DRAFT RARE DISEASE THERAPIES REGULATORY FRAMEWORK

The Brain Tumour Charity's consultation submission - July 2026

About The Brain Tumour Charity

The Brain Tumour Charity is the largest dedicated funder of research into brain tumours globally. This response draws on evidence from our policy reports including, *Unlocking Innovation for Brain Tumours in the UK* and *Barriers to Participation in Research: the experience people with brain tumours*.

We welcome the opportunity to submit to this consultation inquiry and share some our answers on the Draft Rare Disease Therapies Regulatory Framework and considerations for how it could be improved.

The first three questions are about the overall aim of the framework and the involvement of patient views.

1. **In your view, is it desirable for more pharmaceutical treatments for rare diseases to be brought into a regulated pathway rather than used 'off-label' as many are at present? Please explain your answer.**

   The Brain Tumour Charity believes that it is desirable for more pharmaceutical treatments for rare diseases to be brought into regulated pathways, as this supports patient safety, enables more consistent access and strengthens the evidence base. However, this will only be effective if regulatory pathways are sufficiently flexible and proportionate to the challenges of rare disease drug development.

   Regulated pathways play a critical role in ensuring treatments are appropriately evaluated for safety and effectiveness, which is particularly important in rare and complex conditions such as brain tumours. They also provide a structured mechanism for the generation of high-quality evidence, including the increasing use of real-world data, which is essential where traditional trial designs are not always feasible.

   Moving treatments into regulated pathways will also hopefully reduce variation in access. Presently, off-label use may lead to inconsistent availability, with access often dependent on

local clinical practice. A more formalised pathway can support clearer, more transparent decision-making and improve equity for patients across the system.

However, off-label use remains an important route to access in rare diseases, reflecting the high level of unmet need and limited number of approved treatment options for certain conditions.

It is therefore, The Brain Tumour Charity's belief that the focus should be on developing more adaptive and responsive regulatory pathways for rare diseases. This includes enabling earlier access to promising therapies through mechanisms such as conditional approvals or iterative licensing, alongside a stronger emphasis on real-world evidence generation to address ongoing uncertainties. Closer alignment between regulatory approval, health technology assessment, and clinical practice will also be important to ensure that treatments can move efficiently from development into routine care.

It is the Charity's opinion that reducing reliance on off-label use should be a long-term objective, achieved through more flexible and coordinated pathways rather than restriction of clinical discretion. For patients with rare and life-limiting conditions, an effective system will require both accelerated access through regulated routes and the continued ability for clinicians to prescribe off-label where this is supported by emerging evidence and clinical need.

2. The consultation sets out challenges associated with the development and regulation of treatments for rare diseases. Please identify any other challenges you are aware of that have not been considered or elaborate on those already identified. (optional)

The Brain Tumour Charity recognises the challenges associated with evidence generation in small patient populations. However, our recent evidence shows that barriers to rare disease innovation are not limited to evidence generation. They are often structural, spanning the full pathway from discovery through to patient access.

Through our report Unlocking Innovation for Brain Tumours in the UK, we identified barriers across translational research, clinical trials, regulation, health technology assessment, commissioning and adoption. These stages too often operate separately, creating uncertainty for developers and delays for patients.

Access to research is also a major challenge. Our report Barriers to Participation in Research found that only 42% of people affected by a brain tumour had been informed about research opportunities, while only 12% had participated in a clinical trial. This challenge is significant not only for patients, but for the wider research ecosystem. Difficulties identifying eligible patients and recruiting to studies can discourage investment, slow evidence generation and limit the attractiveness of the UK as a destination for rare disease research. In response, The Brain Tumour Charity is supporting the development of Access to Clinical Trials for Brain Tumours (ACT-BT), a national initiative designed to help connect patients with suitable clinical trials and reduce barriers to participation.

Data fragmentation is another key barrier. Our patient-led report A System That Sees Us highlights the need for linked, standardised datasets that can support evidence generation, service improvement and long-term monitoring. Workforce capacity and research infrastructure

also remain significant barriers. Limited research nurse capacity, protected research time and specialist neuro-oncology resource can restrict trial delivery and evidence generation, even where promising therapies exist.

Addressing these challenges will be essential if regulatory flexibility is to translate into meaningful improvements in patient access. A more flexible regulatory pathway for rare diseases should also enable stakeholders to shift their focus from overcoming regulatory barriers to tackling the operational, workforce capacity and capability challenges that can impede trial set-up and delivery. This would help ensure that regulatory innovation results in tangible benefits for patients.

3. Patient engagement is a key feature of the framework. How can patients and their families and carers contribute most effectively to the regulatory process? Please explain your answer. (optional)

Patient engagement is fundamental to ensuring that regulatory decision-making reflects the realities of living with a brain tumour, where prognosis is often poor and treatment options are limited. Patients, families, and carers can contribute most effectively in a number of ways.

First, they should have a critical role in contributing evidence grounded in lived experience. For brain tumour patients, this can include insights on neurological and cognitive symptoms alongside quality-of-life impacts that can be poorly captured in clinical trial endpoints. This evidence is vital for contextualising clinical data and ensuring that benefit–risk assessments reflect outcomes that matter most to patients.

Second, patients and carers should be involved in ongoing engagement throughout the regulatory process, from early-stage development to post-market evaluation. Early engagement can help shape trial design, including the selection of meaningful endpoints such as the ability to maintain independence. Continued involvement can also support the generation and interpretation of real-world evidence, which is particularly important in the Rare Disease space where clinical trial populations are often small.

Third, patient insights are essential in highlighting the full range of unmet need and treatment impact. Brain tumour patients and their families can articulate challenges beyond tumour progression, including the burden of treatment side effects, the impact on daily functioning, and the wider effects on carers. This broader perspective can help ensure that regulatory decisions recognise meaningful benefits, even where clinical gains may be limited.

Importantly, patients can provide crucial input on acceptable levels of risk and uncertainty. Given the often life-limiting nature of brain tumours and the lack of effective treatments, many patients may be willing to accept higher levels of risk in exchange for the possibility of benefit. Capturing this perspective in a structured way can support more proportionate and transparent decision-making, particularly in areas of high unmet need.

Patient involvement should also extend to the development of information materials relating to new therapies, including clear explanations of the available evidence, known risks, and remaining uncertainties or knowledge gaps. The MHRA should work with patients and patient organisations to develop accessible information resources that complement information provided by manufacturers and support clinicians in meeting their consent obligations. This would help ensure that patients are equipped to make informed decisions based on a balanced understanding of both the potential benefits and uncertainties associated with treatment.

Patients should also be involved in the design of evidence generation frameworks, governance arrangements and data collection approaches. Through A System That Sees Us, people affected by brain tumours called for data systems that are more transparent, joined up and shaped by patient priorities. This is particularly important in brain tumours, where outcomes that matter to patients can go beyond traditional clinical endpoints and include cognitive function, neurological symptoms, independence, quality of life and the impact on carers.

The next section has nine questions about elements of the framework

4. **A fundamental question is how much evidence is enough for a decision to be made on the use of a medicine? Using novel approaches to evidence generation the pathway aims to strike a balance between the nature and amount of data needed to support the safety and efficacy of a treatment before patients can access it and the time it takes to generate that data. Do you agree that the proposed approach has found the appropriate balance?**

- **Strongly agree**
- **Agree**
- **Neither agree or disagree**
- **Disagree**
- **Strongly disagree**

Please explain your view on this fundamental consideration (optional)

The Brain Tumour Charity broadly agrees that the proposed approach represents a positive step towards achieving a more appropriate balance between the level of evidence required and timely patient access. In particular, the increased flexibility in approaches to evidence generation and the greater clarity provided to developers on what types of evidence may be considered are welcome. This is especially important in rare and complex conditions, where traditional clinical trial designs are often not feasible and where delays in access can have significant consequences for patients.

However, there is an opportunity to strengthen the approach further by providing clearer guidance on the use and acceptability of international data. Given the small and dispersed patient populations in rare diseases, global data - including real-world evidence and outcomes generated in other healthcare systems - can play a critical role in building the evidence base where UK-specific data is limited. Explicitly recognising how international evidence can be used, and under what conditions, would help maximise the available data, reduce duplication, and support more timely decision-making while maintaining robust standards for safety and efficacy.

The Brain Tumour Charity also believes that greater emphasis should be placed on linked datasets, registry-based evidence and patient-reported outcomes. The increasing use of molecular and genomic profiling may also support stronger assessments of biological plausibility, helping regulators make proportionate decisions where traditional evidence generation is challenging.

A System That Sees Us sets out the importance of better data linkage and interoperability to support care, research and accountability. For rare diseases, robust real-world evidence can provide important insight into treatment effectiveness, quality of life, functional outcomes and long-term safety, helping to address uncertainties that may not be fully resolved through conventional trials.

Overall, while the proposed pathway moves in the right direction, greater clarity on the integration of international data would enhance its effectiveness and ensure it fully delivers on its ambition to balance timely access with robust evidence generation.

5. **Defining rarity is a challenge due to the limitations of using a fixed prevalence (frequency) limit, changing disease classifications and the evolving nature of genetic and molecular disease definitions. Whilst retaining some flexibility, the framework is targeting diseases with a prevalence of around 1 in 50,000 of the UK population, which is deliberately distinct from the orphan designation threshold of 25 in 50,000. Do you consider that this threshold considered appropriate to encourage development of treatments for rare diseases?**

- **Strongly agree**
- **Agree**
- **Neither agree or disagree**
- **Disagree**
- **Strongly disagree**

Please provide your rationale if another threshold should be considered (optional)

https://www.thebraintumourcharity.org/get-involved/campaigning-for-change/what-were-campaigning/cost-of-a-brain-tumour/

The Brain Tumour Charity welcomes the intention to introduce a more targeted framework for rare therapies, but we have reservations about using a prevalence threshold of around 1 in 50,000 as the primary determinant of eligibility.

The consultation acknowledges that rare therapies are currently defined as those intended to treat conditions with a prevalence of no more than 5 in 10,000. The proposed threshold therefore represents a substantial narrowing of scope. While we recognise the rationale for prioritisation, there is a risk that a more restrictive cut-off could exclude conditions where there remains significant unmet need and limited commercial incentive for innovation.

This is particularly relevant to brain tumours, of which there are more than 100 different types. The relationship between prevalence and burden is complex. Some high-grade tumours may have low prevalence because survival remains extremely poor. By contrast, some low-grade tumours may have higher prevalence because people live with the disease for many years, often with significant long-term impacts on cognition, independence, quality of life, employment and education.

This means prevalence alone may not consistently reflect disease burden, unmet need or the case for innovation across different brain tumour types. The Brain Tumour Charity would therefore encourage the framework to ensure that prevalence is not considered in isolation. Where prevalence does not adequately reflect the severity, burden or biological distinctiveness of a condition, there should be sufficient flexibility to consider these factors alongside prevalence when determining eligibility.

Greater clarity is also needed on how the framework will define a rare disease in practice, particularly where treatments are targeted at molecularly defined groups. This will be important

to ensure that biologically distinct brain tumour types are assessed consistently and transparently as scientific understanding continues to evolve.

Additionally, it must be clarified on how this framework aligns with other processes, including health technology assessment, reimbursement decision-making, and system readiness for adoption. Without this alignment, there is a risk that early regulatory support does not translate into timely patient access, weakening the overall incentive for industry.

6. **Do the Scientific Opinion and Designation steps add a tangible incentive for research and development of rare therapies? Are they best delivered at predefined points or on a flexible basis depending on the individual development? Please explain your rationale. (optional)**

The Scientific Opinion and Designation steps do have the potential to provide a tangible incentive for research and development in rare therapies, but their impact will depend on how effectively they are integrated with the wider innovation, regulatory, and access landscape.

Early scientific advice and designation can help to reduce uncertainty for developers by clarifying evidentiary expectations, regulatory requirements, and the potential route to approval. For smaller patient populations, this early engagement may be particularly valuable in providing confidence around the use of adaptive trial designs, real-world evidence and international datasets. In rare disease contexts, where development is often high-risk and patient populations are small, this greater predictability is valuable and can support earlier and more confident investment decisions.

However, these steps in isolation are unlikely to be sufficient to drive meaningful increases in research and development activity. Their value as an incentive will depend on clear alignment with other processes, including health technology assessment, reimbursement decision-making, and system readiness for adoption. Without this alignment, there is a risk that early regulatory support does not translate into timely patient access, weakening the overall incentive for industry. Stronger demand signalling from the system - including clarity on willingness to adopt and pay for innovative treatments in areas of high unmet need - will be crucial to ensuring that these mechanisms effectively influence investment decisions.

To maximise their impact, these mechanisms should be aligned with health technology assessment and reimbursement processes. As set out in Unlocking Innovation for Brain Tumours in the UK, fragmentation between regulation, appraisal, commissioning and adoption can delay patient access even where promising innovation exists. Greater coordination between MHRA, NICE and NHS commissioning bodies would provide developers with a clearer route from regulatory support to patient access.

In terms of delivery, The Brain Tumour Charity believes that a flexible, development-led approach is preferable to rigid predefined points. Rare therapies often follow highly heterogeneous and non-linear development pathways, particularly where adaptive trial designs, repurposing, or real-world evidence generation are involved. Allowing Scientific Opinion and Designation to be accessed at points where they add the most value rather than at fixed stages will better support innovation and enable more tailored regulatory engagement.

7. **Do you agree that open registration of all clinical trials which are linked to the pathway and transparent sharing of safety and efficacy data—especially from early-phase studies—will help in any of the following ways? (optional)**

- **To foster public trust**
- **To enhance scientific learning**
- **To support sustainability of the framework**
- **To support development of treatments for rare (and more common) conditions**

Please add any further comments here (optional)

The Brain Tumour Charity supports open registration and transparent reporting of clinical trials linked to the pathway. As highlighted in Barriers to Participation in Research, research participation in brain tumours remains too limited. In rare diseases, every dataset has value. Transparent reporting helps avoid duplication, supports scientific learning and ensures that the contribution made by patients delivers the greatest possible benefit.

We particularly support transparency around negative and inconclusive findings, as these can still provide important learning for future research.

8. **Proposals for managing market exclusivity have not been addressed in the framework document. How should market exclusivity be managed to balance the potential benefits of incentivising investment with the risk of creating unintended barriers to future innovation? (optional)**

The Brain Tumour Charity recognises the importance of market exclusivity in incentivising investment into rare disease therapies. However, exclusivity arrangements should be proportionate and should not create unnecessary barriers to future innovation, including repurposed medicines, combination therapies or subsequent indications that may deliver meaningful patient benefit. A balanced approach is needed that supports investment while ensuring patients continue to benefit from scientific progress.

The UK must offer a more aligned pathway to rival, if not better, most similar markets around the world, to ensure the UK does not disincentivise first or mutually first therapy launches.

9. **Should decisions regarding market exclusivity and reimbursement be made on the basis of a combination of pre-determined transparent criteria rather than fixed prematurely within the framework? (optional)**

Yes. The Brain Tumour Charity supports decisions being made using transparent and pre-defined criteria. This would improve predictability for developers, increase confidence amongst patients and stakeholders, and allow decision-makers to appropriately balance rarity, unmet need, disease severity, evidential uncertainty and societal impact.

10. **The scope of the framework includes authorised medicines that are being repurposed (being used to treat a different condition). Do you agree that the framework is suitable for these cases?**

The Brain Tumour Charity strongly agrees that repurposed medicines should fall within the scope of the framework. Repurposing offers a potentially faster and more cost-effective route to innovation, particularly where treatment options are limited. This is highly relevant to brain tumours, where patients may currently rely on off-label use because of the lack of approved therapeutic options.

As set out in Unlocking Innovation for Brain Tumours in the UK, people affected by brain tumours face substantial barriers to accessing innovation. The framework should provide a clearer route for generating evidence and securing approval for repurposed therapies where there is a strong rationale and emerging evidence.

11. Below we have listed six elements of the proposed framework. To what extent do you agree with each of these as an important element?; We are interested to hear of your further thoughts on them.

An adaptive regulatory pathway for very small populations (optional)

- **Very important**
- **Important**
- **Moderately important**
- **Slightly important**
- **Not important**

Further comments (optional)

The Brain Tumour Charity welcomes the ambition of the framework and considers an adaptive regulatory pathway particularly important for conditions characterised by high unmet need and small patient populations. However, regulatory flexibility alone will not be enough to improve patient outcomes. Successful implementation will require alignment between regulatory approval, health technology assessment, commissioning and adoption. Without this, promising therapies may still face delays before reaching patients. This challenge is central to Unlocking Innovation for Brain Tumours in the UK.

The framework should also be reviewed over time to ensure eligibility criteria remain appropriate as disease classification and scientific understanding continue to evolve.

Defined entry criteria (such as rarity, severity, unmet need and biological plausibility (optional)

- **Very important**
- **Important**
- **Moderately important**
- **Slightly important**
- **Not important**

Further comments (optional)

early regulatory engagement and designation (optional)

- **Very important**
- **Important**
- **Moderately important**
- **Slightly important**
- **Not important**

Further comments (optional)

the use of prior knowledge, platform data and adaptive evidence generation approaches (optional)

- **Very important**
- **Important**
- **Moderately important**
- **Slightly important**
- **Not important**

Further comments (optional)

ongoing safety monitoring with periodic review (optional)

- **Very important**
- **Important**
- **Moderately important**
- **Slightly important**
- **Not important**

Further comments (optional)

the potential to progress to full marketing authorisation over time (optional)

- **Very important**
- **Important**
- **Moderately important**
- **Slightly important**
- **Not important**

Further comments (optional)

12. **Do you have questions or observations about any aspects of the framework including those we have not specifically asked about? (optional)**

The last three questions ask about your view on the impact of the framework

13. **In your view, will the flexibility and adaptability of the proposed pathway provide sufficient encouragement to developers of treatments for rare diseases to bring them within a regulated pathway? Please explain your answer.**

- **Strongly agree**
- **Agree**
- **Neither agree or disagree**
- **Disagree**
- **Strongly disagree**

Please add any further comments here and if you don't think this aim will be achieved please explain why.

14. In your view, will the pathway achieve its aim of supporting innovation while safeguarding patients and maintaining confidence in regulatory decision-making?

- **Strongly agree**
- **Tend to agree**
- **Undecided**
- **Tend to disagree**
- **Strongly disagree**

Please add any further comments here and if you don't think this aim will be achieved please explain why. (optional)

In principle, the proposed pathway has the potential to support innovation while maintaining patient safety and public confidence in regulatory decision-making. Its emphasis on flexibility, early engagement, and the accommodation of uncertainty is particularly important in the context of rare diseases, where evidence generation is inherently challenging and patient populations are small. These elements should help encourage the development of novel therapies that might otherwise struggle to progress through traditional regulatory routes.

However, whether the pathway ultimately achieves its aim will depend on how it is implemented in practice. Further work is needed to ensure alignment with reimbursement and adoption systems. Without clear and coordinated processes across regulatory approval, health technology assessment, and NHS uptake, there is a risk that innovative therapies will receive approval but still face delays or barriers in reaching patients.

There is also a fundamental question of affordability that must be addressed more explicitly. Therapies for rare and less common conditions are often associated with very high costs, and it is unclear whether the NHS and wider government systems will be able to sustainably fund access at scale. While innovation should be strongly supported, there must be greater transparency from government on how affordability challenges will be managed, including how trade-offs will be handled and how equitable access will be maintained across the system.

Safeguards must also be robust, proportionate, and transparent, particularly where approvals rely on limited or surrogate data. Clear expectations around post-market evidence generation, ongoing monitoring, and the consequences of unmet commitments will be critical to maintaining trust among patients, clinicians, and the wider public.

Patient involvement should be embedded throughout the pathway, ensuring that decision-making reflects lived experience, risk tolerance, and unmet need. Finally, transparency in decision-making, particularly around how uncertainty, value, and affordability are considered, will be key to safeguarding confidence.

With these elements strengthened, the pathway could strike an appropriate balance between enabling innovation and upholding rigorous standards of safety, effectiveness, and sustainability.

15. In your view could this framework reduce barriers to patient access, including time and cost, and in turn help reduce overall treatment costs?

- **Strongly agree**
- **Agree**
- **Neither agree or disagree**
- **Disagree**
- **Strongly disagree**

Please add any further comments here and if you don't think this aim will be achieved please explain why.

Equality Impact

Do you think the proposals risk impacting people differently, or could impact adversely on any of the protected characteristics covered by the Public Sector Equality Duty set out in section 149 of the Equality Act 2010 or by section 75 of the Northern Ireland Act 1998? (optional)

- **Yes**
- **No**
- **No opinion**

There is a risk that a prevalence threshold based primarily on population size could disadvantage some patient groups, including people with molecularly defined disease subtypes, children and young people, and conditions with high unmet need but relatively low prevalence.

As highlighted in Unlocking Innovation for Brain Tumours in the UK and Barriers to Participation in Research, people affected by brain tumours already face inequalities in access to research and innovation. The framework should monitor its impact across different patient groups to ensure it improves, rather than narrows, equitable access.