Rare Disease Individualised Therapies System Information Day

Executive Summary & Insights

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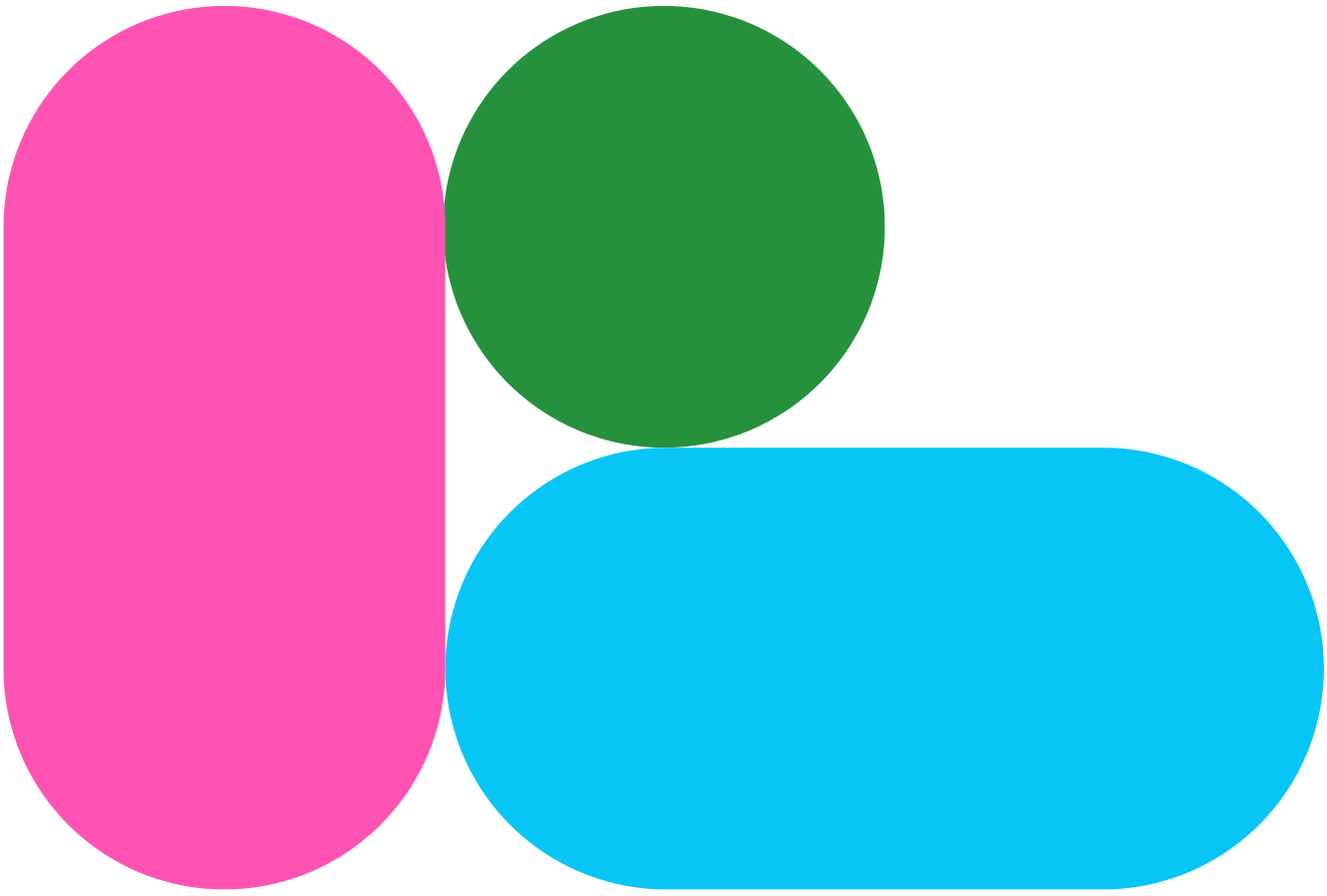

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Aim of the day

Understand the specific challenges of truly individualised therapies, including their regulation, reimbursement, and administration, while exploring emerging technologies and identifying pathways for UK advancement. Fostering collaboration among stakeholders such as MHRA, NICE, and NHSE as a key to developing actionable solutions, considering both 'platform' approaches and individual agents, and fostering innovative perspectives on these critical issues.

Agenda

Time	Title	Speaker
10.00 – 10.30	Arrival & coffee	
10.30 – 10.45	Introduction	Prof. Matt Brown, Chief Scientist, Genomics England.
10.45 – 10.55	Framing the issue	Kath Bainbridge, Head of Rare Diseases and Emerging Therapies Department of Health and Social Care
10.55 – 11.10	Delivery in the NHS and lessons from other countries	Fiona Marley, Head of Highly Specialised Commissioning NHS England
11.10 – 11.30	The patient experience	Mel Dixon, Trustee at Cure DHDDS
11.30 – 12.00	Individualised ASOs and the potential for future therapies	Prof. Stephan Sanders, Professor of Paediatric Neurogenetics at University of Oxford
12.00-12.30	Lunch	
12.30 – 13.00	An actionable path to CRISPR cures	Prof. Fyodor Urnov: Professor of Molecular Therapeutics UC Berkley (virtual)
13.00 – 13.45	Panel discussion – ongoing initiatives in the field	Chaired by Ana Lisa Tavares, Clinical Lead for Rare Disease Research Genomics England.
13.45 – 14.00	Coffee break	
14.00 – 14.50	Workshop – how can the healthcare system change to meet these needs?	
14.50 – 15.00	Summary and close	Kath Bainbridge/ Matt Brown

Summary

The Rare Disease Individualised Therapies System Information Day brought together stakeholders to understand, and start to think about solutions for the challenges in the development and implementation of therapies tailored to rare diseases.

Professor Matt Brown highlighted the limitations in research funding, regulatory inefficiencies and disparities (e.g. FDA, EMA, MHRA), and challenges in patient recruitment for clinical trials. He emphasised the need for collaborative approaches to accelerate diagnosis and therapy development, with initiatives like WGS via Genomics England and the Rare Therapies Launch Pad working to provide vital pathways.

Kath Bainbridge discussed the UK Rare Disease Framework, emphasising faster diagnosis, improved access to care, and the need for pioneering research. She outlined the governance structure supporting these goals, involving NHS England, MHRA, and other delivery partners, and highlighted the draft 2025 England Rare Diseases Action Plan as a possible route to making a commitment to integrating individualised therapies into the NHS. For further background in 2024 please see England Rare Diseases Action Plan 2024: main report.

Fiona Marley shared NHS England's perspective on integrating individualised therapies into the health system and outlined the action NHS England had put forward for the 2025 action plan. She emphasised the importance of creating a robust operational framework for delivering these therapies, including considerations for patient pathways, genomic testing, and evidence generation. Lessons from international models demonstrated the value of centralising expertise in condition-specific centres (i.e. expertise with the condition rather than drug administration in the centre. The ability to administer these therapies is more widespread).

Mel Dixon provided a patient's perspective, sharing the journey of addressing ultra-rare conditions, in her case with DHDDS variants. She underscored the challenges of isolation, funding, and the need for collaboration, while highlighting the importance of building international research networks and initiating drug repurposing projects. The need for accessible therapies locally, without reliance on international travel, was a recurring theme. For more information please visit: Cure DHDDS.

Professor Stephan Sanders elaborated on the potential of ASOs (antisense oligonucleotides) and CRISPR technologies in treating neurodevelopmental and genetic disorders. He presented examples of successful therapies and outlined the hurdles in safety, regulatory approval, and cost-efficiency. He emphasised the transformative impact of individualised therapies and the opportunities these technologies present in advancing precision medicine, but noted the need for systemic changes in research and regulation to realise their full potential.

Professor Fyodor Urnov outlined a path for CRISPR cures, emphasising its potential to revolutionise treatment for rare genetic conditions. He highlighted the current regulatory hurdles that treat each CRISPR guideRNA adaptation as a new product, driving up costs and delays. This was showcased with his Jammie Dodger analogy: Changing the filling of a Jammie Dodger from raspberry to strawberry doesn't require re-evaluating the entire regulatory process for every ingredient in the biscuit; only the new filling undergoes review. Similarly, a focused regulatory approach could be applied to CRISPR technologies, where modifications are assessed individually without revisiting established components. He proposed platform-based approaches to pool patients by syndrome and streamline manufacturing and regulatory processes. He underscored the UK's unique position, with its single-payor integrated

healthcare and genomic infrastructure, to be able to lead globally in precision medicine by adopting accelerated approvals and collaborative pipelines for severe paediatric diseases.

The panel discussion and subsequent workshop explored actionable strategies for changing healthcare systems to meet these needs. Stakeholders identified the importance of streamlined regulation, collaboration across sectors, and robust data collection frameworks to support therapy efficacy and safety. The day concluded with commitments to further refine strategies in the upcoming Rare Disease Action Plan.

Key Highlights

1. Challenges in Rare Disease Treatment

- Limited basic research and funding.
- Regulatory hurdles, with frameworks tailored for common diseases.
- Poorly understood natural history of rare conditions and lack of outcome measures.
- High costs of clinical trials and challenges in patient recruitment, possibly due to the limited patient pool for rare diseases and the lack of comprehensive patient registries.

2. Innovative Therapies

- Focus on CRISPR and antisense oligonucleotides (ASOs) as transformative tools.
- Platform-based approaches to expedite development and regulatory pathways. (Jammie Dodger analogy).
- Highlighted individualised therapies like n=1 ASOs, enabling bespoke treatment for ultra-rare genetic variants.

3. Collaborative Initiatives

- Rare Therapies Launch Pad (RTLP): A pilot program developing infrastructure, pathways and policy for individualised therapies.
- Nucleic Acid Therapy Accelerator (UPNAT): Focused on patient selection guidelines and streamlining translation to clinics.
- Centres of Research Excellence (CoRE): aiming to advance the development of innovative therapies for diseases that currently lack effective treatments (e.g. MRC Centre of Research Excellence in Therapeutic Genomics).

4. Patient Stories

- Personal testimonies underscored the urgency of accessible therapies.
- A handful of committed parents have had success in building research collaborations and securing funding for ultra-rare conditions like DHDDS, HLH, FOP and many more. This is not scalable or equitable.

5. Framework Development

- Proposed operational need for a framework by NHS England for individualised therapies put forward for the 2025 England Rare Diseases Action Plan.

- Will need clarity from MHRA and NICE on their approach to evaluating these therapies
- Emphasis on safety, cost-effectiveness, and efficient pathways for treatment delivery.

6. Global Lessons and UK's Role

- Learning from international examples to create centres of excellence.
- Learning from other regulators e.g. FDA guidance for Individualised ASOs
- Aligning with the 2025 England Rare Diseases Action Plan and strengthening the UK's position in life sciences.

Action Points:

1. Accelerate Diagnostic Pathways

- Expand genome sequencing programs (e.g., Long Read Sequencing) to improve diagnostic rates.
- Enhance data-sharing platforms to facilitate research and patient identification.

2. Develop a Unified Regulatory Approach

- Engage MHRA, NICE, and NHS England to tailor approval and reimbursement processes for individualised therapies.
- Establish guidelines for n=1 ASO therapy and CRISPR applications.

3. Invest in Platform Technologies

- Promote scalable manufacturing and toxicology models for small-batch ASOs.
- Support a platform-based regulatory and delivery system to pool resources across similar conditions.

4. Build Collaboration Networks

- Strengthen ties between researchers, clinicians, and patient groups. Reduce fragmentation.
- Foster partnerships with international initiatives like n-Lorem, N=1 Collaborative, RTLP and UPNAT to streamline therapy development.

5. Enhance Patient Support

- Provide resources for families to connect with researchers and advocacy groups post-diagnosis.
- Develop tools to clearly explain individualised therapies and their risks and benefits
- Develop clear pathways to access experimental therapies locally, reducing the burden of travel and costs.

6. Monitor and Evaluate Outcomes

- Create robust data collection frameworks for tracking therapy efficacy and adverse events.
- Use insights to refine clinical trial /treatment pathway designs and approval processes.

Key Takeaways

The Rare Disease Individualised Therapies Information Day emphasised the importance of integrating patient-centric approaches with cutting-edge science and streamlined policies. It highlighted the need for the different public bodies involved in genomics, research, regulation and service delivery to work together to overcome challenges and enable safe, cost-effective access to these therapies. Stakeholders committed to advancing diagnostics, developing actionable frameworks, and fostering global collaborations to ensure timely, equitable access to life-changing treatments. Each body represented at the meeting expressed intent to explore potential commitments for inclusion in the2025 England Rare Diseases Action Plan.