WORKSHOP REPORT

UK Regulatory Access and Frameworks in Rare Disease

Current Status, Opportunities and Challenges

19 – 20 November 2025

Co-organized by Rare Disease Research UK (the coordination Hub and nodes CAPTIVATE and UPNAT), LifeArc Centre for Acceleration of Rare Disease Trials (ARDT) and Rare Therapies Launch Pad (RTLP)

Rare Therapies Launch Pad

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UK Platform for Nucleic Acid Therapies - UPNAT

Rare Disease Research UK.
Changing Clinical Practice Through Innovative Trial Designs – CAPTIVATE

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UK Regulatory and Access Frameworks in Rare Disease – Current Status, opportunities and challenges

1. Introduction

Held over 2 days, on 19th and 20th November 2025, this workshop was convened by 5 projects/initiatives[1] operating at the cross-rare disease level in the UK. It emerged from complimentary tasks being undertaken by these programmes, with the following objectives:

- To bring together a broad range of stakeholders to better understand the goals and plans of key projects and structures working on this topic
- To share and reflect on recent survey data on the status quo of regulatory processes and access in the UK, relevant to rare disease (RD)
- To discuss and build consensus, at a high level, on a range of relevant topics under the broad heading of 'regulatory and access processes and frameworks'
- To develop and clarify current and future collaborative plans for further work or workshops to advance the more specific topics and questions under this broad area (in light of MHRA and other bodies' activities ongoing in this space)
- To agree how to maximise the benefits of ARDT, RTLP, RDR UK Hub, CAPTIVATE and UPNAT, avoiding duplications and examine where the opportunities for collaboration lie.

The workshop united over 40 experts from academia, industry, patient organisations, regulatory bodies, the policy sphere, and more, to unite insights from these 5 organising structures with perspectives and experience from the wider UK rare disease landscape.

2. Programme

Topic	Speakers	Session type
'State of the Nation' for Rare Disease Regulation and Access	Steph Croker Dr Jon Beaman Professor Devin Peipert	Presentation
Survey Highlights - what can this tell us about perspectives on the UK regulatory framework for rare diseases?	Anna Halstead	Presentation
Panel discussion: • What conclusions can we draw from this data? • Where do we feel regulation and access is working well, and what needs to be 'fixed'? • What does the survey not tell us/not capture?	Vicki Hedley (Chair) Professor Paul Gissen Tori Homer Dr Vanessa Newman Professor AJ McKnight Nick Meade	Panel discussion

[1] The workshop was co-organised by: Rare Disease Research UK (the coordination Hub and nodes CAPTIVATE and UPNAT); the LifeArc Centre for Acceleration of Rare Disease Trials (ARDT); and the Rare Therapies Launch Pad (RTLP)

Plans from key programmes with respect to UK regulatory frameworks for rare disease	RDR UK Hub: Vicki Hedley UPNAT Node: Professor Haiyan Zhou CAPTIVATE Node: Tori Homer LifeArc ARDT: Professor AJ McKnight RTLP: Dr Vanessa Newman	Presentation
The MHRA Rare Disease Consortium – plans and principles	Dr Jon Beaman	Presentation
NICE – Plans and priorities for assessing rare disease therapies	Dr Christian Griffiths	Presentation
Enabling Access to Rare Disease Therapies across the 4 nations: invitation to share future plans and priorities from key stakeholders	Dr Chris Garland	Presentation
How can regulation be a driver for change?	Facilitators: Dr Dan O'Connor Professor Carlo Rinaldi	Breakout discussion
How to rethink clinical trial design and conduct for robust decision-making	Facilitator: Tori Homer	Breakout discussion
How might evidence needs be met by the data sources we have, and how can the potential of these be leveraged?	Facilitator: Professor AJ McKnight	Breakout discussion

The presentations can be viewed here.

3. High-level results of the pre-workshop survey

To better inform discussions in the cross-project workshop, a survey was developed across these initiatives, earlier in 2025, to assess perspectives from the wider UK rare disease community regarding the status quo of regulation and access to rare disease therapies. 45 responses were received, from a broad range of stakeholders (ranging from academics to clinicians, patient advocates to researchers, industry experts to independent consultants).

The workshop regarded this survey data as a very useful starting-point for discussions on the status quo across regulatory and access processes; however, it was acknowledged that the topic is rather specialist and consequently, although respondents typically provided substantial -and very valuable- qualitative feedback in the form of free-text comments, the *number* of responses to most individual questions is probably too small to draw definitive conclusions from this data alone. Findings were therefore explored and developed further across the 2 days of the workshop. **The full analysis of this survey can be found as an Annex to this report.**

Main messages

In terms of ease or otherwise of progressing through a range of processes connected to regulation and access across the UK, and clarity of the requirements, there is definitely room for improvement (NB it is important to note that the numbers of respondents rating each of these specific activities was only a fraction of the total respondents ranging from 10-40% each time)

- **Marketing Authorisation** – the 9 respondents who gave a rating here were evenly split between ratings of 'straightforward' and 'difficult'.
- **CE/UKCA** (Conformité Européenne/ UK Conformity Assessed) Marking – only 5 people expressed a view here, and of those, 3 ranked 'difficult', 1 'straightforward', and 1 neutral ('neither straightforward nor difficult'). Comments suggested this is straightforward for low-risk devices but increasingly complex for high-risk or rare disease diagnostics, with system inconsistencies and adoption barriers adding further challenges.
- **Health Technology Assessment** – 16 people felt able to make a judgement here, with three quarters of them deeming it either difficult (8 people) or very difficult (4 people) to progress through UK HTA processes. 3 rated this as 'neither straightforward nor difficult' and only 1 opted for 'straightforward'. Comments show this is the perception particularly for rare and high-cost therapies. Demonstrating cost-effectiveness is challenging due to limited data, small patient populations, and high treatment prices, which can deter companies from entering the UK market
- **NHS Commissioning** – of the 18 respondents who answered this sub-question, 89% rated it 'difficult' or 'very difficult' to progress through the process (split evenly between these 2 responses). 1 reported 'neither straightforward nor difficult' and 1 ranked positively as 'very straightforward'. Respondents described this process as slow, bureaucratic, and underfunded, creating a major barrier to patient access. The responses highlight the overly complex and outdated processes, fragmented decision-making, and lack of accountability, with delays often lasting years
- **Post-Market Surveillance** – opinions here seemed less fixed than for the activities above. Of the 10 respondents willing to make an assessment, 60% felt this was neither straightforward nor difficult, with 30% rating 'straightforward' and 10% opting for 'difficult'. Comments explained that surveillance is most effective when supported by funded registries, as relying on clinicians alone adds to workload and risks limiting patient access. Current approaches are seen as overly burdensome, with calls for

4. Breakout discussion summaries

4.1. How can regulation be a driver for change?

In considering the broad but fundamental question of how regulation can act as a driver for change, workshop participants discussed a range of interrelated topics.

System alignment: Participants emphasised the need for significantly greater alignment between regulators and health technology assessment (HTA) bodies, highlighting

opportunities for increased collaboration and joint approaches. At a UK level, improved alignment across the four nations was identified as a priority (indeed, as the uncertainty surrounding new and personalised products increases, the need for a joined-up approach to data and evidence gathering, across all 4 nations but also actually globally, also increases). It was also noted that alignment efforts must extend *beyond* regulators and HTA bodies to include other parts of the healthcare ecosystem, most obviously payers; however, it is also important to think even broader, including expanding national screening programmes, to support coherent end-to-end patient pathways.

Utility of clinical models: The UK was recognised as having a strong environment for discovery science relative to other countries. However, participants noted inherent limitations in clinical and pre-clinical models for small population research, which must be acknowledged and appropriately accounted for within regulatory and decision-making processes.

Are we all on same page in defining rare? It is challenging to define what constitutes "rare", and it was noted that there are differences between regulators. For instance, the FDA accepts rare subsets of common conditions based on stages of illness or molecular markers of disease, which is a different approach to that in Europe. This is important, as many companies operate globally, and there are obviously potential policy and funding implications. For patients, that label of having a rare condition is generally very important, and if new developments in the MHRA, for instance, seek to change this in any way, there could be a major impact for patients and families. Some participants proposed that rather than focus too much on strict numerical definitions, any innovation or initiatives need to be sure to encompass the areas of higher unmet need, and this should be driven by the data and what is really needed to show that a treatment works. It may be more helpful to think in terms of personalised or targeted therapies for all, rather than simply considering the rarity of the condition. Participants suggested that a government or regulator-led mapping exercise could help clarify the current crowded landscape and identify opportunities in under researched conditions, supporting a shared understanding of rarity.

Use of external control and real-world data: Participants explored how real-world data could be better integrated into clinical development, noting that strong patient engagement in the UK could support this approach. The importance of robust, high-quality data was emphasised. We are seeing examples from the cancer space – e.g. with the DETERMINE precision medicine trial- in which data from patients with a common cancer is being included to offset the much smaller body of data on rare cancer patients.

In theory, data from DMD patients with more common genetic variants could support studies in the much rarer subsets. The group agreed that regulatory guidance was essential to ensure that developers *understand* expectations at an early stage, with rational, functional outcome measures being in place; however, the challenge is establishing that balance, and it may be that this will always need a case-by-case approach. Proposed solutions included the development of a practical minimum dataset for real-world evidence or a standardised data collection protocol.

How do we maximise novel approaches to evidence generation? The discussion considered how novel evidence-generation approaches could be better leveraged, including the potential role of regulators in mandating certain elements, such as the integration of natural history data into development programmes. Participants stressed the importance of encouraging early engagement with regulators, enabling developers to seek advice and test data collection plans in advance.

Platform and process approvals: Participants discussed the potential for generalisable knowledge generation, shared learning, and access to existing data. Multidisciplinary team (MDT) assessments were identified as important for agreeing meaningful parameters and determining which data should be collected. While some aspects of data collection may be generalisable, it was recognised that efficacy assessments would be largely disease-specific.

What are rare challenges we need to solve?
The aetiology of too many conditions and the modifiers of severity are still unknown, with many conditions under researched and under investigated.

It is challenging to appropriately assess Quality of Life (QoL) in rare conditions, as QoL is perceived differently by different individuals, and as symptoms can vary significantly, day to day in some rare conditions: the traditional approaches (EQ5D) are sometimes not sensitive enough, and ideally need supplementing with wearable data that allows the capturing of fluctuations. QoL also needs to be assessed based on social care, as well as more traditional health dimensions. It may be necessary to think in terms of core sets of outcome measures relevant to broad groups of rare conditions, with the ability to also have flexibility around such a clustering approach.

It was also observed that while regulators appear increasingly open to engagement with industry, access and support can be more limited for academia, despite early discovery science often originating in academic settings. Some highlighted the fact that academics have traditionally been more reluctant to seek advice from regulators (perhaps failing to recognise the value of the expertise and insights that regulators can bring – there is a tendency to think of regulators as bureaucrats, overlooking the innovation and scientific advice on offer). But nonetheless, it is important to assess if there are barriers hampering this interaction, beyond the historical lack of awareness. Early engagement with regulators and HTA in a joint setting, from academics driving discovery, is especially important in instances where companies have acquired a product *from* academia and come to NICE without a clear ability to explain the development pathway taken. It is essential that joint scientific advice between MHRA and NICE becomes more and more the standard approach.

Data and the need for single version in the health system: Health data is not owned by regulators, but regulators are in a good position to drive policy and advocate for change and innovation in the data space. A joined-up approach to data collection and sharing across all 4 nations would support not only better regulation of therapies but also build knowledge on our rare disease populations. Participants asked how feasible it is, today, to find out how many patients we have across the UK as a whole with a given condition, factoring in our national registries, the Genomics England databases, the CPRD, etc;

however, the group also noted that these resources and datasets only cover the populations in England at present, which is a major barrier to leveraging the power of this precious data.

In silico methods and data standardisation: The discussion noted that high-quality, standardised data must be available to support in silico modelling approaches. Participants considered whether industry could be incentivised to share data and emphasised the need for clearly defined regulatory pathways for approval. System changes are required, for example the ability to contact patients for follow-up.

Regulatory incentives for developers: Participants discussed how developers could be incentivised to invest in the UK. It is regrettable that the UK no longer has a pre-authorisation drug designation step – this allowed for a more visible route for early engagement with regulators, and has been lost post-Brexit. Perhaps there is a way to still align with the EU here, so that somehow designation may be made based on non-clinical data, rather than being assessed only at the point of marketing authorisation. Other suggested incentives included reviewing intellectual property and exclusivity periods to better reflect development investment and introducing concierge-style support mechanisms such as priority review vouchers, similar to FDA schemes (albeit ideally without the current potential for exploitation of such schemes). The group emphasised that incentives should be proportionate to the needs and circumstances of both academic and commercial developers, including consideration of waiving consultation fees for academia, as has been done by the EMA. It was also acknowledged that regulators themselves require adequate resources and capacity to support these initiatives and thus expanding them/encouraging more early access and scientific dialogue will incur a resourcing cost.

Funding opportunities and timing to engage with regulators: The UK was recognised as having increased funding opportunities in the space between pre-clinical and clinical (the so-called "valley of death") but the group highlighted the need for more. While the UK performs well in translational science, better coordination and alignment of expertise is still necessary. A significant gap in funding for the establishment and maintenance of high-quality registries and data collection infrastructure was also identified.

4.2. How to rethink clinical trial design and conduct for robust decision making

The session focused on rethinking trial design and conduct for robust decision-making and began with trying to identify the major challenges. The challenges identified were endpoint validation, identifying patient relevant questions, the lower population sizes, improvement rates, and navigating the push to always need gold standard RCT designs.

The group discussed the acceptable levels of uncertainty and evidence standards and concluded that a lower level of uncertainty might be accepted for a rare disease, but that doesn't necessarily mean a lower level of *evidence* standards should be accepted, raising the question of how might evidence standards vary with severity or prevalence of disease.

The discussion then considered whether trials could be reconceptualised as single-phase studies, rather than the traditional two- or three-phase designs. It was suggested that evaluating treatments within a single, integrated phase could improve efficiency, accelerate decision-making, and enhance access to therapies for patients with rare diseases.

A discussion around outcome measures concluded that a well-set and well-defined research question is required, and some challenges with primary outcomes were attributed to a lack of clarity in trial design. There is a need to balance what is required from a regulatory and reimbursement perspective vs what is feasible to collect.

The recent developments in wearables and collective technology make patient reported outcomes easier to collect, and the group considered if this meant we should be shifting more towards their use in clinical trials and regulatory processes. There is a possibility that information captured in this way by patients is not sufficiently robust, but it can certainly act as a supplementary dataset. This led to considering the utility of PROs when it comes to regulatory decision making and how they are generally only collected in clinical trials and not in real world data.

A discussion on innovative designs began by considering the difference between platforms and master protocols and if we should strive to set up platform trials for rare diseases. This type of model would require funding to ensure sustainability. Some aspects of innovative design, such as Bayesian design or use of synthetic data and the idea of digital twins is still very much in the academic world and the group acknowledged that meaningful adoption of these approaches within regulatory frameworks would require a significant cultural and organisational shift.

4.3. How might evidence needs be met by the data sources we have, and how can the potential of these be leveraged?

This breakout session explored data sources including what data exists, the key challenges related to data standards and interoperability, barriers to data access and opportunities for repurposing data.

In relation to data packages, the group considered the most critical evidence needs to support recruitment and the extent to which these needs are met by existing data sources. The discussion also addressed the most critical evidence needs for regulatory approval and examined what is currently available as well as identifying the gaps.

Other topics discussed included:

- The importance of adopting more innovative ways of working, given that technological advances now enable home-based health consultations, remote video assessments, and cloud-based data sharing.
- A consensus that sustained funding is required to support a national data infrastructure across all four UK nations, with clearly defined mandates, governance, and requirements.

- The need to further explore how artificial intelligence (AI) and machine learning approaches can be used more effectively, for example in the screening of primary and secondary care datasets to boost diagnoses, or to mine multiple large datasets to more easily count how many patients have any given condition.
- The importance of linking UK Biobank data and patient-identified biobank data with electronic health records and routinely collected healthcare datasets.
- The development of a standardised and dynamic consent model that allows individuals to amend or update their consent over time, including the ability to consent selectively to specific uses of their data (e.g. research, commercial use, pharmaceutical development, or AI modelling).
- Consideration of the role of registries and real-world evidence in supporting regulatory approvals. While such data sources may capture changes in treatment, they often fail to record the clinical decision-making processes underlying those changes, highlighting the need for mechanisms to capture this information.
- Advocacy for the further development of national rare disease registries, informed by best practice from established national cancer registries. There is limited knowledge of how the 4 national registers function, who can access what kinds of data, etc. A public awareness campaign is very much needed here. It may also be worth considering if, down the line, any data collected by national funders like NIHR should by default be submitted to the national registry for rare disease. However, for national registers to take on additional responsibilities and really deliver on the potential, there needs to be a greater involvement of the wider rare disease research community in contributing to their vision, as well as more resourcing for core registry experts to deliver these services.
- Recognition that disease-specific models for every rare condition are not feasible, and that the development of a minimum dataset applicable across multiple rare conditions would provide some value.

5. Key Messages and conclusions

The workshop organisers have prepared a review for publication (the link will be updated here once available). This paper really emphasises the importance of collaboration between all the initiatives currently exploring or seeking to amend regulatory and access frameworks for rare disease therapies in the UK, particularly the five projects co-organising this workshop. What is clear, however, is that considering the whole pathway from research and innovation through regulation, HTA and access, there is a lot of room for improvement. The challenges and 'pain points' may well differ from one disease area to another, and it is likely that different fields will require different solutions depending on characteristics such as prevalence of the condition, age of onset of symptoms, severity and speed of symptom progression, etc. Therefore, when making changes to the UK's regulatory framework (through ongoing -as of Q2 2026- MHRA proposals[2]) but also in contemplating any changes

[2] The *Draft Rare Disease Therapies Regulatory Framework* opened for consultation in May https://www.gov.uk/government/consultations/draft-rare-disease-therapies-regulatory-framework/draft-rare-disease-therapies-regulatory-framework

to HTA or access arrangements, it will be important to avoid disrupting systems and processes that *do* work and are already viewed as appropriate and effective.

The participants agreed that follow-up workshops, dedicated to more specific aspects of some of the topics explored in this initial meeting, would be beneficial, whilst acknowledging that it will be necessary to observe how some of the major shifts and developments on the horizon actually materialise and evolve.

Annex 1 – Detailed Survey Report

UK Regulatory and Access Frameworks Survey Summary

Background

Rare Disease Research UK (RDR UK) and the LifeArc Centre for the Acceleration of Rare Disease Trials (ARDT) conducted a survey to capture the experiences of the UK rare disease research community with regulatory pathways and frameworks. The survey gathered insights on bringing medicines, devices, and diagnostics to patients, including interactions with UK regulatory authorities (e.g. MHRA), HTA agencies across the four nations, and NHS partners. It aimed to identify common challenges, community needs, and priorities for improving regulatory frameworks and market access processes in rare disease.

Method

The survey was structured as a mix of multiple-choice and open-text responses. Participants were first asked to indicate the UK nation(s) their experience derived from, and whether they had direct engagement with regulatory bodies. They were then invited to reflect on their experiences with specific stages of regulatory processes for rare disease including

- Marketing authorisation for medicines
- CE/UKCA marking or conformity assessment for devices or diagnostics
- Health Technology Assessment (HTA)
- NHS commissioning or service adoption
- Post-market surveillance or safety/data reporting

Respondents rated the **ease, timeliness, clarity, and predictability** of progressing through these processes. They were also asked to describe any support received from regulatory agencies, and to comment on what works well, what does not work well, and what challenges they have faced in their journey.

Finally, the survey sought views on effective international practices and asked participants to propose one change they would prioritise for the future of UK regulatory frameworks in rare disease.

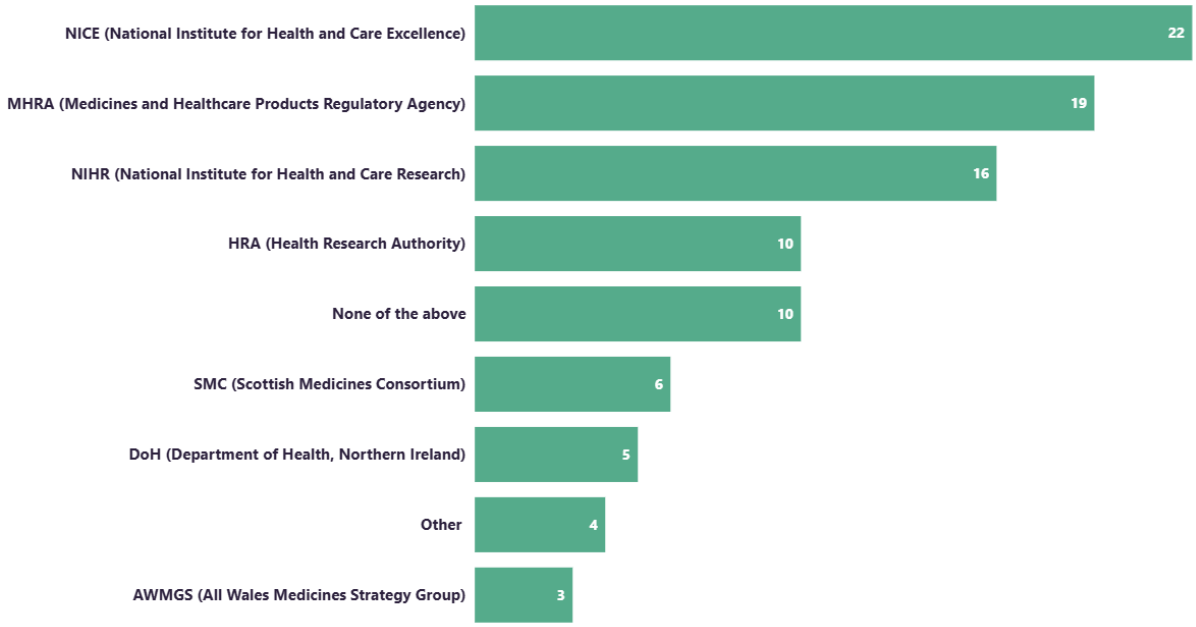
Findings

A total of 45 responses were received. Respondents included senior lecturers, consultants, researchers, patient advocates, and healthcare professionals, representing a range of organisations such as universities, hospitals, charities, biotech companies, and independent professionals.

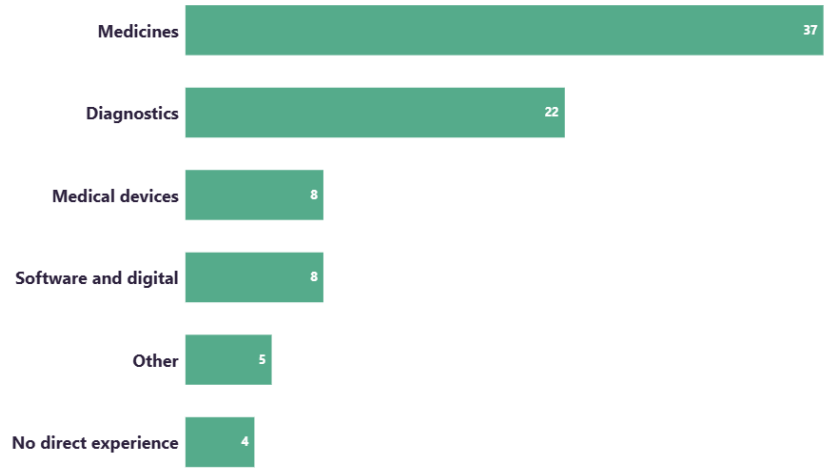
31 respondents reported experience solely from England, 6 had UK-wide experience, 1 from both England and Wales, 3 from Northern Ireland, and 1 each from Scotland and Wales.

Respondents came from a range of backgrounds. 7 were linked to industry, while the majority were from healthcare or academia/research. 13 had lived experience of rare disease, and 15 were involved in patient advocacy or charity work. Others included founder/ CEO of start-up and NHS Commissioner.

Respondents were asked whether they had direct experience engaging with UK organisations in relation to regulatory and access processes. As this was a multiple-choice question, respondents could select more than one organisation. The highest level of engagement was reported with NICE, followed by MHRA and NIHR. Other organisations included HTA HFEA and NHS.



Respondents were asked which areas their experience related to, with the option to select more than one. The majority reported experience with medicines, followed by diagnostics, while fewer noted involvement with medical devices, software and digital health.

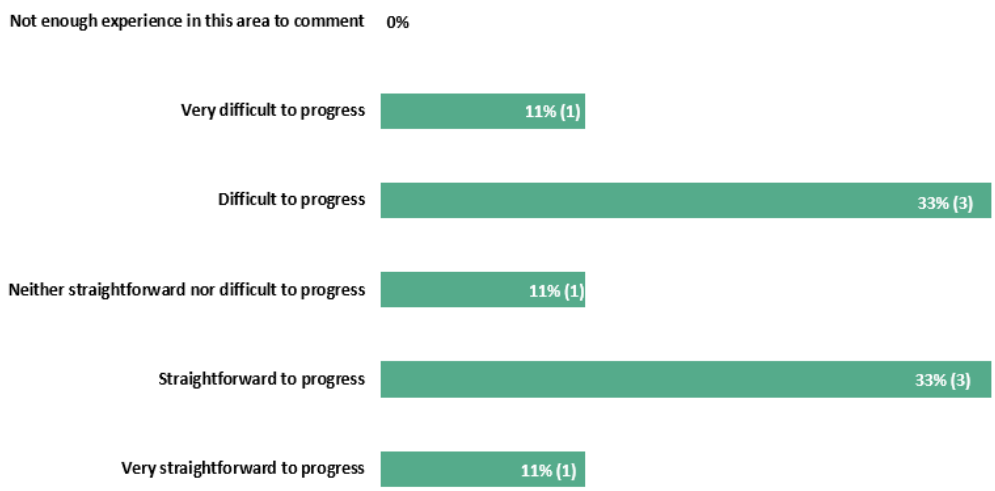


Do you believe that overall, it is straightforward or difficult to progress through these current UK processes and that requirements and processes from agencies in the UK are clear?

NB as each of these questions were only answered by a subset of the overall respondents, the numbers are small and trends should therefore be viewed with caution and be interpreted against the wider body of comments.

UK Marketing Authorisation

In terms of ease of progressing through UK marketing authorisation processes, respondents were evenly split between ratings of 'straightforward' and 'difficult'.



Key challenges highlighted include financial and market barriers, with small companies facing high costs and limited margins that discourage entry, often delaying patient access. The system is also complex and bureaucratic, with slow and opaque processes at MHRA, NICE, and SMC, where outcomes can depend more on committee discretion than clear evidence standards. Rare and genetic medicines face additional uncertainty due to unclear regulatory requirements and limited clinical data, making conventional pathways often unsuitable. While mainstream medicines with robust data navigate the system more smoothly, rare and novel therapies frequently encounter significant delays, restricting timely patient access.

In terms of clarity, UK marketing authorisation processes are generally clear and well-defined, with guidance from MHRA, NICE, SMC, and AWMSG providing a transparent framework. However, the pathways are often poorly suited to rare disease therapies, creating practical challenges despite the clarity of the rules. Increasing complexity and bureaucracy add administrative burden, with limited perceived benefit beyond regulatory oversight, making timely access to treatments for rare disease patients difficult.

Comments

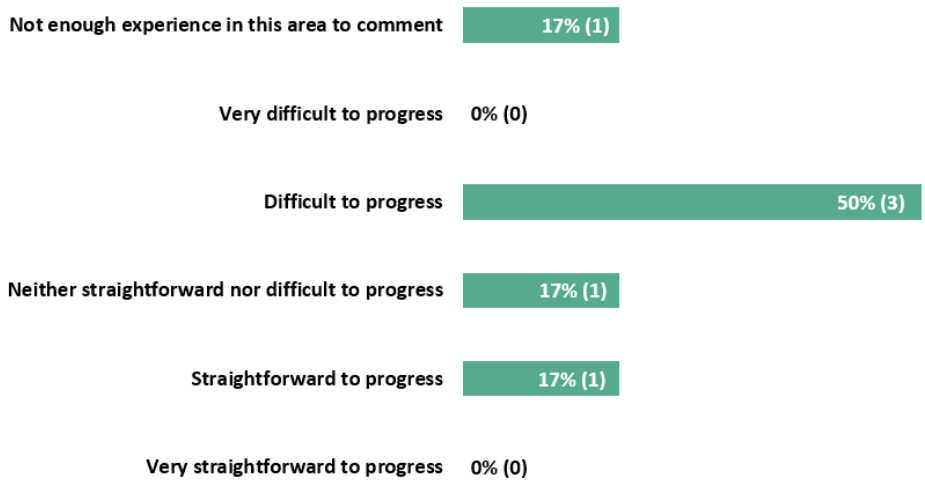
'Clarity with regards to the path of a genetic medicine to the clinic is needed. What proportionate data package is needed to get marketing authorization?'

'In general, I know the cost of having to do all of this again after doing the US and EU is making it very difficult for small companies to make the commitment to entering the UK market'

'The regulatory processes for mainstream medicines are clear, and if the submitted data is acceptable, straightforward. Rare disease - especially individualised therapy is much more difficult in regulatory terms due to the paucity of data. For individualised therapies it is possible to have no in human data at all. In these cases, the conventional regulatory system leading to a Marketing Authorisation is untenable.'

CE/ UKCA Marking

Overall, UK CE/UKCA marking is straightforward for low-risk devices but increasingly complex for high-risk or rare disease diagnostics, with system inconsistencies and adoption barriers adding further challenges.



Progress through UK CE/UKCA marking varies by device type and risk classification. Low-risk devices are relatively straightforward to self-certify, though this may not provide sufficient evidence for NHS adoption. High-risk devices and diagnostics, particularly for rare diseases, face challenges due to limited patient populations and underpowered clinical studies. Differences between UK and EU requirements, such as the need for a Notified Body opinion in Northern Ireland but not in Great Britain add complexity, and overall adoption of innovative devices remains difficult. Clearer guidance could help streamline the process and improve access.

CE/UKCA data requirements are generally clear for medical devices. However, in vitro diagnostics (IVDs) are less straightforward due to limited guidance and ambiguity around whether pre- or post-certification studies are needed to demonstrate clinical utility, making planning and compliance more challenging.

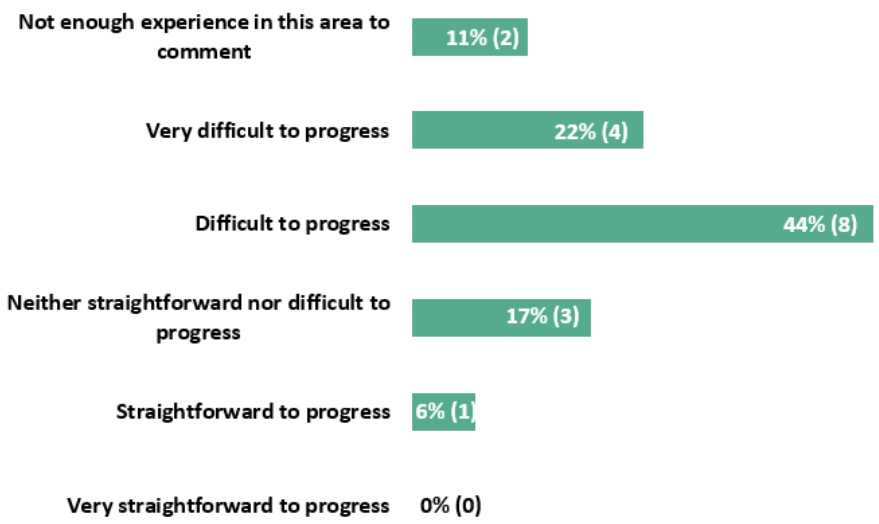
Comments

'Differing device requirements in UK and EU mean that it is difficult to apply for a UK MAA with an integral device since in GB MHRA do not require a Notified Body Opinion/CE mark and in Northern Ireland they do (as they are under EU MDR). Consistency in device requirements/Health authority oversight between the two territories as was achieved with the Windsor Framework for medicines would help eliminate this discrepancy.'

'There's limited documentation and support, the best I've found is on the IRAS system which details the types of studies which classify as performance evaluations for the EU. There's often an argument as to whether an IVD can be used interventionally before UKCA / CE marking to demonstrate utility (as you can sometimes do with medical devices), or whether you need a follow-on study after certification. Definitely muddier for IVDs.'

Health Technology Assessment

Progress through UK Health Technology Assessment (HTA) is widely regarded as difficult, particularly for rare and high-cost therapies. Demonstrating cost-effectiveness is challenging due to limited data, small patient populations, and high treatment prices, which can deter companies from entering the UK market.



The multi-step approval process, including complex negotiations with NHS R&D offices, often causes substantial delays and wastes research funding. Standard HTA methodologies, such as ICER-based assessments, are poorly suited to ultra-rare diseases, meaning many therapies fail to achieve approval despite clinical benefit. Overall, the system creates financial, evidential, and procedural barriers that limit timely patient access and discourage industry investment.

In terms of clarity, HTA processes are generally clear in principle, but in practice they are often unsuitable for rare diseases. Standard cost-effectiveness methodologies and rigid appraisal expectations fail to account for small patient populations, unclear trial design pathways, and limited registry or data infrastructure. While agencies such as MHRA and NICE provide transparent guidance, the system remains complex, slow, and burdened by multiple approval bodies and inconsistent expert involvement. Ultimately, clarity on paper does not translate into workable processes, with cost and methodological barriers making HTA particularly challenging for rare disease therapies.

Comments

'A better structured interface with registries would improve this considerably. EMR are not constructed for the purposes to report these findings'

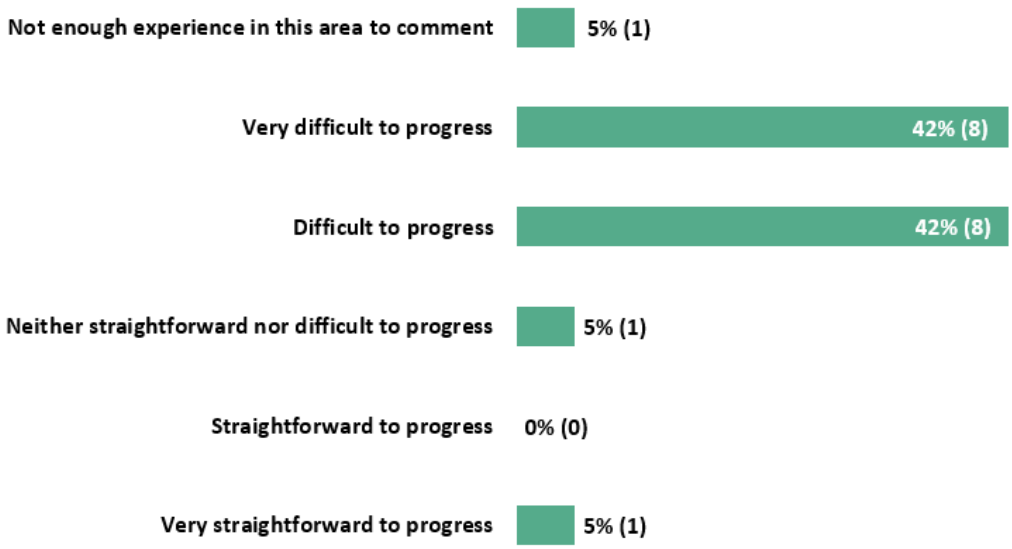
'The complex set of bodies who each need to give approval makes the whole process awkward, cumbersome and slow.'

'Often described as difficult to demonstrate cost-effectiveness, due to evidence limitations and (relatively) high prices for orphan medicines.'

'Complex negotiations with NHS R&D Offices, who are often overloaded. This ends up slowing progress very substantially, wasting a lot of research funding as months go by while we wait for each of a series of approval steps.'

NHS Commissioning

NHS commissioning is widely regarded as difficult. It is slow, bureaucratic, and underfunded, and creates a major barrier to patient access. The responses highlight the overly complex and outdated processes, fragmented decision-making, and lack of accountability, with delays often lasting years.



Limited funding and short-term planning further restrict adoption, while insufficient infrastructure prevents delivery of approved therapies. These challenges are particularly damaging for rare disease populations, where treatment delays can mean missed opportunities for benefit.

In terms of clarity, NHS commissioning requirements and processes are only partly clear. While the steps may be transparent in theory, in practice staff themselves are often unsure of procedures, particularly for amendments to existing documents. The system's complexity, coupled with a lack of accessible guidance or a clear roadmap, creates confusion. Although some flexibility can be helpful, it often adds to inconsistency, leaving commissioning processes perceived as bureaucratic, flawed, and difficult to navigate.

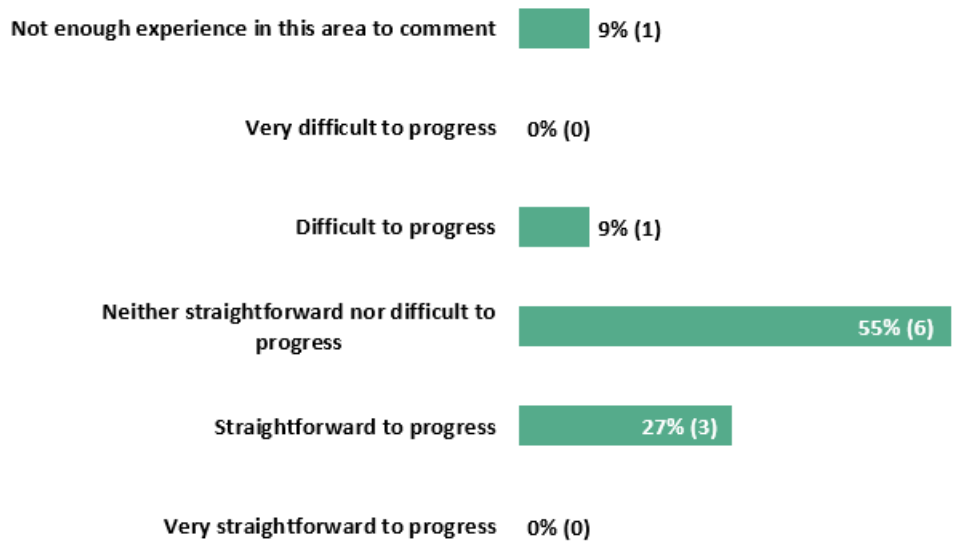
Comments

'The process of NHS commissioning is very lengthy and bureaucratic.'

'The adoption and commissioning process starts too late and as we know rare disease populations cannot wait too long as disease progression can reduce the opportunity to benefit from new therapies and solutions. The system needs to work more closely with the industry to reduce the time lag between approval and adoption. There is a risk the new NHS structure may fragment this even further.'

Post-Market Surveillance

Opinions on post-market surveillance appeared less fixed than for the activities above, with the most popular response being neither straightforward nor difficult overall. Difficulty is to navigate without dedicated funding or clear, consistent requirements. Respondents stressed that surveillance is most effective when supported by funded registries, as relying on clinicians alone adds to workload and risks limiting patient access. Current approaches are seen as overly burdensome, with calls for simpler, light-touch systems.



Additionally, inconsistencies between UK and EU requirements, particularly for integral devices, create unnecessary complexity.
UK post-market surveillance and safety/data reporting requirements are technically defined but increasingly viewed as overly complex and bureaucratic. Clinicians and researchers report growing administrative burdens without clear evidence of patient or therapeutic benefit, suggesting that while the processes exist in principle, their practical value and clarity are undermined by unnecessary layers of bureaucracy.

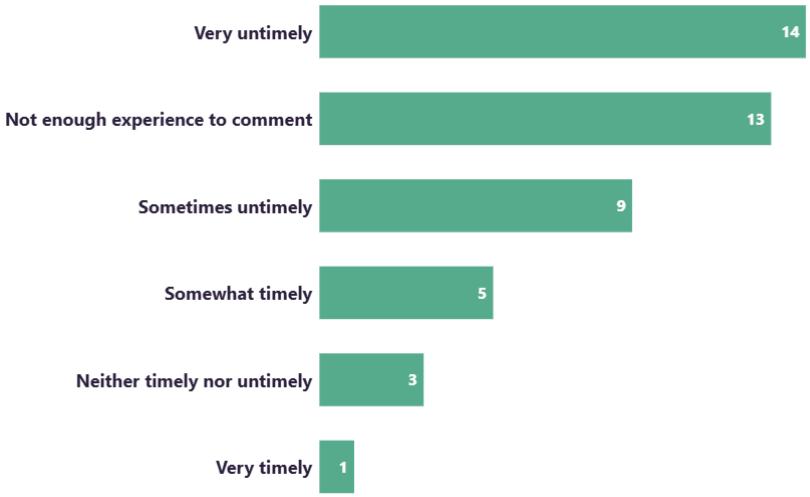
Comments

'Post-marketing surveillance is most effective when registers are funded either by pharma (as a licensing requirement) or by public funds. Expecting doctors to just take this risks fueling resentment (for adding to the "invisible" work we do and the barriers we experience getting treatments to our patients- who often end up not getting the treatment they need as a result) so needs a simple format/light touch.'

Overall, UK processes are seen as highly challenging to navigate, especially for rare diseases. Patients face significant knowledge and awareness gaps, with delays and misdiagnoses common due to limited clinician understanding. Navigating the system requires persistence, as services are fragmented, points of contact unclear, and bureaucracy extensive. Rare disease therapy development is particularly constrained by high costs, lengthy timelines, and unsuitable regulatory approaches, while limited funding and short-term planning further hinder progress. Even when therapies reach clinical trials, lack of clear guidance and low success rates mean many fail to progress to approval, leaving patients without access to potentially life-changing treatments.

UK agency requirements and processes are generally clear in principle, with MHRA providing structured guidance under the existing framework, but practical challenges remain. Future regulatory pathways are uncertain, making planning difficult, and rare diseases often lack tailored guidance, leading to inconsistent treatment and high costs. Accessibility of information is also a barrier, with even official resources proving difficult to navigate. Overall, while processes are transparent in theory, gaps in clarity, accessibility, and rare disease focus limit their effectiveness in practice.

How would you rate the timeliness of the regulatory and market access processes for rare disease research or product development?



UK regulatory and market access processes for rare disease therapies are widely seen as too slow and complex. Lengthy timelines mean approvals often take years, leaving patients waiting far longer than in the US or EU. These delays are compounded by regulatory agency inefficiencies, with slow coordination between MHRA, NICE, and SMC further hindering timely access. The system complexity, including extensive and sometimes unrealistic evidence requirements, creates drawn-out reviews and discourages companies from launching in the UK. These challenges are particularly acute for rare diseases, where small patient populations and severe, fast-progressing conditions make conventional timelines and rigid requirements unworkable. Even when regulatory approval is achieved, evidence gaps can prevent adoption if data does not align with NHS or NICE expectations. Overall, while processes are clear in principle, in practice they are slow, bureaucratic, and poorly adapted to the needs of rare disease patients.

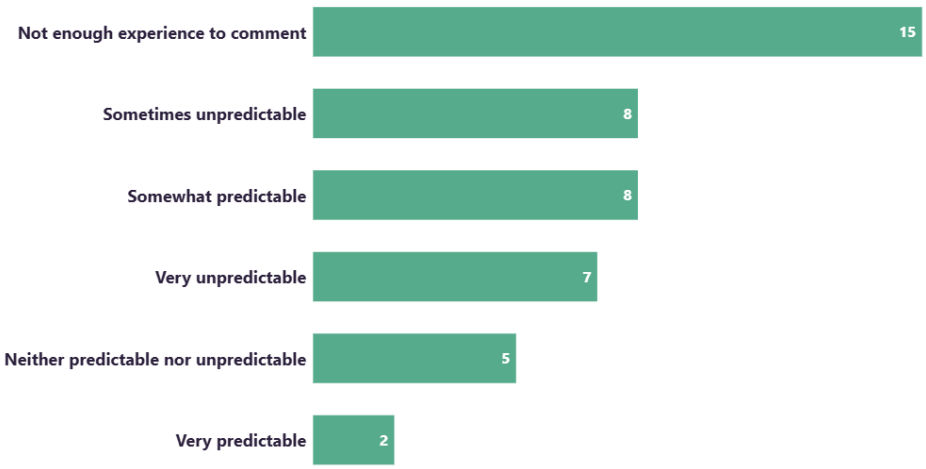
Comments

'In our experience the MHRA procedure was quick and efficient, but the NICE procedure has very long timelines.'

'The process is very demanding and asks for information that is either not available today, may not be available in the short to medium or long term especially given the small population in rare. This means the process is drawn out as these uncertainties cannot be reconciled. Unrealistic demands are made which has resulted in a number of therapies not being approved or not even planning a launch in the UK.'

'Conventional approvals take a long time to process. My experience would be c 1 year periods consecutively for MHRA and NICE. This may have improved in the last few years - but using the example of the baby in the news from US recently given a gene therapy for a metabolic disorder, 2 years is not going to work in that setting where a therapy is designed for one individual.'

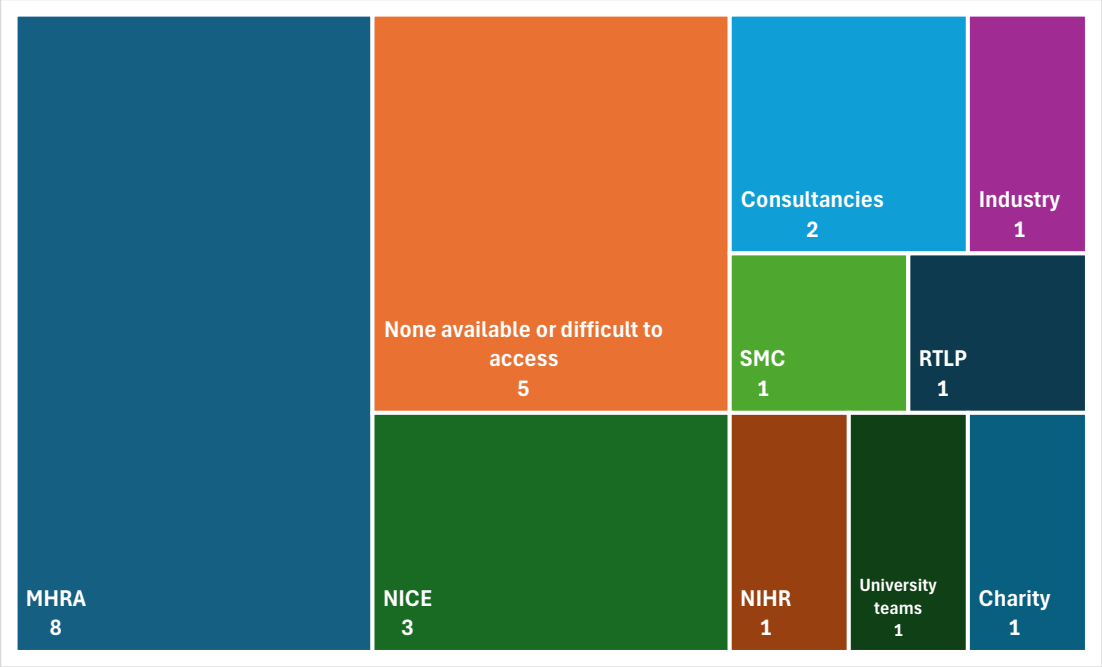
How would you rate the predictability of the regulatory and market access processes for rare disease research or product development?



The system is widely seen as unpredictable for rare disease as the data requirements are often unclear. A distinction is made between common diseases where a large, randomised control trial with plentiful data makes assessment easier and more predictable, and rare diseases where less data is available, leading to discussion, unpredictability and delay.
If there was more expertise in rare diseases in assessment panels, processes would become more predictable.

Please tell us about any form of support that you have been able to access from regulatory agencies in the past, or from your host organisation or other third party.

The survey asked respondents to give details of support that they had been able to access from regulatory agencies, their host organisation or other third parties. This was to help us understand the different types of support that are available, and also how useful that support is. Feedback around the support received was generally positive. However, some believe that support is difficult to access, or that it does not exist.
The majority of support accessed was through the MHRA, followed by NICE. Individuals commented that they had each received support from Industry, SMC, RTLP, NIHR, their university or a charity.
In general, comments show that support is available, but that it is not always necessarily easy or straightforward to access. The level of support available also varies across organisations, and even when available, it is not always timely. The MHRA's processes are viewed to be clearer than those of other agencies and their willingness to work with patient organisations is highlighted.



Comments

"We have had good liaison from MHRA, and SMC though the SMC procedure is not yet complete. NICE has been helpful in general, although their public messaging has complicated the situation."
"Working with MHRA is the most clear of the pathways compared to the other agencies/ processes."
"MHRA provides useful support through their queries process. However, recently this took 10 months to get a reply around IVD study design."
"It is very difficult to access support for the academics either from the regulatory agencies or the academics."
"The MHRA is keen to work with patient organisations. They are easy to make contact with and go out of their way to help. They have prioritised review of clinical trial amendments and applications when we have highlighted delays and their impact."
"Zero. Just blocking tactics"

Please tell us what you think works well in the UK regulatory and access frameworks for rare disease research or product development.

This question received a broad range of responses. A wide range of positive experiences was shared, but the feedback from other respondents was that nothing or not very much is working well. In terms of what does not work well, the points raised are summarised as follows:

- Rare disease is disadvantaged in the system
- Processes are not timely enough
- MHRA less collaborative than other agencies

In terms of what does work well, the support and advice that is available is welcomed and agencies' flexibility and willingness to innovate is seen as a very positive aspect of the UK's framework. Agencies are viewed as being open to engagement with the community and

their willingness to be innovative and open to new ways of working is welcomed, including efforts to make adaptions for rare disease and new, emerging personalised therapies.

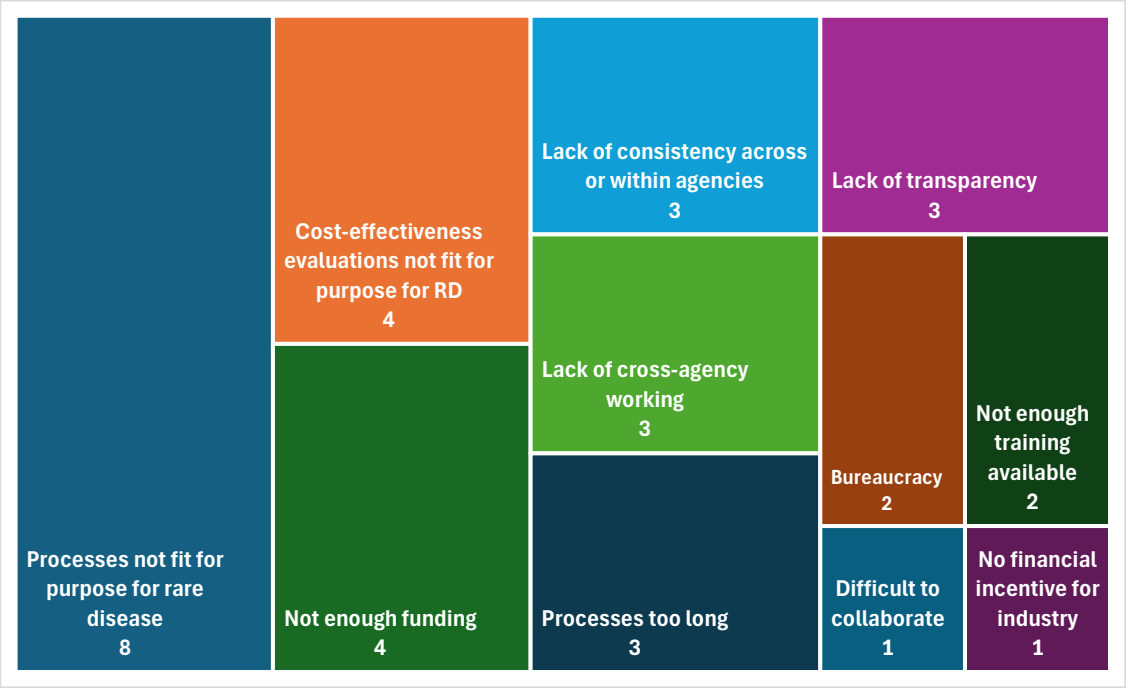
Comments

"The quality of the MHRA assessment is second to none and the appropriateness of the risk/ benefit clearly taken into consideration"
"MHRA is an innovative regulatory agency and should be proud of their willingness to address tough regulatory issues/challenges, specifically as they relate to rare disease. They appear to be taking the lead in establishing a new regulatory framework for uniquely rare, SDLT indications (similar to mRNA cancer vaccines) for which they should be commended."
"I think there is a robust framework however, I feel chronic rare diseases are disadvantaged compared to cancer. It is difficult to show a dramatic benefit easily quantifiably even when there is plus, of works then patients can be on lifelong reducing cost effectiveness for chronic disease compared to cancer."
"Great that the UK is starting to think about how we get medications to those with rare diseases (in the case of ultra-rare diseases, we need real vision to see how we can get medicines to people who are not cute babies). One rare disease I work with has benefitted from an active patient organisation, well-defined pathogenesis of disease- particularly from companies wanting to try out new technologies."
"MHRA are friendly and happy to help small patient groups (although don't always have the answers to questions). They are trying to improve their patient engagement and are transparent in their strategy and progress, and accept feedback (positive and negative)."

Tell us what you think does not work well in the current UK regulatory and access frameworks for rare disease research or product development or what challenges you have faced.

The most recurring theme of the responses was that processes are not fit for purpose for rare disease, where respondents highlighted the difficulties in gathering data for rare

diseases, the need for evidence standards to be proportionate to the number of patients and the need for innovative approaches towards treatments for individualised therapies where conventional methods will not work. Respondents also commented that cost-effectiveness evaluations are not fit for purpose for rare disease.
There is a view that agencies are not consistent, resulting in conflicting advice and requirements, and that there is a lack of collaboration between agencies. Additionally, it is perceived that requirements are not aligned between agencies, leading to a longer and more complex pathway.
Comments on bureaucracy and length of time for processes were also seen frequently.



Comments

“Difficult to gather data on rare diseases, funding limitations make it hard to convince regulatory bodies and commissioners of value.”
“Innovative approaches are required for treatments for RD/individualised therapies. Conventional methods will not work.”
“Using current Health Economic metrics, e.g. QALYs, the cost-effectiveness at a population level is essentially capped due to the extremely low prevalence, with rare disease screening being a difficult business case for NICE to recommend the testing. If more societal metrics were used, beyond the individual patient QALY, such as costs of family counselling and support, we might see a better argument for adoption of rare disease diagnostics.”
“Financially not worth anyone investing in rare diseases for the most part.”
“A solution requires coordination across agencies and probably a new regulatory framework that can adapt to information sharing across related genetic medicines. Balancing safety and cost effectiveness with progress is challenging.”

"Working better alongside HTA bodies to better align on both regulatory and HTA requirements is needed."

Are you aware of any international practices or approaches which you feel are particularly effective in terms of regulatory processes for rare conditions

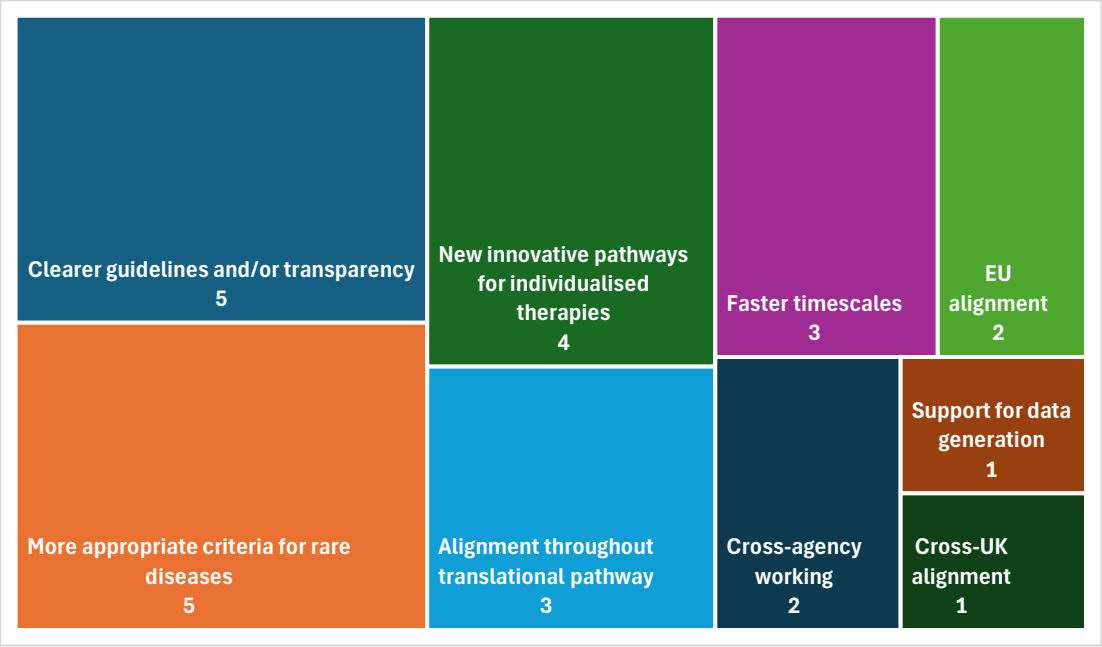
Respondents gave a number of examples of international practices, which included:

- Support for registries by NHS (or similar) tariffs.
- FDA 510k clearance (USA). Applies to medical devices and can work well for rare disease where studies would typically be underpowered due to lower numbers of participants.
- Accredited centres for bone marrow transplant. (Netherlands and Germany)
- USA Orphan Drug Act.
- Approved PKD Guidelines adopted by medical teams (USA)
- Providing access to drugs before the final decision on reimbursement is made (Germany)
- EMA approval or orphan designation is sufficient for commissioning (France and Germany)

What is the one change that you would like to see made in the future in relation to UK regulatory frameworks

The final question asked for respondents to give one change that they would like to see made in the future in relation to regulatory frameworks in the UK.

Answers highlighted that the community wants to see clearer guidelines and transparency and more appropriate criteria for rare diseases. It is also evident that there is a wish for more innovation around pathways for individualised therapies and N=1 trials. Other common responses included alignment throughout the translational pathway and faster timescales.



Comments

“An innovative pathway allowing n of 1/a few to be treated and reimbursed, with data collection leading to retrospective assessment.”

“The different bodies systematically working together (eg NICE and MHRA) and being aligned on the data that they want.”

“Shorter Time to certification and considerable reduction in costs, especially for startups and SMEs.”

“Fair and even services for all rare diseases.”

“Clear guidelines. Easy access for advice as developing programs.”

“Differential criteria for assessing drug re-imbursement for rare diseases that are not 'ultra-rare'.”