Operational framework for individualised genetic therapies, NHS England

Draft scope for engagement

November 2025

Remit

This scoping document relates to the planned development of an **operational framework** to support the **piloting** of access to individualised genetic therapies that are not currently eligible for NICE appraisal (due to small patient treatment numbers) and **not currently commissioned or funded by the NHS** in England.

The purpose is to:

- ensure appropriate and safe service delivery arrangements in NHS facilities where treatment is funded from non-NHS sources
- help further explore and understand operational and process issues relevant to any future research and / or commissioned pathways. This would include future potential approaches to patient consent / assent, product regulatory licensing, treatment centre selection and / or accreditation, data collection and evidence generation.

The operational framework does not infer or cover how future decisions on public funding and funding prioritisation for individualised genetic therapies will be made and will therefore only apply during an initial pilot phase where external (non-NHS) funding for the treatment and related service costs has already been identified.

Defining individualised genetic therapies

Individualised genetic therapies (including some described as 'n-of-1' therapies) are personalised medicines for patients with a rare disease that has an underlying genetic cause. Of particular interest in terms of this framework are those which are excluded in NICE's criteria for appraisal of highly specialised technologies.[1]

Key dependencies

The operational framework will help identify and understand regulatory, health technology assessment and national clinical policy considerations and requirements which may differ for individual genetic therapies compared to other more commonly used medicines/indications.

The framework may particularly support the Rare Therapies Launch Pad pilot on antisense oligonucleotides (ASOs), treatments that are designed to bind to specific ribonucleic acid (RNA) sequences which can target disease-causing genes.

[1] NICE HST routing criteria 3 states that: no more than 300 people in England are eligible for the technology in its licensed indication, and the technology is not an individualised medicine, https://www.nice.org.uk/process/pmg46/resources/highly-specialised-technologies-nice-prioritisation-board-routing-criteria-15301445581/chapter/hst-routing-criteria#criterion-3-the-technology-should-be-limited-to-the-population-in-its-licensed-indication

Funding

Newly licensed treatments are usually funded subject to a positive recommendation for access in the NHS in England via NICE technology appraisal or highly specialised technology (HST) guidance. However, NICE's HST routing criteria explicitly exclude individualised genetic therapies from selection to that programme, and this route to routinely funded NHS access therefore does not apply.

To date, funding of individualised genetic therapies and associated treatment delivery costs have typically come from either research funding, not-for-profit or philanthropic sources. As a new and developing area of treatment, there is currently no funding source identified in the NHS for delivery of these therapies for the spending review period up to 2028/29. However, the operational framework will apply to cases fully funded from non-NHS sources at this time, essentially on a pilot basis. This will help inform future NHS funding decisions, including potential approaches to pricing and reimbursement.

Background

1. Advances in genomic medicine mean that we can now sequence the whole genome, including for those with a suspected rare disease caused by a variation in their DNA. Technological advances also mean that it is now possible, in some cases, to develop highly personalised therapies specific to this DNA variation targeting the root cause of the condition. This can include using cutting edge techniques such as gene editing (for example, CRISPR), antisense oligonucleotides (ASOs) or mRNA therapies.

2. For some rare conditions this presents the potential of a life-changing or life-saving treatment, by generating personalised or even individualised therapies for those who have a unique variant in their DNA, or are one of only a handful of people living with a condition linked to a specific DNA variation. Therapies to treat such rare conditions are often referred to as individualised therapies or n-of-1 therapies, irrespective of the technology underpinning the treatment. These therapies are new and will pose particular challenges for regulation, reimbursement and service delivery. For example, it is not possible to run standard randomised and comparative clinical trials when a therapy is specifically designed for an individual or very small number of individuals (as discussed in an article published by Nature Reviews Drug Discovery).

3. Recognising the potential of these technologies, the Government is making significant investments in research to support their development. This includes through the UK Platform for Nucleic Acid Therapy for rare disease treatment (UPNAT), funded by the Medical Research Council (MRC) and the National Institute for Health and Care Research (NIHR) as part of the £14 million Rare Disease Research UK platform. The Nucleic Acid Therapy Accelerator (NATA), funded through the MRC, operates at the intersection of academia, preclinical research and industry to advance the development of nucleic acid therapies and associated technologies.

4. In December 2024, the MRC launched the first 2 MRC centres of research excellence (CoRE), both studying gene therapies, an investment of up to £50 million over 14 years. The MRC CoRE in therapeutic genomics aims to achieve transformative impact for rare genetic disorders and will develop processes to take successful genetic therapies and

re-programme them to treat new disorders, enabling the development of individualised therapies at scale.

5. This investment in research, combined with the UK's capabilities in diagnostic genomics (which enables the identification of people who could benefit from these therapies), a single payer healthcare system, a track record of innovation adoption in the NHS, and a responsive and flexible regulator, gives the UK the opportunity to play a world-leading role in treating rare disease with advanced therapeutics. This will bring benefits for both patients and the UK life sciences sector.

6. Alongside UPNAT, the Rare Therapies Launch Pad (RTLP) will be key to developing thinking and testing to approaches to a risk-proportionate regulatory system, patient and genetic variant identification, ethics and consent, data requirements and reimbursement. This will initially focus on antisense oligonucleotides (ASOs) as a pilot for other individualised therapies.

The role of NHS England in individualised therapies

7. NHS England recognises the opportunities that individualised therapies may offer in terms of providing potentially life-changing treatments for certain rare disease patients but also the challenges these therapies could pose in terms of funding, prioritisation and service delivery. Some of these therapies are being produced by not-for-profit organisations or are otherwise funded by benefactors who are able to offer the therapy free of charge (and sometimes also cover linked treatment and delivery costs). It may therefore be the case that we have individuals in the UK with very specific genetic variant who could benefit, for whom non-NHS funding may be offered.

8. NHS England will explore the development of a highly specialised service operational framework to enable the piloting of service delivery of individualised therapies to patients within a NHS setting, and informing potential future commissioning requirements. This will initially focus on ASOs as a pilot topic, but could be built upon for other individualised therapies. This will include specifying what constitutes an optimal and safe service model and how to select an appropriate service provider(s). It will build on experiences in other countries. As with other innovative treatments, the framework will need to help inform future decisions on the value and affordability of the therapies.

9. Building on work by UPNAT and the RTLP, MHRA and NICE, the framework will need to help clarify the clinical criteria for identifying which patients might be suitable for treatment. NHS England will work with partners, including MHRA and NICE, around linked approaches for regulation and evaluation of these therapies. Such pathways would need bespoke processes for consent, regulation, evidence gathering, reimbursement and patient identification, striking a balance between aligning with other more routine arrangements for medicines but also recognising differences linked to evidence generation and the numbers of potentially eligible patients.

10. The planned output will be a national operating framework to support the piloting of access to individualised genetic therapies for patients within NHS settings, which may include bespoke models for specific technologies (for example, ASOs). The scope of the framework will be agreed by February 2026 and reported in the England Rare Diseases

Action Plan. In the longer term, the framework aims to support the safe and affordable provision of individualised therapies to eligible patients within the NHS.

What the operational framework will cover

1. How individualised genetic therapies will be delivered to patients within NHS settings under pilot arrangements
2. The principles that should apply to the piloting of individualised genetic therapies in the NHS
3. Which medical conditions an individualised genetic therapy might be available for under the pilot
4. How potentially clinically eligible patients are identified, including:
    a. Are there relevant genetic similarities between their genomic profile and that of someone who has already received an individualised genetic therapy?
    b. Is the treatment going to be given at an earlier stage of the disease (not end-stage)?
5. Which providers should offer individualised genetic therapies being piloted and how they will be selected
6. An end-to-end patient pathway detailing how individualised therapies will be delivered in the NHS under pilot arrangements
7. Consideration of appropriate approaches to the generation and licensing of intellectual property generated through a treatment's pilot delivery in the NHS
8. How any individualised genetic therapy clinical evidence generation, interpretation and evaluation methodology may translate into future clinical policy determination
9. The practical considerations for delivering the individualised therapy
10. What (and how) data (including real-world evidence) will be collected to support future patient and clinical decision making, future commissioning decisions, regulation, HTA and long-term outcome monitoring
11. Best practice for delivery, informed by international practice

What the operational framework won't cover

12. Clinical decision making on who might be suitable to receive an individualised genetic therapy
13. Funding strategy, prioritisation and process, including how an individualised genetic therapy and any associated service costs might be funded in the future
14. Identifying treatments for people where no individualised genetic therapy currently exists
15. Study approvals, including approach to patient consent / assent and research ethics
16. Clinical evidence interpretation and evaluation
17. Regulatory requirements and methodology for individualised therapies
18. Health technology assessment requirements and methodology for individualised therapies
19. Commercial strategy and pricing / supply negotiation mechanisms for individualised therapies

How will the framework be developed?

An internal NHS England think group will oversee the development of the operational framework. NHS England will work closely with DHSC, MHRA, NICE and NIHR during its development to ensure it aligns with the requirements of these bodies.

The operational framework will be tested with relevant patient organisations. It will also be tested with other key stakeholders (e.g. Genomics England, Office of Life Sciences).