once the guidance review has been completed.

6.20 Progress with data collection will be reviewed regularly. An annual report, provided by the company or the organisation collecting the data, will be

submitted to NICE to check whether the data collection is on track, and to establish whether any additional action is needed. Guidance may be considered for review before the published review date if there is significant new evidence that either supports the original case for clinical and cost effectiveness, or when the evidence points to the likelihood that the original recommendations are not valid. The steps involved are shown in tables 6, 7 and 8 and figure 12.

6.21 The published guidance will be withdrawn, and the drug removed from the Cancer Drugs Fund, if the company stops data collection for reasons other than an early guidance review.

6.22 Review of guidance for cancer drugs funded by the Cancer Drugs Fund will be scheduled into the technology appraisal work programme to coincide with the end of the data collection period determined at the point of entry of the drug into the Cancer Drugs Fund. This will normally not be longer than 24 months. If NICE considers it reasonable to review the published guidance earlier than at the end of the designated data collection period, the decision to do so will be subject to consultation with consultees and commentators.

6.23 The guidance review will be done through a shortened technology appraisal process, which will normally take a maximum of 6 months. The company will have 28 calendar days to submit the new evidence from data collection, and the evidence review group (ERG) will have 28 calendar days to critique the new evidence (see table 7).

6.24 Following the ERG critique, the technical team will compile the technical report within 21 calendar days and issue it for technical engagement with consultees and commentators for 14 calendar days.

6.25 The Cancer Drugs Fund guidance review will take into account the data that have become available since the original appraisal, together with any change to the patient access scheme or commercial access agreement proposed by the company. No changes to the scope of the appraisal will be considered.

6.26 Companies must provide an evidence submission to support the Cancer Drugs Fund guidance review. The managed access agreement signed at the time of the original appraisal includes this obligation.

6.27 After the first committee meeting for the guidance review, a FAD will be produced if its recommendations are consistent with the original conditions for use in the Cancer Drugs Fund. In all other circumstances, an ACD will be produced.

Table 6 Expected timelines for the Cancer Drugs Fund guidance review – shortened technology appraisal process

		Calendar days (approx.)
Step 1	NICE invites organisations to participate in the guidance review as consultees or commentators	0
Step 2	NICE receives evidence submission from company holding the marketing authorisation	28
Step 3	NICE requests clarification from the company on the evidence submission	35
Step 4	NICE invites selected clinical experts, NHS commissioning experts and patient experts to attend the appraisal committee meeting	
Step 5	NICE creates the technical report	55
Step 6	NICE issues the technical report for engagement with consultees and commentators	60
Step 7	NICE sends the technical report to the appraisal committee	80

*Timelines may change in response to individual appraisal requirements.

Table 7 Expected timelines for the Cancer Drugs Fund guidance review using the shortened appraisal process if an ACD is produced*

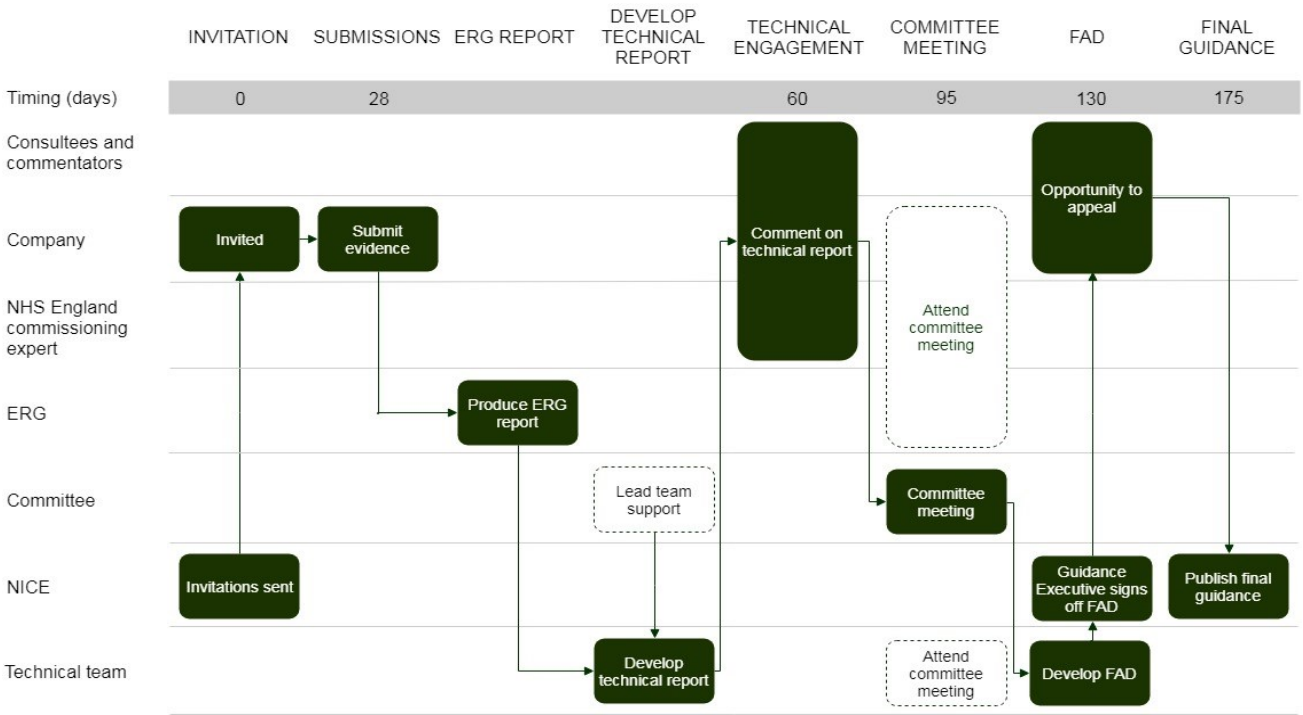
		Calendar days (approx.)
Step 7	Appraisal committee meeting.	95
Step 8	The ACD is produced. NICE distributes the ACD and publishes it on the website 7 calendar days later.	116
Step 9	Fixed 28 calendar day consultation period on the ACD.	144
Step 10	Appraisal committee meeting to consider comments on the ACD from consultees and commentators, and comments received through the consultation on the NICE website. Appraisal committee agrees the content of the FAD.	155
Step 11	The FAD is produced. NICE distributes the FAD and publishes it on the website 7 calendar days later.	190
*Timelines may change in response to individual appraisal requirements.		

Table 8 Expected timelines for the Cancer Drugs Fund guidance review using the shortened appraisal process if an ACD is not produced*

		Calendar days (approx.)
Step 7	Appraisal committee meeting to develop a FAD.	95

Step 8	The FAD is produced. NICE distributes the FAD and publishes it on the website 7 calendar days later.	130
*Timelines may change in response to individual appraisal requirements.		

Figure 12 Summary of the Cancer Drugs Fund guidance review using a shortened technology appraisal process



7 Further information

Process working group

A process working group, from NICE's Centre for Health Technology Evaluation, developed this document.

Jenniffer Prescott (Project lead)	Associate Director
Jenna Dilkes (Chair)	Programme Manager
Elisabeth George	Associate Director
Frances Sutcliffe	Associate Director
Carl Boswell	Programme Manager
Andrew Kenyon	Programme Manager
Jeremy Powell	Project Manager
Stephanie Yates	Project Manager
Michelle Adhemar	Project Manager
Joanna Richardson	Technical Adviser
Alex Filby	Technical Adviser
Sally Doss	Technical Adviser
Nicola Hay	Technical Adviser
Jasdeep Hayre	Technical Adviser
Frances Dixon	Technical Adviser
Rebecca Albrow	Technical Adviser
Bernice Dillon	Technical Adviser

Ross Dent	Technical Analyst
Mary Hughes	Technical Analyst
Victoria Kelly	Technical Analyst
Thomas Strong	Technical Analyst
Aminata Thiam	Technical Analyst

Glossary

Abstract

A 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.

Appraisal committee

A standing advisory committee of NICE. Includes people who work in the NHS, lay members, people from relevant academic disciplines and the pharmaceutical and medical device industries.

Appraisal consultation document (ACD)

Sets out the appraisal committee’s preliminary recommendations to NICE.

Carer

In this guide the term 'carer' refers to a person who provides unpaid care by looking after a relative, friend or partner who needs support because of ill health, frailty or disability.

Cancer Drugs Fund

New technology appraisal processes and methods were implemented in line with the new operating model of the Cancer Drugs Fund. A modified appraisal process for cancer drugs was introduced on 1 April 2016. Information on the new Cancer Drugs Fund operating model is available on NHS England’s website.

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 done in accordance with the published appraisal process and methodology.

Clinical effectiveness

The extent to which an intervention produces an overall health benefit, taking into account beneficial and adverse effects, in routine clinical practice. It is not the same as efficacy.

Clinical expert

In technology appraisals, clinical experts act as expert witnesses to the appraisal committee. They are selected on the basis of specialist expertise and personal knowledge of the technology and/or other treatments for the condition. They provide a view of the technology within current clinical practice, and insights not typically available in the published literature.

Commentator

An organisation that engages in the appraisal process but is not asked to prepare a submission. Commentators are invited to comment on the draft scope document, the assessment report and the appraisal consultation document (ACD). They receive the final appraisal document (FAD) for information only. These organisations include relevant comparator technology companies, Healthcare Improvement Scotland, relevant National Collaborating Centres, related research groups and other groups as appropriate.

Commercial in confidence

See ‘In confidence material’.

Committee papers

The committee papers that are issued and published with an ACD or a FAD include all of the evidence seen by the appraisal committee. They are made up of the technical report, ERG report, written submissions, and the personal statements of patient experts and clinical experts, as well as comments received on the technical

report. For second and subsequent committee meetings they will also include consultation comments and responses.

Company

The company that manufactures or sponsors either the technology being appraised, or the comparator technology.

Comparator

The standard intervention against which the intervention under appraisal is compared. 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 carry out 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

An organisation that takes part in the appraisal of a technology. Consultees can comment on the draft scope, the assessment report and the appraisal consultation document (ACD) during the consultation process. Consultee organisations can nominate clinical experts, commissioning experts and patient experts to present their personal views to the appraisal committee. All consultees are given the opportunity to appeal against the final appraisal document (FAD).

Cost effectiveness

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

Decision problem

A clear description of the interventions, patient populations, outcome measures and perspective adopted in a health technology evaluation, relating specifically to the decision(s) that the evaluation is designed to inform.

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 needed, 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 and Social Care

The Department of Health and Social Care 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 such as environmental hazards to health, infectious diseases, health promotion and education, the safety of medicines, and ethical issues.

Early access to medicines scheme

The Medicines and Healthcare products Regulatory Agency's (MHRA) early access to medicines scheme (EAMS) aims to give patients with life-threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation. It provides an opportunity for important drugs to be used in UK clinical practice in parallel with the later stages of the regulatory process.

It is anticipated that medicines with a positive EAMS scientific opinion could be made available to patients 12 to 18 months before formal marketing authorisation.

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.

European Medicines Agency

A decentralised agency of the European Union responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union.

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 and/or patients/carers).

Evidence review group (ERG)

An independent assessment group commissioned by the National Institute for Health Research Health Technology Assessment Programme to produce an independent assessment of the evidence submitted by the company with a technology being appraised within the standard technology appraisal process.

Final appraisal document (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.

Guidance executive

A team comprising the executive directors and centre directors at NICE who are responsible for approving the final appraisal document before publication.

Health-related quality of life

A combination of a person's physical, mental and social wellbeing.

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 medical technologies.

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 difference in the mean costs of a technology compared with the next best alternative to the differences in the mean outcomes.

Indication

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

Lay member

A lay member is a committee member with a patient, service user, carer or community background. The lay member's role is the same as other committee members, and additionally includes contributing a lay perspective and highlighting patient and carer issues.

Lead team

The lead team consists of 3 committee members; 1 who focuses on cost effectiveness; 1 on clinical evidence and 1 on patient and carer evidence (called the lay lead).

Marketing authorisation

An authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA) or European Commission to market a medicinal product.

Medicines and Healthcare products Regulatory Agency (MHRA)

The Executive Agency of the Department of Health and Social Care. 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 Institute for Health Research – Health Technology Assessment 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 Programme on behalf of the NIHR. The aim of the 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 treatment with a preventive or therapeutic intervention. Outcome measures can be either intermediate or final end points.

Patient Access Scheme Liaison Unit

The Patient Access Scheme Liaison Unit (PASLU) at NICE advises NHS England on the feasibility of patient access scheme proposals. When assessing a patient access scheme proposal, the PASLU considers the key principles for implementing patient access schemes in England and Wales as outlined in the 2014 Pharmaceutical Price Regulation Scheme.

Patient expert

Acts as an expert witness to the appraisal committee. Patient experts have used the technology either personally or as part of a representative group. Patient experts attend as individuals; they may be either somebody with personal experience of the condition, and if possible the technology, or a member of a patient and carer organisation for the condition being appraised.

Pharmaceutical Price Regulation Scheme (PPRS)

The 2014 PPRS is a non-contractual voluntary scheme. The parties to this agreement are the Department of Health and Social Care and 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). The scheme aims to ensure that safe and effective medicines are available on reasonable terms to the NHS.

Public Involvement Programme (PIP)

The PIP is the team at NICE that supports and develops public involvement across NICE's work programme. A PIP public involvement adviser is assigned to each appraisal and supports patient and carer consultee organisations, their representatives, and individual patients or carers throughout the appraisal. The PIP public involvement adviser also supports the lay members of the appraisal committees.

Redacted

If documents contain confidential information, it must be redacted, that is, academic in confidence and commercial in confidence information should be replaced with asterisks and then highlighted in black.

Remit

This is the brief the Department of Health and Social Care 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.

Systematic review

Research that summarises the evidence on a clearly formulated question according to a predefined protocol. Systematic and explicit methods to identify, select and

appraise relevant studies, and to extract, collate and report their findings are used. Statistical meta-analysis may or may not be used.

Technical engagement

A period of 28 calendar days when the technical report is sent to consultees and commentators and experts to seek their views on the judgements made by the technical team and to specify any remaining clinical uncertainties.

Technical report

A report created to provide the preliminary scientific judgements of the technical team to the appraisal committee. It is created following consideration of the company submission, the ERG report, consultee and commentator and expert statements and any discussions with the company or experts about the appraisal.

Technical team

A team comprising members of the NICE appraisal committee (including the committee chair or vice chair) and NICE staff, who are responsible for considering submissions and providing preliminary scientific judgements and advice to the appraisal committee.

Technology appraisal

The process of developing recommendations on the use of new and existing health technologies within the NHS in England.

Technology assessment

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

Terminated appraisal

The standard technology appraisal process relies on companies 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 company did not make an evidence submission when making local decisions on whether to offer the treatment.

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