NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interim Process and Methods of the Highly Specialised Technologies Programme

Principles

1. Our guidance production processes are based on key principles, outlined in our Social Value Judgments document, that define how we work. The principles are:

   - Scientific rigour
   - Inclusiveness
   - Transparency
   - Independence
   - Challenge
   - Review
   - Support for implementation
   - Timeliness

2. The application of these principles has been fundamental to our success and they are valued highly by our stakeholders. Therefore the process for the new programme needs to adhere to these principles and set the same standard of excellence for which the Institute is recognised world-wide.

Process for the evaluation of highly specialised technologies

3. An outline process is described below. The core of the process is an evidence submission by the manufacturer or sponsor of the technology on key aspects of the decision making framework for which they can reasonably be expected to hold the evidence base. This allows for speedy review and also has the advantage of being able to be undertaken whilst formal marketing authorisation approval is being sought.

4. A review of the manufacturer or sponsor submission will be undertaken by an external group to NICE (the 'review group'). Its remit will be to critically evaluate the submission, clarify where necessary (see also below), identify its strengths and weaknesses and supplement it with their own explorations or re-modelling, where appropriate. On occasion, the NICE Decision Support Unit will be asked to provide advice or further analyses.

5. The review group will further be asked to provide evidence, and synthesis of that evidence, for aspects of the decision making framework that are less likely to be provided by the company. This includes consideration of evidence provided by other consultees, particularly from the patient/carer groups.

6. The review group will contribute to the scoping phase, provide technical input into interactions the Institute may have with evidence submitters and provide other information and evidence when necessary, particularly where it concerns aspects of the decision making framework that are less likely to be addressed by the company.

7. Consultee and commentator organisations will be identified for each highly specialised technologies evaluation (i.e. patient, professional and commercial organisations that have an interest in the technology, plus the NHS, NHS Commissioning Board, and the DH). Statements from interested parties, particularly patient/carer groups and professional organisations on current management of the disease and patient experience will be sought, and nominated experts (clinical, patient, NHS) will be invited to attend the evaluation committee meeting(s), as will two company representatives. Arrangements for selection of specialists and experts follow those set out for Technology Appraisals at NICE.

8. Specific evidence submissions will be sought from individual consultees, particularly patient/carer groups, where appropriate. The need for this will be determined at scoping for the topic.

9. Formal clarification of aspects of the evidence submissions from the company, review group, or occasionally other consultees, will be sought by the Chair and Lead Team (see below) in advance of the meeting of the full Evaluation Committee.

10. A report for Committee will be developed by NICE on behalf of the Chair and the Lead Team, based on the evidence submission by the company, submissions by other consultees and review by the independent group.

11. NICE advisory committee meetings are, in part, open to members of the public and press. There may be occasions when a meeting will be entirely closed because it is not possible to conduct any discussion without referring to confidential information. Committee decisions are normally based on consensus. If a vote is taken, it will be noted in the minutes. Clinical specialists, NHS commissioning experts, manufacturer representatives and patient experts respond to questions from the Committee and provide clarification. They contribute to the debate with the Committee but do not make a formal presentation to the Committee. Arrangements for attendance at public meetings are similar to those used for other advisory committee meetings, specifically those for Technology Appraisals.

12. Formal consultation will only take place if the recommendations emerging from the Committee are substantively restrictive. A substantively restrictive recommendation will be one that is more limited than the terms of

regulatory approval (or, in the absence of a regulatory approval process, the claims of the sponsor for how the technology should be used), to an extent judged to be significant in clinical practice.

13. When required, the consultation phase will be similar to the existing technology appraisal consultation process: a request for feedback on the preliminary recommendations from consultees and commentators plus the opportunity for feedback from members of the public via our website. Consultees and commentators will be supplied with an evaluation report at this point, comprising all the evidence seen by the evaluation committee, except that which is designated commercial-in-confidence by the manufacturer, and including any economic models developed by the company or used to inform exploratory analyses by the review group. Responses to consultation will be considered by the Evaluation Committee at a second meeting and final recommendations will be prepared.

14. The purpose of the consultation is to seek views on the Evaluation Committee's provisional recommendations and to determine whether they are an appropriate interpretation of the evidence considered. NICE invites comments on whether:
    - all the evidence available to the Evaluation Committee has been appropriately taken into account
    - the summaries for benefits and costs are reasonable interpretations of the evidence
    - the provisional recommendations are sound and constitute a suitable basis for guidance on national specialised commissioning
    - there are any equalities-related issues that need special consideration that are not covered in the ACD.

15. At the consultation stage, the Centre or Programme Director must agree to accept any new evidence before it is submitted. New evidence will only be accepted if it is likely to affect the provisional recommendations. The new evidence must be presented as a separate appendix to the general comments to be submitted in response to consultation. NICE may need to extend timelines to allow for new evidence to be considered.

16. If the recommendations emerging from the first meeting of the Evaluation Committee broadly support use consistent with the approved indications of the technology, final recommendations will be prepared. The NICE project team undertakes a last review of the final recommendations, signs them off, and submits a report to NICE's Guidance Executive (made up of NICE's Executive Directors and Centre Directors). The Guidance Executive checks that the Evaluation Committee has appraised the technology in accordance with the terms of the Secretary of State for Health's referral, the scope and the programme's methods and processes. If satisfied, the Guidance Executive approves the final recommendations

for publication on behalf of the NICE Board. Consultees and commentators will be also supplied with an evaluation report at this point, comprising all the evidence seen by the appraisal committee, except that which is designated commercial-in-confidence by the manufacturer.

17. Appeals can be lodged against the final recommendations by any of the consultees engaged in the appraisal. We anticipate using the grounds proposed in the regulations laid before parliament: in making the assessment/evaluation that preceded the recommendation, NICE failed to act fairly, or exceeded its powers, or the recommendation is unreasonable in the light of the evidence submitted to NICE.

18. We envisage a formal step of 'reconsideration' of the case for national commissioning at a limited number of time points. These reconsideration steps will provide the opportunity for the company and NICE to address one or more of a number of elements that may support the case for national commissioning. These elements include:

    identification of sub-group(s)
    volume of sales
    cost per patient
    service delivery issues
    pricing arrangements (akin to those now available as Patient Access Schemes)
    conditions for approval with research.

19. Reconsideration is expected to be normally led by the company at the public consultation stage of the process, and NICE-led after the final recommendations have been developed and any appeals are held.

20. The core process requires approximately 17 weeks from receipt of submissions from stakeholders, excluding consultation, reconsideration and without an appeal. In case of public consultation this will be extended to 27 weeks. Additional process elements will add to this and will necessitate (re)use of core process elements.

Action	By	Duration (weeks)	Time from submission (weeks)
Core process			
Consultation on the scope	Company, patient groups and other consultees	4	n.a.
Preparation evidence submission	Company, patient groups and other consultees	8	0
Evidence review, collection and synthesis	Review group	8	8

Report for Committee	NICE on behalf of Chair and Lead Team	2	10
Committee meeting and drafting of consultation document*	Evaluation Committee, NICE	3	13
Public consultation**	Consultees	4	17
Consideration of comments received	Chair, lead team and NICE	3	20
Committee meeting and drafting of final recommendations	Evaluation Committee, NICE	4	24 or 14***
Appeal consideration	Consultees	3	27 or 17***
Additional process			
Formal clarification of evidence submission(s)	Chair, Lead team, Review group, NICE, Company (occasionally other consultees)	3 (2 for company, 1 for NICE review)	
Reconsideration	Company, NICE, NHS-CB, Review group	4 (2 for company, 2 for NICE review)	
Appeal	Consultee(s), NICE	8 weeks	

* Positive opinion from the relevant regulatory body must have been received

** Marketing authorization must have been granted.

*** Without public consultation.

21. Topics will be scheduled so that the Evaluation Committee first considers a topic as soon as possible post positive opinion by the Committee for Medicinal Products for Human Use or the equivalent committee at MHRA. Draft recommendations cannot be published without receipt of marketing authorisation for the technology, and are anticipated to be issued within approximately 3-4 months of confirmation from the European Commission that a marketing authorization has been granted.

22. Topics to be evaluated through the programme will be formally referred by Ministers to NICE. Criteria for topic selection will be the same as those used currently by AGNSS (see above). The criteria will be reviewed over the next months, to ensure that they continue to align with the work by the NHS Commissioning Board on the commissioning of highly specialised services.

23. The process for selection of topics for the highly specialised technologies programme will be similar to that of the current process for the selection of technology appraisals. The topic selection process will use five distinct decision points, involving expert input from external clinicians and NICE at the filtering stages, and from consultees and commentators during the scoping stage (including at scoping workshops). Decisions on progression

of a topic to scoping and subsequently to recommendation for referral will be made by representatives from NICE, the Department of Health and the NHS Commissioning Board. A procedural note to assist those involved will be published, the draft of which is included in an appendix to this paper.

24. Referrals to the programme will be phrased as follows:

    'To evaluate the benefits and costs of <technology x> within its licensed indication for the treatment of <disease y> for national commissioning by the NHS Commissioning Board'.

25. Guidance published by the programme will be phrased as follows:

    '<Technology x> is recommended as an option for the treatment of <disease y> in the context of national commissioning by the NHS Commissioning Board'

26. Regulations laid before parliament indicates that the guidance will include the recommendation that the NHS Commissioning Board […] provide funding within a specified period to ensure that the highly specialised health technology can be made available for the purpose of treatment of patients.

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

28. NICE develops the review proposal after gathering relevant information and undertaking a literature search. NICE identifies new indications for the appraised technology, searches for new related technologies, assesses the progress of ongoing trials, and gathers new available evidence. NICE also asks manufacturers and sponsors to provide information relating to marketing authorisation (or equivalent) or any extensions to the marketing authorisations. NICE's Guidance Executive uses this information to consider the review proposal and decides if and how the published guidance should be updated.

29. NICE must ensure that the manufacturer or sponsor prepares the best possible evidence submission for the Evaluation Committee. NICE's technical leads do not validate the submission but they help to clarify substantive issues. If, after all reasonable requests for clarification, NICE is not satisfied that the evidence submission is adequate for the Evaluation Committee to make a decision or no evidence submission has

been received, the Centre Director will recommend to NICE's Guidance Executive that the highly specialised technology evaluation should be terminated. NICE will return an inadequate evidence submission to the manufacturer or sponsor noting that no submission has been received. NICE will subsequently advise the NHS that the evaluation has been terminated and that 'NICE is unable to recommend the use in the NHS of the technology because no evidence submission was received from the manufacturer or sponsor of the technology'. NICE will also provide an explanation to help the NHS make local decisions on making the technology available. A terminated appraisal can be re-initiated if the manufacturer or sponsor indicates that they wish to make a full evidence submission.

30. Information submitted to NICE will be handled in line with obligations, processes and procedures in place for the Institute in general and Technology Appraisals programme specifically. NICE publishes unconfirmed minutes of the Committee meeting on its website within 15 working days of the meeting. When the Committee has approved them, NICE publishes the confirmed minutes on its website normally within 6 weeks of the meeting. The minutes of a Committee meeting provide a record of the proceedings and a list of the issues discussed.

Methods for the evaluation of highly specialised technologies

31. The Evaluation Committee is an independent advisory body. Members include people who work in the NHS, patient and carer organisations, relevant academic disciplines, and pharmaceutical and medical devices industries. The Evaluation Committee makes recommendations to the Institute regarding the benefits and costs of highly specialised technologies for national commissioning by the NHS Commissioning Board. It is also the role of the Evaluation Committee to recommend against the use of a technology if the benefits to patients are unproven or costs of technology are unreasonable. The Institute is responsible for the dissemination of the final guidance to the NHS.

32. When formulating its recommendations to the Institute, the Evaluation Committee has discretion to consider those factors it believes are most appropriate to each evaluation.

33. The Evaluation Committee takes into account advice from the Institute on the appropriate approach to making scientific and social value judgements. Advice on social value judgements is informed by the work of the Citizens Council, NICE advisory bodies, and NICE's Board, as well as legislation on human rights, discrimination and equality as reflected in NICE's equality scheme. Principles that describe the social value judgements that should, generally, be considered by the Evaluation Committee have been provided in the Institute's document, 'Social value judgements: principles for development of NICE guidance, second edition'.

34. A Lead Team consisting of the Chair and a limited number of specialist members of the Committee meets in advance of the full Committee to seek formal clarification of the evidence submissions received from the company, the review group, or occasionally other consultees.

35. The decision making framework to be used by the Highly Specialised Technologies Evaluation Committee builds on the work by AGNSS, and incorporates NICE's exploratory work on appraising medicines and technologies, including the 2004 exploratory work on 'ultra-orphan drugs'.

36. Given the very small numbers of patients living with these very rare conditions a simple utilitarian approach, in which the greatest gain for the greatest number is valued highly, is unlikely to produce guidance which would recognise the particular circumstances of these vary rare conditions. These circumstances include the vulnerability of very small patient groups with limited treatment options, the nature and extent of the evidence, and the challenge for manufacturers in making a reasonable return on their research and development investment because of the very small populations treated.

37. In order to form the guidance, the Committee will take account of the following criteria:

Nature of the condition

- Disease morbidity and patient clinical disability with current standard of care
- Impact of the disease on carers' quality of life
- Extent and nature of current treatment options

Impact of the new technology

- Clinical effectiveness of the technology
- Overall magnitude of health benefits to patients and, when relevant, carers
- Heterogeneity of health benefits within the population
- Robustness of the current evidence and the contribution the guidance might make to strengthen it
- Treatment continuation rules

Cost to the NHS and Personal Social Services

- Budget impact in the NHS and PSS
- Robustness of costing and budget impact information
- Patient access agreements

Value for money

- Technical efficiency (the incremental benefit of the new technology compared to current treatment
- Productive efficiency (the nature and extent of the other resources needed to enable the new technology to be used
- Allocative efficiency (the impact of the new technology on the budget available for specialised commissioning)

Impact of the technology beyond direct health benefits

- Whether there are significant benefits other than health
  - Whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services;
  - The potential for long-term benefits to the NHS of research and innovation;

The impact of the technology on the delivery of the specialised service

- staffing and infrastructure requirements, including training and planning for expertise

38. The Committee will consider each of the criteria listed above and, after

reviewing the evidence and commentary, reach a consensus on whether

the highly specialised technology can be recommended for national commissioning.

39. The Evaluation Committee's judgement on clinical effectiveness will also take account of:

    The nature and quality of the evidence derived from:
    - The submission from the manufacturer
    - The commentary provided by the independent academic groups
    - The written submissions of the consultees
    - The views expressed by the clinical specialists, particularly their experience of the technology in clinical practice
    - The view of the patient experts and carers on the experiences of patients with the condition and those who have used the technology

    Uncertainty generated by the evidence and differences between the evidence submitted for licensing and that relating to effectiveness in clinical practice.

    The possible differential benefits or adverse outcomes in different groups of patients.

    The impact of benefits and adverse outcomes associated with the technology as seen from the patient's perspective.

    The position of the technology in the overall pathway of care and the alternative treatments that are established in clinical practice.

    The extent to which these factors are taken into account when making judgements about the evidence of clinical effectiveness is a matter for the Committee's discretion which will be exercised in the light of the particular features of the condition and the technology.

40. When considering a treatment continuation rule, the Committee will consider:

    the robustness and plausibility of the end point on which the rule is based;

    whether the 'response' criteria defined in the rule can be reasonably achieved;

    the appropriateness and robustness of the time at which response is measured;

    whether the rule can be incorporated into routine clinical practice;

    whether the rule is likely to predict those patients for whom the technology is particularly cost effective;

    considerations of fairness with regard to withdrawal of treatment from people whose condition does not respond to treatment.

41. When evaluating cost to the NHS and PSS, the Committee will take into account the total budget for specialised services, and how it is allocated, as well as the scale of investment in comparable areas of medicine. The committee will also take into account what could be considered a reasonable cost for the medicine in the context of recouping manufacturing, research and development costs from sales to a limited number of patients.

42. When the evidence of clinical effectiveness or impact of a highly specialised technology on other health outcomes is either absent, weak or uncertain, the Evaluation Committee may recommend that the technology is used only in the context of research or the technology is recommended as an option, but that research is conducted. Before issuing such recommendations the Committee will consider the following factors:

    - the need for and potential value to the NHS of additional evidence that can inform the development of NICE guidance and clinical practice on the use of the technology and
    - the uncertainty in the analysis and what could be gained by reconsidering the decision in the light of research findings
    - whether the research is feasible in circumstances when the Evaluation Committee recommends the intervention for NHS use outside of the context of research
    - irrecoverable costs incurred from introducing the technology
    - the likely net benefits for all NHS patients of use only in research setting during the time that the recommended research is being conducted.

    In considering these factors the Committee will balance the potential net benefits to current NHS patients of a recommendation not restricted to research with the potential net benefits to both current and future NHS patients of being able to produce guidance and base clinical practice on a more secure evidence base.

43. Recommendations on the use of technologies only in the context of research will not include consideration of which organisation (public or private) will fund the research. The Evaluation Committee will consider:

    - the likelihood that the research needed will be commissioned and successfully report
    - the time it is likely to take for research findings to be available to inform subsequent NICE guidance and clinical practice
    - other factors that may impact on the value of evidence generation, such as other research that is underway or likely to be commissioned and completed.

In considering these factors the Committee may seek advice from research commissioners, the wider research and clinical communities and consultees.

44. Where the Committee both recommends a technology and that further research is conducted, it will consider the factors set out above and be satisfied that the additional research is feasible in the circumstances in which the intervention has been recommended.

45. When technologies are being considered for recommendation only in the context of research, the Committee will explore whether overall, the potential value to the NHS of the recommended research is likely to represent good value in the context of limited research resources.

46. The Evaluation Committee will not normally make recommendations regarding the use of a technology outside of the terms of its marketing authorization, as published in the manufacturer's summary of product characteristics, unless requested to do so by the Secretary of State. Evidence related to the use of a technology under evaluation outside of the terms of the marketing authorization may be considered during the assessment phase of the evaluation and may inform the Committee's deliberations regarding the licensed use of the technology.

47. The Evaluation Committee can consider as comparator technologies that do not have a marketing authorization for the indication defined in the scope when they are considered to be part of established practice for the indication in the NHS. Specifically when considering an 'unlicensed' medicine, the Committee will have due regard for the extent and quality of the evidence, particularly for safety and efficacy, for the unlicensed use.

NICE

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