National Institute for Health and Care Excellence

Highly specialised technologies NICE prioritisation board routing criteria

1 The vision

The Highly Specialised Technologies (HST) Programme evaluates technologies for ultra-rare diseases (defined in NICE strategic principles, and previously referred to as 'very rare'). These ultra-rare diseases are often very severe and debilitating and need specific consideration by the HST Programme. The vision for the HST Programme was last consulted on in 2021. Specifically, it evaluates technologies that:

- meet the definition of an HST, as described in legislation in Schedule 4 of the NHS Commissioning Board and Clinical Commissioning Groups (Responsibilities and Standing Rules) Regulations 2012, or may potentially need nationally coordinated delivery approaches, and
- need consideration using the methods and processes of the HST Programme, as identified through the HST routing criteria.

NICE's standard technology appraisals methods and processes are designed to be flexible, and adaptable for all technologies and conditions. So, they are suitable for most technologies that treat rare conditions and small populations.

The HST Programme is designed to be used in exceptional circumstances. Its purpose is to evaluate technologies for ultra-rare diseases that have:

- small numbers of patients
- limited or no treatment options
- challenges for research and difficulties with collecting evidence because of the uniqueness of the disease.

The HST Programme aims to:

- encourage research on, and innovation for, ultra-rare diseases when there are challenges in generating an evidence base that is robust enough to bring the product to market
- secure fairer and more equitable treatment access for very small populations with ultra-rare diseases
- recognise that an approach that maximises health gain for the NHS may not always be acceptable because it could deliver results that are not equitable.

The HST Programme acknowledges that:

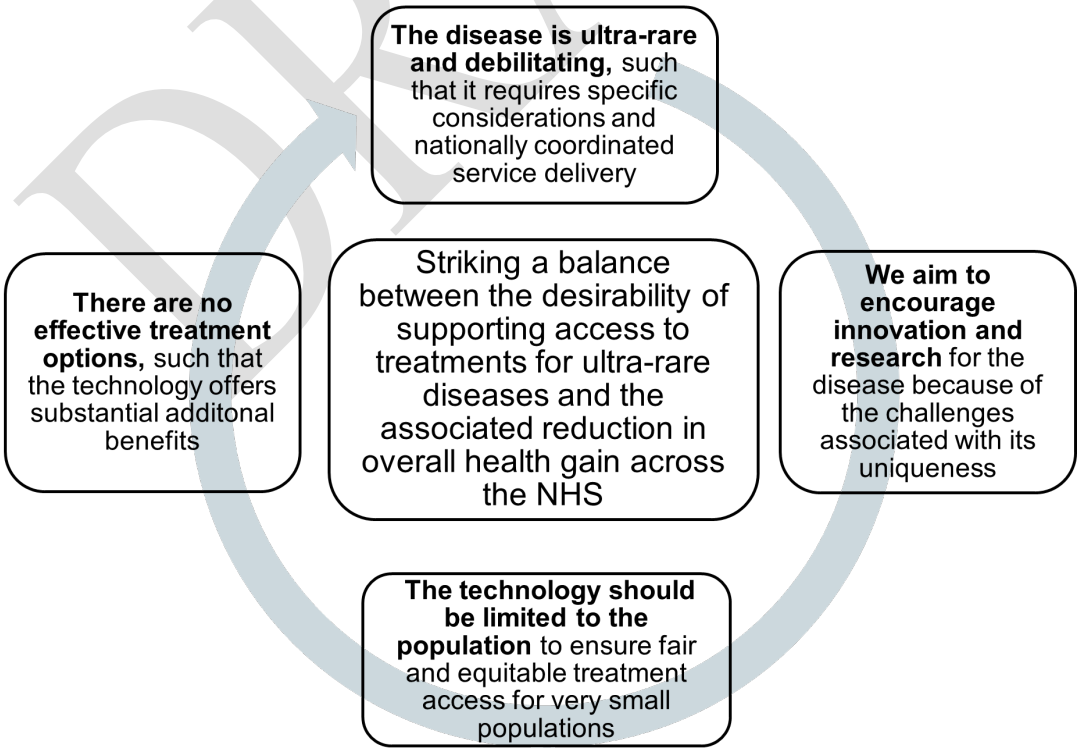
- It is important for NICE to apply appropriate constraints to the ultra-rare diseases' populations who can potentially be routed to the HST Programme. This is because the HST Programme is a deliberate departure from the standard technology appraisal process. It values the benefits of HSTs more by having a much higher incremental cost-effectiveness ratio (ICER) threshold for the reasons outlined above.
- Each time NICE routes a topic to the HST Programme and if the technology is recommended, it is deciding that the NHS must commit to allocating resources that would otherwise have been used for activities that would be expected to generate greater health benefits.
- NICE has sought to strike a balance between the desirability of supporting access to treatments for ultra-rare diseases against the resulting inevitable reduction in overall health gain across the NHS. Both considerations are valid and important, and neither can be given absolute priority over the other. So, the HST routing criteria and their anticipated application do not intentionally seek to capture every case in which there are challenges in generating an evidence base, or when there is a small population with an ultra-rare disease.
- This approach ensures that technologies routed to the HST Programme fulfil the vision of the programme and manages the displacement in the

wider NHS. How the context of the HST vision is linked to the HST routing criteria is illustrated in figure 1.

But it can be challenging to identify the exceptional circumstances when the HST methods and processes should be used. This is because of the difficulty in getting the information needed at the point of a routing decision. Proxy information is often relied on and used to make judgements. The HST routing criteria identify which technologies should be routed to the HST Programme. These criteria help the NICE prioritisation board make judgements that are as informed, justifiable, consistent, predictable and transparent as possible. NICE's capacity to develop HST guidance can react to need. Also, there is no limit on the number of technologies that can be routed to the HST Programme.

For the purpose of this refinement work, see the separate 'supporting information'.

Figure 1: Summary of the vision of the HST Programme



2 Proposed refinements to the HST routing criteria

Technologies will be considered eligible for routing to the HST Programme if the NICE prioritisation board agrees that all 4 routing criteria have been met (see section 3). Each criterion has a set of definitions that help to explain how it will be assessed. The criteria should not be assessed in insolation. The NICE prioritisation board will always consider all the definitions when assessing each routing criterion.

2.1 The disease is ultra-rare and debilitating

Description of the HST Programme's vision

The rarer a disease is, the more challenging it is to do research and generate an evidence base that is robust enough to bring an effective technology to market. The HST Programme's vision aims to encourage research when it is most challenging.

Not all ultra-rare diseases are debilitating. The vision focuses on ultra-rare diseases that cause ongoing debilitating symptoms and an exceptional burden on the people with them. This is to justify prioritising access to HST technologies over overall population health.

Routing criterion 1

The disease is ultra-rare and debilitating, that is, it:

- is defined as having a point prevalence of 1:50,000 or less in England (NICE strategic principles for rare disease)
- is lifelong after diagnosis with current treatment, and
- has an exceptional negative impact and burden on people with the disease.

Definitions

These definitions have been developed to help define what an ultra-rare disease is, and the debilitating nature of the disease. Relevant information should be collected by NICE (from the company, and other research or academic sources) to explain how each definition is considered by the NICE prioritisation board.

- The first 2 bullet points of routing criterion 1 are about the 'disease', not about the symptoms associated with the disease (regardless of whether the symptom or set of symptoms are the dominating feature).
- 'Disease' refers to a condition for which a diagnosis can be made based on the International Classification of Diseases (ICD-10 or ICD-11) developed by the World Health Organization (WHO). Diagnosis is based on a unique set of signs and symptoms (characteristics) identified using:
  - clinical examination
  - patient history
  - imaging or laboratory tests that are, or can be made, available in the NHS in England.
- 'Disease' does not refer to subgroups based on age, sex, severity or genetic subtype when these are not clinically meaningful (that is, associated with a unique and clinically distinct phenotype, prognosis or treatment options).
- 'Point prevalence' refers to the point prevalence of the 'disease' in England. It counts the number of people with a diagnosis of the disease thought to be alive in England on a given index date compared with the total population of England at that time (NHS England).
- 'Lifelong' indicates that the disease the people currently have:
  - needs ongoing clinical management, supportive care or both
  - is not relapsing–remitting, with periods when a person is free of symptoms and disease burden.

- ‘Exceptional negative impact’ refers to shortened length of life or severely impaired quality of life. The precise assessment of what these are needs an element of subjective judgement.

2.2 We aim to encourage innovation and research

Description of the HST Programme’s vision

This criterion is designed to uphold the HST Programme’s vision to encourage innovation and research into ultra-rare and debilitating diseases for which there is poor service provision within the NHS (for example, delay in diagnosis, no treatment options beyond supportive care). Without these incentives from the HST Programme, the technology may not be available either after launch, or during development or testing of the technology in England and Wales. The availability of the innovation can also reshape NHS services and advance awareness.

Routing criterion 2

The technology is an innovation for the ultra-rare disease.

Definitions

These definitions have been developed to help define what is an innovative technology. Relevant information about the technology should be collected by NICE from relevant sources (for example, the Medicines and Healthcare products Regulator Agency [MHRA], ongoing trials, registries and others) to explain how each definition is considered.

- ‘Innovation’ refers to a technology or medicine such as an advanced therapy medicinal product (ATMP), a new chemical or biological entity, or a novel drug device combination that brings additional health gains to people with the disease (compared with existing treatment or best supportive care).
- To ensure the technology is an innovation for the ultra-rare disease, the technology should:

  - not be a repurposed technology
  - the indication for the technology should not be a significant extension of an indication from another population or disease
  - the technology should not currently be being explored in clinical trials for other indications.
- A repurposed technology means new uses for medicines that are outside the scope of the existing licence for the medicine. This typically involves taking an existing medicine that already has a marketing authorisation or licence for human use for a particular condition, and then using it to treat another condition (Repurposing medicines in the NHS in England).

2.3 The technology should be limited to the population in its licensed indication

Description of the HST Programme's vision

This criterion is designed to establish the acceptability of the technology as an effective use of NHS resources because of the significantly higher ICER per quality-adjusted life year (QALY). So, the eligible population needs to be small. This is to strike a balance between the desirability of supporting access to treatments for ultra-rare diseases against the inevitable reduction in overall health gain across the NHS because of a higher ICER threshold. A small subpopulation within a population with a common disease would not be suitable for the HST Programme.

Routing criterion 3

No more than 300 people in England are eligible for the technology for its licensed indication, and the technology is not an individualised medicine.

Definitions

These definitions have been developed to help define what kind of licensed indication is suitable for a technology to be considered for routing to the HST Programme, and to help explain what an individualised medicine is. Relevant

information about the licensed indication of the technology should be collected by NICE to explain how each definition is considered.

- ‘Eligible’ refers to everyone who could have the technology under its marketing authorisation (obtained or in the process of being obtained) in England.
- To promote innovation, the ‘technology’ should only be developed for the ultra-rare disease, so the eligible population is small. The technology:
  - has to be the first treatment for the 'licensed indication' under consideration
  - should not be for an extension of an existing indication for another population or disease, or for a subgroup of people with the ultra-rare disease
  - is unlikely to be suitable for other subgroups of the population with the ultra-rare disease in the future who are outside of its first indication, or other populations with other diseases
  - is not a repurposed technology.
- ‘Individualised medicine’ refers to a medicine that is developed based on a person’s unique genetic profile (n of 1), or on the genetic profile of monozygotic twins or triplets.

2.4 There are no effective treatment options

Description of the HST Programme’s vision

This criterion is designed to address the lack of effective treatment and access to NHS services for some ultra-rare diseases. To justify prioritising treatment access for ultra-rare diseases over overall population health, the technology indicated should provide substantial health benefits to people with the disease over existing clinical management and supportive care.

Routing criterion 4

The technology is likely to offer substantial additional benefit for people over existing established clinical management, and the existing established clinical management is considered inadequate.

Definitions

These definitions have been developed to help define what is substantial additional benefit, and to help to explain the meaning of no other treatment options. Relevant information should be collected by NICE to explain how each definition is considered.

- 'Substantial additional benefit' means that the technology demonstrably extends the reduced length of life or demonstrably improves the severely impaired quality of life attributable to the disease, as exemplified by research data on relevant patient-reported outcome measures (PROMs).
- 'The technology' means:
  - if the technology is a disease-modifying treatment (including curative treatment), there is no other disease-modifying treatment available in the NHS in England and Wales for the same ultra-rare disease at the time of routing decision, or
  - if the technology treats a symptom or set of symptoms unique to the ultra-rare disease, there is no other treatment available in the NHS in England and Wales for the same symptom for which the technology is indicated at the time of routing decision.

For comparisons of the existing HST routing criteria with the proposed refined criteria, see appendix A.

3 Routing deliberation and decision

To ensure transparency and consistency of routing decisions, an HST routing assessment checklist (see appendix B) will be used to collate all relevant information by the NICE technical team, This information will be presented by

the NICE technical team to the NICE prioritisation board for discussion and deliberation. At the end of the discussion and deliberation, the NICE prioritisation board members will vote on each routing criterion as 'met' or 'not met'. All 4 HST routing criteria need to be voted by the NICE prioritisation board as 'met' (that is with a majority vote of being met) for the technology to be routed to the HST Programme. If the NICE prioritisation board thinks more information is needed for them to discuss and deliberate, the decision will be deferred until there is more information. Rationales for the routing decisions will be captured in the HST routing assessment checklist. If there are split votes (50% compared with 50%) for any individual criterion, the NICE prioritisation board chair will have the deciding final vote.

All HST routing decisions will be available on the NICE prioritisation board webpage, This will also have the rationales for the decisions supplemented by the completed HST routing assessment checklist, and the timeframe to participate in the clarification process.

4 HST routing decision clarification process

The aim of the clarification process is to explain NICE's reasons for its HST routing decision(s) that are queried by industry or stakeholders. For more details on clarification process, see section 12 of the NICE-wide topic prioritisation: the manual (PMG46).

Appendix A Comparisons of existing and refined HST routing criteria

The existing and proposed refined HST routing criteria

Existing HST routing criteria	Proposed refined HST routing criteria

Criterion 1
The disease is very rare, defined by 1:50,000 in England.
Criterion 3
The very rare disease for which the technology is indicated significantly shortens life or severely impairs its quality.
	The disease is ultra-rare and debilitating
	Routing criterion 1
	The disease is ultra-rare and debilitating, that is, it:
	• is defined as having a point prevalence of 1:50,000 or less in England (NICE strategic principles for rare disease)
	• is lifelong after diagnosis with current treatment, and
	• has an exceptional negative impact and burden on people with the disease.
	Definitions
	• The first 2 bullet points of routing criterion 1 are about the 'disease', not about the symptoms associated with the disease (regardless of whether the symptom or set of symptoms are the dominating feature).
	• 'Disease' refers to a condition for which a diagnosis can be made based on the International Classification of Diseases (ICD-10 or ICD-11) developed by the World Health Organization (WHO). Diagnosis is based on a unique set of signs and symptoms (characteristics) identified using:
	  ○ clinical examination
	  ○ patient history
	  ○ imaging or laboratory tests that are, or can be made, available in the NHS in England.
	• 'Disease' does not refer to subgroups based on age, sex, severity or genetic subtype when these are not clinically meaningful (that is, associated with a unique and clinically distinct phenotype, prognosis or treatment options).
	• 'Point prevalence' refers to the point prevalence of the 'disease' in England. It counts the number of people with a diagnosis of the disease thought to be alive in England on a given index date compared with the total

	population of England at that time (NHS England).
	• 'Lifelong' indicates that the disease the people currently have:
	  ○ needs ongoing clinical management, supportive care or both
	  ○ is not relapsing–remitting, with periods when a person is free of symptoms and disease burden.
	• 'Exceptional negative impact' refers to shortened length of life or severely impaired quality of life. The precise assessment of what these are needs an element of subjective judgement.

Not applicable	**We aim to encourage innovation and research**
	Routing criterion 2
	The technology is an innovation for the ultra-rare disease.
	Definitions
	• 'Innovation' refers to a technology or medicine such as an advanced therapy medicinal product (ATMP), a new chemical or biological entity, or a novel drug device combination that brings additional health gains to people with the disease (compared with the existing treatment or best supportive care).
	• To ensure the technology is an innovation for the ultra-rare disease, the technology should:
	  ○ not be a repurposed technology
	  ○ the indication for the technology should not be a significant extension of an indication from another population or disease
	  ○ the technology should not currently be being explored in clinical trials for other indications.
	• A repurposed technology means new uses for medicines that are outside the scope of the existing licence for the medicine. This typically involves taking an existing medicine that already has a marketing authorisation or licence for human use for a particular condition, and then using it to treat another condition (Repurposing medicines in the NHS in England).

Criterion 2	**The technology should be limited to the population in its licensed indication**

Normally, no more than 300 people in England are eligible for the technology for its licensed indication and no more than 500 across all its possible indications	**Routing criterion 3**
	No more than 300 people in England are eligible for the technology in its licensed indication, and the technology is not an individualised medicine.
	Definitions
	• 'Eligible' refers to everyone who could have the technology under its marketing authorisation (obtained or in the process of being obtained) in England.
	• To promote innovation, the 'technology' should only be developed for the ultra-rare disease, so the eligible population is small. The technology:
	  ○ has to be the first treatment for the 'licensed indication' under consideration
	  ○ should not be for an extension of an existing indication for another population or disease, or for a subgroup of people with the ultra-rare disease
	  ○ is unlikely to be suitable for other subgroups of the population with the ultra-rare disease in the future who are outside of its first indication, or other populations with other diseases
	  ○ is not a repurposed technology.
	• 'Individualised medicine' refers to a medicine that is developed based on a person's unique genetic profile (n of 1), or on the genetic profile of monozygotic twins or triplets.

Criterion 4 There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options	**There are no effective treatment options** **Routing criterion 4** The technology is likely to offer substantial additional benefit for people over existing established clinical management, and the existing established clinical management is considered inadequate. **Definitions** • 'Substantial additional benefit' means that the technology demonstrably extends the reduced length of life or demonstrably improves the severely impaired quality of life attributable to the disease, as exemplified by research data on relevant patient-reported outcome measures (PROMs). • 'The technology' means:

	○ if the technology is a disease-modifying treatment (including curative treatment), there is no other disease-modifying treatment available in the NHS in England and Wales for the same ultra-rare disease at the time of routing decision, or ○ if the technology treats a symptom or set of symptoms unique to the ultra-rare disease, there is no other treatment available in the NHS in England and Wales for the same symptom for which the technology is indicated at the time of routing decision.

Appendix B: Highly specialised technology (HST) routing assessment checklist

Introduction

The NICE HST routing assessment checklist highlights when a technology meets or does not meet the criteria for routing it to the HST Programme. All 4 criteria need to be met for a technology to be routed.

HST routing criteria checklist

Criteria	Descriptions of how the criteria are met or not met through assessing the definitions
Criterion 1 **The disease is ultra-rare and debilitating, that is, it:** • is defined as having a point prevalence of 1:50,000 or less in England (NICE strategic principles for rare disease) • is lifelong after diagnosis with current treatment, and • has an exceptional negative impact and burden on people with the disease.	• 'Disease' refers to a condition for which a diagnosis can be made based on the International Classification of Diseases (ICD-10 or ICD-11) developed by the World Health Organization (WHO). Diagnosis is based on a unique set of signs and symptoms (characteristics) identified using: ○ clinical examination ○ patient history ○ imaging or laboratory tests that are, or can be made, available in the NHS in England. • 'Disease' does not refer to subgroups based on age, sex, severity or genetic subtype when these are not clinically meaningful (that is, associated with a unique and clinically distinct phenotype, prognosis or treatment options).

	Has this definition been met or not met?[Yes/No]
	
	Notes and rationales:
	• 'Point prevalence' refers to the point prevalence of the 'disease' in England. It counts the number of people with a diagnosis of the disease thought to be alive in England on a given index date compared with the total population of England at that time (NHS England).
	
	Has this definition been met or not met? [Yes/No]
	
	Notes and rationales:
	• 'Lifelong' indicates that the disease the people currently have:
	  ○ needs ongoing clinical management, supportive care or both
	  ○ is not relapsing–remitting, with periods when a person is free of symptoms and disease burden.
	
	Has this definition been met or not met? [Yes/No]
	
	Notes and rationales:
	• 'Exceptional negative impact' refers to shortened length of life or severely impaired quality of life. The precise assessment of what these are needs an element of subjective judgement.
	
	Has this definition been met or not met? [Yes/No]

Criterion 2 **The technology is an innovation for the ultra-rare disease.**	**Notes and rationales:** • 'Innovation' refers to a technology or medicine such as an advanced therapy medicinal product (ATMP), a new chemical or biological entity, or a novel drug device combination that brings additional health gains to people with the disease (compared with existing treatment or best supportive care). **Has this definition been met or not met? [Yes/No]** **Notes and rationales:** • To ensure the technology is an innovation for the ultra-rare disease, the technology should:

	○ not be a repurposed technology ○ the indication for the technology should not be a significant extension of an indication from another population or disease ○ the technology should not currently be being explored in clinical trials for other indications. **Has this definition been met or not met? [Yes/No]** **Notes and rationales:** • A repurposed technology means new uses for medicines that are outside the scope of the existing licence for the medicine. This typically involves taking an existing medicine that already has a marketing authorisation or licence for human use for a particular condition, and then using it to treat another condition (Repurposing medicines in the NHS in England). **Has this definition been met or not met? [Yes/No]**
Criterion 3 **No more than 300 people in England are eligible for the technology for its licensed indication, and the technology is not an individualised medicine**	**Notes and rationales:** • 'Eligible' refers to everyone who could have the technology under its marketing authorisation (obtained or in the process of obtaining) in England. **Has this definition been met or not met? [Yes/No]** **Notes and rationales:** • To promote innovation, the 'technology' should only be developed for the ultra-rare disease, so the eligible population is small. The technology: ○ has to be the first treatment for the 'licensed indication' under consideration ○ should not be for an extension of an existing indication for another population or disease, or for a subgroup of people with the ultra-rare disease ○ is unlikely to be suitable for other subgroups of the population with the ultra-rare disease in the future who are outside of its first indication, or other populations with other diseases ○ is not a repurposed technology. **Has this definition been met or not met? [Yes/No]**

	Notes and rationales: • 'Individualised medicine' refers to a medicine that is developed based on a person's unique genetic profile (n of 1), or on the genetic profile of monozygotic twins or triplets. **Has this definition been met or not met? [Yes/No]**

Criterion 4
The technology is likely to offer substantial additional benefit for people over existing established clinical management, and the existing established clinical management is considered inadequate.
	Notes and rationales:
	• 'Substantial additional benefit' means that, the technology demonstrably extends the reduced length of life, or demonstrably improves the severely impaired quality of life attributable to the disease, as exemplified by research data on relevant patient-reported outcome measures (PROMs).
	
	Has this definition been met or not met? [Yes/No]
	
	Notes and rationales:
	• 'The technology' means:
	  ○ if the technology is a disease-modifying treatment (including curative treatment), there is no other disease-modifying treatment available in the NHS in England and Wales for the same ultra-rare disease at the time of routing decision, or
	  ○ if the technology treats a symptom or set of symptoms unique to the ultra-rare disease, there is no other treatment available in the NHS in England and Wales for the same symptom for which the technology is indicated at the time of routing decision.
	
	Has this definition been met or not met? [Yes/No]

	Overall routing decision: [HST/TA] **Other comments:**