



Department
of Health &
Social Care

The UK Strategy for Rare Diseases

Rare Diseases implementation plan for England

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Foreword

As co-chairs of the Rare Disease Policy Board we welcome the joint publication by NHS England (NHSE) and the Department of Health and Social Care (DHSC) of their implementation plans for meeting the commitments in the UK Strategy for Rare Disease. This document sets out an overarching view and the actions which DHSC will take to coordinate the delivery of the commitments by its partner organisations, which fall within its remit. It should be read in conjunction with its sister plan published by NHS England, which sets out the actions against the commitments owned by NHS England. Between them, both documents cover all of the 51 commitments made in the Strategy.

The UK Rare Diseases Policy Board has provided advice on, and welcomed, both implementation plans as important milestones in providing greater transparency of all the good work that is being done across the sector in implementing the Strategy. Taken together, these plans demonstrate a commitment to maintaining improvement to services and support to patients and their families across the spectrum from basic research to the planning and delivery of care.

Highlights covered in this implementation plan include the following activities:

- The creation of opportunities for patient engagement through the Rare Disease Policy Forum and a new digital platform for the Forum.
- A new annual conference by the UK Rare Diseases Policy Board to listen to feedback from the rare diseases community and the Rare Disease Policy Forum in particular.
- The establishment of a task and finish group to look at, and improve, the 'diagnostic odyssey' of rare diseases patients.
- The continuing progress and success of the 100,000 Genomes Project.
- The launch and progress of the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS).
- The UK's involvement and leading role in the European Reference Networks.
- The ever increasing research activities through National Institute for Health Research (NIHR) and creation of a unique infrastructure that significantly improves the national capability to undertake and support research studies.

The UK Rare Diseases Policy Board will continue to consider progress against the actions in England's implementation plans and of course take a view across the devolved nations as well.

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Executive Summary

The publication of the 2013 UK Strategy for Rare Diseases (from here on referred to as ‘the Strategy’), an effort by all four health departments in the UK to recognise and respond to the needs of all those affected by rare diseases, was generally seen as a landmark for patients with rare diseases. Since then, much has been achieved in implementing the various elements of the Strategy although no formal implementation plan for the activities under the Strategy in England had been published.

On 28 March, Department of Health and Social Care ministers announced that there would be an implementation plan for those of the 51 commitments of the Strategy for which NHS England has lead responsibility and that for those commitments that fall outside NHS England’s remit, the Department of Health and Social Care (DHSC) would work collaboratively across stakeholders to contribute to the implementation plan for England. This means that the implementation plan for England is published in two parts – one by DHSC and the other by NHS England (NHSE).

DHSC has worked in close collaboration with colleagues at NHSE to facilitate the implementation of the commitments in the Strategy, engaged with key stakeholders, and sought the advice of the UK Rare Diseases Policy Board which oversees the implementation of the Strategy across all four UK nations.

This document covers an overview of the implementation plan for those commitments in the Strategy where DHSC has taken a lead on coordinating input. It sits alongside the implementation plan by NHSE, which can be accessed through NHSE’s [highly specialised services webpage](#).

In producing this plan, we have worked in close collaboration with many of our partner organisations to capture their work in implementing the Strategy. It represents a first step in mapping the delivery landscape and we will continue to work with our partners to recognise the breadth of relevant activities, and importantly maintain the relevance of the Strategy’s vision in light of challenges and opportunities for the benefit of rare diseases patients and their families.

This document and its annexes describe key achievements and future activities by our delivery partners across the five themes of the Strategy, which are:

- (i) empowering those affected by rare diseases
- (ii) identifying and preventing rare diseases
- (iii) diagnosis and early intervention
- (iv) coordination of care
- (v) the role of research

This main document provides a strategic overview of the rare disease landscape as it stands and our vision for the future. In annex 1 we then list in full actions by DHSC and its partner organisations against the relevant commitments in the Strategy.

In annex 2, we present our initial efforts to link the commitments covered in this document to metrics where possible. As we go forward, we will continue to seek the advice of the UK Rare Diseases Policy Board regarding our progress and will annually publish updates to annexes 1 and 2 of this plan via an annually convened Implementation Plan Group.

Background

To date, six to eight thousand rare diseases have been discovered and new diseases are regularly described in the medical literature ([Orphanet](#)). Approximately 80% of rare diseases are of genetic origin ([UK Strategy for Rare Diseases](#)). Despite being described as 'rare', collectively rare diseases affect the lives of around 3 million people in the UK. **1 in 17 people will suffer from a rare disease at some point in their lives**; therefore, they are often termed 'individually rare, collectively common'.

With the aim of improving the lives of all those affected by a rare disease, the UK Government published the Strategy in 2013, a high-level framework containing 51 commitments which sets out a 7-year strategic vision (2013-2020) covering five key areas:

- (i) empowering those affected by rare diseases
- (ii) identifying and preventing rare diseases
- (iii) diagnosis and early intervention
- (iv) coordination of care
- (v) the role of research

The actions taken to implement the 51 commitments in the Strategy in England are covered jointly in this plan and in the [NHSE implementation plan](#). This plan sets out the delivery contributions by DHSC and its partner organisations and will be updated with new activities on an annual basis as we continue our mapping of activity across the health and social care and life sciences sectors, and as actions and their impact clarify.

The rare disease landscape has been much transformed since the Strategy was published in 2013 especially considering EU Exit, the evolving legacy of the 100,000 Genomes Project, new emerging technologies such as genome editing, and seminal publications of 2017 such as the independent CMO report '[Generation Genome](#)', the sector-led '[Life sciences: industrial strategy](#)' (LSIS), and recently published '[Life sciences: Sector Deal](#)' - all of which refer to the importance of genomics for health, including rare diseases. Going forward, we will ensure that we harness the opportunities presented by these developments for the benefit of rare disease patients and their families.

Governance Framework

In response to the publication of the Strategy, DHSC established the **UK Rare Disease Forum** to oversee and coordinate how the Strategy is delivered across the UK after its publication in 2013. The Forum's membership included representation from the rare diseases community, industry, academics and researchers.

In October 2016 revised governance arrangements were introduced. The **UK Rare Disease Policy Board** was established to focus on UK-wide policy development and meeting the 51 commitments in the Strategy. The Board is a UK-wide body with responsibility to facilitate the co-ordination of policy development and meeting the commitments set out in the Strategy.

As well as supporting policy development and implementation, the Board considers how delivery of the Strategy could be improved by harnessing the outputs from across the broader genomics and rare diseases landscape, and works collaboratively with the UK Rare Disease Forum. The next UK-wide progress report from the Policy Board will be published in early 2018.

The Chief Medical Officer's 2016 Annual Report 'Generation Genome' outlined a clear vision for genomic medicine and the opportunities to build on initiatives like the 100,000 Genomes Project. Her first recommendation was for a **National Genomics Board (NGB)**, chaired by a Minister, to facilitate collaboration and effective delivery of key action. This recommendation was accepted by Ministers in July and the establishment of the NGB was announced in November 2017. Its vision is 'to make sure that the UK remains the world's leading centre for genomic medical research, and to leverage this position to deliver quantifiable benefits for NHS patients and for the life sciences sector'. The NGB will oversee the implementation of the Generation Genome report as well as implementation of the genomics component of the Life Sciences Industrial Strategy and the Life Sciences Sector Deal. Together with the NHS it will establish the world's first Genomics Medicine Service, propagate economic growth, and help articulate the "genomics dream" of faster and better diagnosis and treatment - especially for patients with rare diseases and cancer.

The **Rare Diseases Advisory Group (RDAG)** makes recommendations to NHS England and the devolved administrations of Scotland, Wales and Northern Ireland on developing and implementing the Strategy and highly specialised services. The membership of RDAG is broad and includes representatives from Royal Colleges, commissioners, patient and public voice representation and professionals such as a geneticist and an ethicist.

RDAG has advised NHSE in terms of the activities described in our sister plan – the [NHSE implementation plan](#).

Implementing the Commitments of the Strategy

Much progress has been made in implementing the Strategy since its publication in 2013. While implementation plans were developed in [Scotland](#), [Wales](#) and [Northern Ireland](#), no formal implementation plan for England had been published until now.

The activities described in this plan are shared between DHSC and a number of partner organisations, including but not limited to the National Institute for Health Research (NIHR), Public Health England (PHE), Health Education England (HEE), National Screening Committee (UKNSC), Office for Life Sciences (OLS), Medicines and Healthcare products Regulatory Agency (MHRA), Health Research Authority (HRA), and Genomics England. For each of the Strategy's five themes, this document sets out the relevant commitments, provides a current strategic overview and, importantly, outlines where we want to be in the future. In annex 1 we have listed in greater detail the actions DHSC and our partner organisations will take in delivering the commitments for which we have taken lead responsibility, thereby complimenting the commitments owned by and covered in [NHS implementation plan](#).

We have also begun to identify performance measures and metrics (Table 2; annex 2). Recognising that 'positive patient experience', while not easily measurable, is likely the most important outcome measure of the Strategy, we will continue to develop and refine these metrics over the coming two years to enable as comprehensively as possible an evaluation of progress in the final Progress Report on the Strategy in 2020.

The rare diseases landscape is changing rapidly, yet we believe that the five themes of the Strategy remain relevant. Under the leadership of the NGB, we will ensure that opportunities presented through initiatives such as the 'Life sciences: Sector Deal' and pertinent recommendations in '[Generation Genome](#)' (pp 18-21) are harnessed for the benefit of the rare diseases community, keeping the Strategy relevant 5 years on.

Finally, we want to ensure continued relevance of this plan. To this effect we will convene an annual review meeting with representatives from our key delivery partners and NHS England with the aim to:

- identify new actions and update our indicators for measuring progress (as per annexes 1 and 2);
- identify any constraints and develop solutions; and
- seek the advice from the UK Rare Diseases Policy Board on progress against the actions in England set out here, including on measuring progress.

In its first Progress Report, published in 2016, the UK Rare Disease Forum identified three key issues that they felt required further attention. These were: **collaboration** (at every level, across the UK and internationally), **evaluation** (particularly developing concise and tangible metrics against which implementation of the UK Strategy can be measured) and **consolidation** (building and transforming the best of existing provision to fully realise their potential). These key issues have informed the activities set out in the following sections and annexes.

Theme 1 - Empowering Those Affected by Rare Diseases

The concept of 'patient empowerment' is underpinned by knowledge and understanding of the condition, skills and confidence in the use of health information, and by patients being involved as active partners in their care. But it is not just patients who require access to high quality information and data. Because any rare disease is just that, rare, in many cases, GPs, clinicians and other involved parties often have not had previous exposure and experience of a specific condition. Hence, access to quality data and information benefits all involved – patients, healthcare providers, commissioners and clinicians.

The same holds true for raising awareness of rare diseases more generally, leading to better informed support networks for rare disease patients and their families in the community, and empowering patients to have a say in the development of policies that affect them.

Where we are now

A number of enablers and activities are now in place which will help meet the above eight commitments.

Regarding **patient empowerment at policy level**, in October 2016, the Government established the UK Rare Disease Policy Board to focus on UK-wide policy development and meeting the commitments in the Strategy. Membership of the Board, which includes two patient representatives, is published on [Gov.uk](https://www.gov.uk). The Board is working collaboratively with the UK Rare Disease Forum through an online networking and communication platform, which was launched in 2017. Key aims of the platform include the provision and management of a discussion forum for the submission of questions/discussion points to the quarterly UK Rare Disease Policy Board meetings; reporting back on these questions/discussion points to the Forum; thereby formalising communication and working between the UK Rare Disease Policy Forum and Policy Board.

As part of this continued communication and work between the Forum and Board, DHSC organises an annual Rare Disease Forum conference. The first annual forum conference was held in November 2017 at Birmingham Hospital for Children. It was attended by more than 50 participants including members of the UK Rare Disease Forum, UK Rare Disease Policy Board, clinicians, professionals and patient representatives and industry. The conference provided an opportunity for feedback, discussion and development of ideas concerning the implementation of the Strategy. More details of the conference will be published in the 2018 Progress Report.

The importance of **patient engagement in research** is a key concept in the Strategy. We know that input from patients and their families can improve both the quality and effectiveness of research at all stages of the process. Much progress has been made in improving patient engagement in research; for example, through [INVOLVE](#), the National Institute for Health Research (NIHR) actively promotes and leads on activities to encourage greater patient and public involvement, engagement and participation in research. This included the "Ok to Ask" campaign to raise awareness about clinical research opportunities amongst the public and health professionals and, more recently in 2017, the "[I Am Research' campaign](#)". "I Am Research" gives patients, the public and health and social care research professionals a voice to raise awareness about the benefits of research and the positive impact it has on people's lives.

Patient engagement in care is a key objective for NHSE and this is formalised through the 2017 'Framework for patient and public participation in specialised commissioning', which sets out how 163 patient and public members are included in their governance structures. In addition, NHSE involves patients in the working groups that develop clinical commissioning policies and service specifications, as do regulators and organisations such as MHRA and HRA in their decision making.

One example of this is MHRA, who have established a **Patient Group Consultative Forum** (PGCF). This Forum brings patients into the MHRA to discuss pertinent issues and provide patient insight to inform the organisation's operations, acting as an agency-wide resource. The PGCF currently has nearly one hundred individual members, representing between them 58 different patient groups and research charities operating across a wide variety of health constituencies including rare diseases. Recent topics, of direct relevance to rare diseases, have included the Accelerated Access Review and patient attitudes to risk/benefit of medicines, which featured a presentation from the Duchenne Children's Trust, patient views on the pathways to innovation in connection with regenerative medicine and a workshop on the Agency's Operational Transformation programme; which examined opportunities for greater patient involvement in MHRA's services including the Early Access to Medicines Scheme.

High quality data and the value that can be derived from it, is central to any healthcare system and its patients. It underpins high quality patient care, research, commissioning decisions, public health and much more. Collecting data on common diseases is challenging but in the field of rare diseases, data can be scarce and often fragmented, adding particular complexity. On 1 April 2015, PHE launched the **National Congenital Anomaly and Rare Disease Registration Service** (NCARDRS). Data are collected on all suspected and confirmed congenital anomalies and rare diseases in England identified *in utero*, at birth, in childhood or as an adult. Before its launch less than half the country collected data on congenital anomalies. For the first time, England has national coverage of congenital anomaly registration with the aim to expand data collection on other rare diseases.

Where we want to get to

The Government is as committed as ever to empower those affected by rare diseases. We know that patient empowerment requires knowledge, understanding, skills and confidence in the use of health information with patients involved as active care partners. Therefore, in going forward into the remaining two years of the Strategy, DHSC and its delivery partners have three overarching aims:

1. to raise public and service provider awareness of rare diseases;
2. to strengthen the provision of information; and
3. to involve patients in research and policy activities.

In England, as well as on a UK-wide level, we will continue to seek the advice of the UK Rare Diseases Policy Board and UK Rare Disease Forum to ensure we understand, learn from, and act upon the insights of patients and other stakeholders, including through the annual forum conference, our online discussion platform and via the biennial publication of the progress report (the next progress report is due to be published in February 2018) – raising awareness and involving patients at every level.

Increasingly, registry data is used to support and empower patients, inform research and drive wider healthcare system aims, e.g. as a data source for NHS commissioners, clinical audits, to monitor and evaluate programmes, and to evaluate treatments. PHE's NCARDRS will provide a comprehensive national registration service for all congenital anomalies and rare diseases diagnosed and treated in England to support these activities. Such a national register of conditions and information collection is important for a number of reasons. For example, it:

- provides a resource for clinicians to support high quality clinical practice
- supports and empowers patients and their carers (by providing information relevant to their disease or disorder)
- provides epidemiology and monitoring of the frequency, nature, cause and outcomes of these disorders
- supports research into congenital anomalies, rare diseases and precision medicine including basic science, cause, prevention, diagnostics, treatment and management
- informs the planning and commissioning of public health and health and social care provision
- provides a resource to monitor, evaluate and audit health and social care services, including the efficacy and outcomes of screening programmes

In addition, in 2018, NCARDRS will be exploring the feasibility of a patient portal to enable patients to self-register on the service.

Please see annex 1 for the specific actions DHSC and its partner organisations will take to meet the commitments under this theme of the Strategy. Further actions by NHS England are described in the [NHSE implementation plan](#).

Theme 2 - Identifying and Preventing Rare Diseases

Many rare diseases are present at birth. Detection and early intervention can prevent or lessen serious illness in children. Screening has an important role in facilitating an early diagnosis. Patients can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition.

The UK National Screening Committee (UKNSC) advises ministers and the NHS in the 4 UK countries about all aspects of population screening and supports the implementation of screening programmes. Using scientific evidence, pilot studies and economic evaluation, the Committee assesses the evidence for national screening programmes against a set of internationally recognised criteria covering the condition (as judged by its frequency and/or severity), the diagnostic test, and the availability of interventions for the condition and the effectiveness and acceptability of the screening programme.

Where we are now

The newborn period is a particularly important window of opportunity for rare conditions. The current newborn screening programme in the UK is based on the blood spot test (heel prick, dried onto a piece of filter paper) and screens for nine rare but serious conditions: sickle cell disease, cystic fibrosis, congenital hypothyroidism, phenylketonuria (PKU), medium-chain acyl-CoA dehydrogenase deficiency (MCADD), maple syrup urine disease (MSUD), isovaleric acidaemia (IVA), glutaric aciduria type 1 (GA1) and homocystinuria (pyridoxine unresponsive) (HCU). Often this can mean early and effective referral to specialist centres for further diagnosis and treatment.

The UKNSC has considered and recommended screening programmes for rare diseases, including structural anomalies through the antenatal scans, infectious diseases through blood tests in early pregnancy, rare conditions through the bloodspot screening programme and for rare causes of hearing loss through the newborn hearing screening programme.

As of March 2017, there are 11 managed NHS population screening programmes in England.

Antenatal and newborn	Young person and adult
<ul style="list-style-type: none"> sickle cell and thalassaemia 	<ul style="list-style-type: none"> diabetic eye
<ul style="list-style-type: none"> fetal anomaly 	<ul style="list-style-type: none"> abdominal aortic aneurysm
<ul style="list-style-type: none"> infectious diseases in pregnancy 	<ul style="list-style-type: none"> breast cancer
<ul style="list-style-type: none"> newborn and infant physical examination 	<ul style="list-style-type: none"> cervical cancer
<ul style="list-style-type: none"> newborn blood spot 	<ul style="list-style-type: none"> bowel cancer
<ul style="list-style-type: none"> newborn hearing 	

Table 1. Current managed NHS population screening programmes (England)

Where we want to get to

To aid the quicker identification and prevention of symptoms of rare disease, a key delivery aim is to improve the utilisation of screening to identify rare diseases early in cases where this is beneficial and by taking advantage of the **latest technological advances** to stay ahead of the curve. For example, in 'Generation Genome', Dame Sally Davies raised the possibility of incorporating New Generation Sequencing into new born screening programmes to enable the earliest identification of potential problems, and therefore recommended that UKNSC conducts a systematic evaluation of the **opportunities offered by genomics** for present and potential screening practices. This will be considered by UKNSC as it continues to assess new evidence for the effectiveness and acceptability of novel screening programmes, working with NHS England to ensure that an appropriate NHS service is available for any newly approved test.

Increasing awareness of rare diseases across healthcare is a key step in strengthening the ability to identify rare diseases. NHS England will secure greater involvement of other clinical specialties in identifying and characterising rare diseases and **design and test optimal pathway arrangements for patients** with rare diseases.

Research to help the quicker identification and prevention of rare diseases can be hindered by the scarcity of available patients as well as patient tissues for research purposes. The recently published '**Life sciences: Sector Deal**' announced Government support to Whole Genome Sequencing (WGS) of UK Biobank and the extension of the cancer genome pathway. Genomics England will continue to work with relevant regulatory bodies to explore the feasibility of accessing additional cohorts of patients through partnerships with other projects (subject to appropriate participant consent) such as UK Biobank, East London Genes and Health and NIHR Bioresource, a panel of thousands of volunteers who are willing to be approached to participate in research studies investigating the links between genes, the environment, health and disease. This will substantially increase the data set available to researchers and clinicians thereby increasing our understanding of rare diseases or treatments.

Annex 1 describes in detail the specific actions DHSC and its partner organisations will take to meet the commitments under this theme of the Strategy. Actions by NHSE are described in the NHSE implementation plan.

Theme 3: Diagnosis and Early Intervention

Early and accurate diagnosis of rare diseases is essential for the best outcome and care for rare disease patients. Delays in diagnosis often mean that opportunities for timely interventions can be missed or patients may be given unsuitable drugs to treat their misdiagnosed condition.

Over half of patients wait for more than one year after first symptoms arise and some can wait over 20 years for a diagnosis. This is termed the 'diagnostic odyssey' and causes uncertainty and distress for those affected as well as considerable costs for health and social care budgets.

Where we are now

A number of key enablers and activities are now in place which will help meet the commitments in the Strategy.

Understanding in detail the diagnostic pathway of a patient suffering from a rare disease is the first step in finding ways to improve diagnosis and subsequent early intervention. In early 2017, the '**Diagnostic Odyssey** of rare diseases patients' task and finish group was established by the UK Rare Diseases Policy Board. It follows on from work carried out by the Policy Innovation Research Unit (PIRU), funded through DHSC, which explored whether an accurate, robust and cost-effective method can be developed for the routine measurement of rare disease diagnostic odysseys. The Diagnostic Odyssey task and finish group aims to identify and describe the diagnostic journey of three exemplar rare diseases (Bardet-Biedl Syndrome; Tuberous Sclerosis; and ANCA vasculitis) and will report its initial findings in 2018.

The **100,000 Genomes Project** has shown to be successful in addressing parts of this unmet diagnostic need. Sequencing of the individual's genome is increasingly utilised as a diagnostic tool for individuals with unrecognised signs and symptoms and to support the diagnosis of a rare disease. About 25% of patients sequenced through the Project now receive a diagnosis for the first time. Importantly, despite an often chronic and progressive nature, associated long-term complications can be targeted early and addressed for some rare diseases if diagnosed in a timely manner.

A £20 million **Genomics Education Programme** (GEP) was launched to equip NHS staff with knowledge, skills and experience to ensure that the health service remains a world leader in genomic and precision medicine. This responded to a need identified in the Strategy for high-quality training and education of NHS staff as a key prerequisite to reducing the time it takes to diagnose a rare disease, ensuring that the skills of NHS staff can be utilised appropriately and efficiently. See the case study below.

The Strategy called for a better and more holistic approach to data collection. Data (such as occurrence and life-expectancy of a specific rare disease or treatments received by patients with the same condition) is an essential tool for informing clinicians and rare disease patients but such data had thus far not been collated in a systematic manner. In response to the Strategy, PHE launched the **National Congenital Anomaly and Rare Disease Registration Service** (NCARDRS) in April 2015. Before this less than half the country collected data on congenital anomalies. As of 2017, PHE established for the first time national coverage of congenital anomaly registration and is further expanding to collect data on other rare diseases.

In addition to a timely diagnosis, early intervention is a key theme in the Strategy. In 2016, the **Accelerated Access Review**, chaired by Sir Hugh Taylor, set out a vision for the UK of getting the best technologies to patients more quickly and more cheaply. The review made recommendations to take advantage of opportunities to streamline the pathways to patients for breakthrough products while delivering improved value to the taxpayer. In its response 'Making a reality of the Accelerated Access Review', the Government endorsed the vision of the review and set out its strategy to implement its recommendations.

Following public consultation, NICE introduced changes to its methods for the evaluation of highly specialised technologies (HST) topics in April 2017. Under the revised methodology, products that are evaluated through the HST program will be assessed against a sliding scale, so that the more additional quality-adjusted life years (QALYs) a treatment offers, the greater the cost per QALY level it will attract, starting at £100,000 per QALY, rising to a maximum of £300,000 per QALY. This will also be covered in the 2018 Rare Disease Progress Report on the UK Strategy for Rare Disease (publication date - 28th February 2018).

Case Study - Genomics Education Programme

The Genomics Education Programme (GEP) is a £20 million programme in which HEE is working in partnership with key stakeholders to lead the education contribution of the 100,000 Genomes Project, driving the development of a genomics-knowledgeable workforce.

Since the launch of the GEP in 2014, the programme has made substantial progress in each of these aims. Notable achievements include:

- The funding and delivery of more than 550 Master's places in Genomic Medicine (**which includes a module focusing on the genetics of common and rare diseases**) across 10 Higher Education Institutes in England, both successfully and ahead of schedule.
- The delivery of more than 60,000 CPD sessions to date (formal, online or face-to-face education or training, informal, self-directed study), which exceeds the 2018 target of 52,000 educational episodes.
- Funding for 27 extra First Higher Specialist Scientist Training (HSST) places for Genetics and 11 places in Molecular Pathology of Acquired Disease. The first cohort of HSST bioinformaticians are now in training and the first round of registrations have been achieved through Health and Care Professionals Council (HCPC).
- **In support of clinical and scientific workforce development in rare diseases**, the development of a scientist training programme in Genomic Counselling which has been approved by the HCPC and has full recruitment to the first cohort of 15. This has been incorporated into HEE business as usual with subsequent recruitment to a second cohort of 10 in 2017.
- Launch of the first Whole Genome Sequencing Massive Open Online Course (MOOC), achieving more than 14,000 learner registrations in its first year.

Where we want to get to

The Government is committed to shortening and improving the quality of the diagnostic journey for rare disease patients. An early and correct diagnosis reduces the time that patients and families have to spend searching and visiting a multiplicity of healthcare professionals.

Improving diagnosis also means that patients and families can be signposted quickly to services that are expert in the care of their disease.

As a research project, the 100,000 Genomes Project has proven successful in addressing unmet diagnostic needs. In late 2018/19, the NHS will launch a **Genomic Medicine Service** for England, embedding genomic medicine into routine care pathways by building on the success of the 100,000 Genomes Project and using the infrastructure developed by the NHS and Genomics England. NHSE is continuing to develop and implement England's genomic testing strategy for the NHS, including determining which tests will be recommended for which disease from single gene tests to multiplex panels and WGS.

Through NCARDRS, developed by PHE, a coherent approach to collect data has been introduced that will support NHS commissioners and clinicians in their work. PHE will work to ensure that by 2020 every clinician has **access to high-quality data and information** about rare diseases, their prevalence and trends in a clear, accessible and useful format.

It is the Government's ambition to bring forward patient access to selected, highly beneficial and affordable innovations. From April 2018, Government will introduce an **Accelerated Access Pathway** (AAP) that aims to streamline regulatory and market access decisions, getting innovative treatments to patients more quickly.

Annex 1 describes in detail the specific actions DHSC and its partner organisations will take to meet the commitments under this theme of the Strategy. Actions by NHSE are described in the [NHSE implementation plan](#).

Theme 4 - Co-ordination of Care

A multidisciplinary, yet coordinated, approach is vital in providing better care to patients affected by rare diseases. This is of particular importance when several specialists and hospital departments are involved in support of the primary care-giver (GP) and rare disease patient and their family. We know that rare disease patients can have difficulty accessing the full breadth of health services available in a timely manner and suboptimal coordination among existing health services can result in delays of diagnosis and care. To add to this, it is important to ensure that healthcare professionals have access to educational opportunities, easily accessible information and expert advice to support patients with rare diseases.

The number of patients who collectively suffer from diseases classified as rare is significant at approximately 3 million in the UK. This covers a great many different conditions, yet we know that the issues facing those with rare diseases are often universal, not just in the UK but in other countries as well. The scarcity of rare disease expertise and patients suffering from any given condition in any single country means that diagnosis, treatment and management of rare diseases strongly benefit from cross-border collaboration.

Where we are now

The UK is a leader in the treatment of rare diseases and in sharing of information, data, knowledge and best practice internationally and across Europe. The UK has been instrumental in promoting better engagement on rare diseases policy at an EU level. For example, through DHSC, we have played a leading role in the development of **European Reference Networks (ERNs)** set up in March 2017. ERNs act as centres of knowledge, skills and expertise in the field of rare diseases and complex conditions. They enable the principles of better access for patients to highly specialised services and support European co-operation on highly specialised healthcare, knowledge sharing and improved diagnosis and care in medical domains where expertise is limited. ERNs can also be focal points for medical training and research.

There are currently 24 ERNs across the European Economic Area with 26 member states participating, creating a large network of over 300 highly specialised healthcare providers. The UK is heavily involved by participating in 23 of 24 networks across a total of 113 separate health care providers in England and the devolved nations. UK clinicians lead 6 of the 24 networks, more than any other EU country (see also case study below).

At national level, NHS England is working to improve the better provision of health care to patients affected by rare diseases. One key development is the 'rare disease insert' which will form part of NHS England's contract documentation with providers that deliver specialised services to patients with rare diseases. The insert will be a set of criteria to allow NHS England to hold providers to account for the **care experience of rare diseases patients**. Further details are given in the NHSE implementation plan.

Case Study - An ERN in Action: eUROGEN

eUROGEN is the **European Reference Network** for rare urogenital diseases and complex conditions. It is made up of 29 specialist healthcare providers across 11 member states. The network offers virtual review of rare and very complex cases, including the diagnosis and

treatment of people with highly complex urogenital disorders, those who have rare urogenital cancers and children who have suffered with urogenital disorders from birth.

There are already examples of cross-border benefits for patients:

- Professor Chris Chapple, who leads eUROGEN, recently had a case referred to them where there had been three previous attempted repairs of a vesico-vaginal fistula from a major teaching centre in another Member State.
- They successfully carried out the repair, as they are a subspecialist unit in Sheffield Teaching Hospitals NHS Foundation Trust, which carries out approximately 20 of these procedures per year. The referring department saw one such procedure every 18 months.
- Prior to this surgery, the patient had been unable to work for 18 months and had suffered with incontinence and other functional problems that severely affected her quality of life. The patient is now fully recovered and back at work.

eUROGEN will use high-cost research facilities within its participating healthcare providers more efficiently, reducing costs and stimulating research:

- One of eUROGEN first research activities will be to address one of the gaps in current effective treatments for patients by developing a new safer tissue engineered material for use in urogenital surgery.
- Clinical trials can be run in UK hospitals. Networking knowledge and expertise together will create a European supra-hub of expertise to foster learning and generate research and innovation more attuned to the needs of our patients.

Where we want to get to

We are committed to removing unnecessary barriers and facilitating access to high quality care and treatment for all patients with rare diseases. Key to this will be partnership working at the highest level involving key leaders and decision makers across the health and social care pathway and working in partnership with industry, charities and patient organisations. Under the leadership of the Government's **National Genomics Board**, we will ensure that opportunities presented through initiatives such as the 'Life sciences: Sector Deal' and pertinent recommendations in 'Generation Genome' are harnessed for the benefit of the rare diseases community. Key to this will be the NHS's new **Genomics Medicine Service** from late 2018/19, with the aim to provide faster and better diagnosis and treatment especially for patients with rare diseases and cancer.

As we approach the UK's exit from the European Union, **international collaboration** for the benefit of rare diseases patients will be as important as ever. The Government's policy paper, 'Collaboration on Science and Innovation: A Future Partnership Paper' stresses the importance of continued collaboration with European partners to ensure that the UK remains one of the best places in the world for science and innovation. ERNs for rare diseases patients were cited in the paper as an example of collaboration that the UK and EU need to discuss [in the negotiations], given the mutual benefits. The Government has also stated that there are three principles which will help us rise to the challenge of developing a new regulatory system post Brexit: patients should not be disadvantaged; innovators should be able to get their products into the UK market as quickly and simply as possible; and we continue to play a leading role promoting public health.

Please see annex 1 for the specific actions DHSC and its partner organisations will take to meet the commitments under this theme of the Strategy. Actions by NHSE are described in the [NHSE implementation plan](#).

Theme 5 - The Role of Research in Rare Diseases

Research is critical in creating novel insights and treatments for people with rare diseases. The UK is a world leader in rare diseases research and a first choice partner for research, innovation and technology development.

There are many known rare diseases for which the genetic (molecular) basis is not yet understood. Continued research, including learning from genomic analyses of rare disease patients and their families, is vitally important to further our understanding of rare diseases and their cause so that new treatments can be developed. Government, charity and industry funding all have an important role to play in finding innovative treatments and interventions for rare diseases. Only by working in collaboration will we be able to develop new diagnoses, interventions, treatments and drugs for rare disease patients.

Where we are now

Through the **National Institute for Health Research (NIHR)**, the Government has invested significantly in rare diseases research and infrastructure in England. For example, in October 2012 the NIHR launched a call for Applied Clinical Research on Very Rare Diseases as part of the researcher-led funding streams across six of the NIHR Programmes. This call was issued in support of the UK Strategy for Rare Diseases and in recognition of the need for increased high quality evidence on the organisation of highly specialised services or their commissioning and to improve the health outcomes for patients of rare diseases.

As a result of the call, 48 applications across the six programmes, were received and reviewed by the NIHR boards and committees, considering the scientific quality of the applications and their importance to the NHS, patients and the public. In total over £5 million was committed to research through this call, across 7 projects.

Extending our knowledge of the human genome allows the removal of barriers hindering diagnosis and innovative treatments. The leap in the speed and reduction in the cost of sequencing technologies has opened up the potential of **genomics for mainstream healthcare** – and the UK is at the forefront of this vision. To fulfil this ambition the **100,000 Genomes Project** was launched in late 2012 and has proven to be a key vehicle for delivering against many of the commitments in the Strategy, including those that fall under the themes of ‘Research’ (theme 5) and ‘Patient Empowerment’ (theme 1).

Working in partnership provides opportunities for funding, research and development to reinforce one another, translating research more quickly from perception to clinical trials and most importantly, to the patient. The 100,000 Genomes Project has underpinned collaborative working for the benefit of the patient through Genomics England’s **Clinical Interpretation Partnership (GeCIP)**. Currently, over 2,000 researchers in 342 UK and international institutions participate. Genomics England has also initiated the **Discovery Forum**, which provides a platform for collaboration and engagement between Genomics England, industry partners, academia, the NHS and the wider UK genomics landscape.

Having access to data is a key factor in being able to improve research capability. Recognising this, the NIHR has developed the **Health Data Finder for Research** in partnership with Clinical Practice Research Datalink, Health and Social Care Information Centre, NIHR Health

Informatics Collaborative and Public Health England. It enables researchers to find information about the UK healthcare data sets that are available for research and to request access to these data sets.

The NIHR has also established the **UK Clinical Trials Gateway** (UKCTG) to help patients and the public make informed choices about taking part in clinical trials. It contains all experimental medicine trials registered on ISRCTN (International Standard Randomised Controlled Trials Number) and ClinicalTrials.gov, including those trials focussed on rare diseases. The UKCTG has been improving the presentation and functionality of the website so that it is more user-friendly and has focussed on maximising its potential to be used by patients to identify opportunities to participate in clinical trials.

Input from patient improves and focuses research endeavours. As described earlier (Theme 1 – Patient Empowerment), the NIHR encourages **public involvement** in NHS, public health and social care research through INVOLVE campaigns such as the “Ok to Ask” and the recent “I Am Research” campaign. NIHR supported research projects, programmes and infrastructure also include as a funding requirement active patient/public engagement and involvement in design and conduct.

In conjunction with the devolved administrations, HRA has published the new UK-wide Policy Framework for Health and Social Care Research. This Framework replaced the four separate Research Governance Frameworks (RGFs) in October 2017 aiming **to make the UK an even more attractive place in which to conduct research** by focussing on the benefits of research, the need for proportionate risk management, and by promoting UK wide consistency.

Where we want to get to

Supporting research and innovation is of fundamental importance to the Government. This was recently reaffirmed in the publication of the ‘Industrial Strategy’ in November 2017, which announced an additional investment of £2.3 billion in 2021/22, and – perhaps more pertinently for the rare diseases community – by the publication of the ‘Life sciences: Sector Deal’. Working with research funders in Government, industry and the third sector, the NGB will oversee the genomics elements in the ‘Life sciences: Sector Deal’ and fulfil its vision for the UK to remain the **world’s leading centre for genomic medical research**, and to leverage this position to deliver quantifiable benefits for NHS patients and for the life sciences sector.

Research is a vital tool for increasing knowledge and availability of treatment options for patients with a rare disease. The Government invests significantly in rare diseases research and infrastructure and the UK continues to be at the forefront in this area. As we go forward, we will continue to:

- Strengthen research, including translational research
- Incentivise the development and marketing of medicines for rare diseases
- Improve evidence based evaluation of new tests and treatments

For example, the NIHR will continue to promote and advance public involvement in research, ensuring all research projects, programmes and infrastructure supported by the NIHR have active patient/public engagement and involvement in their design and conduct. Importantly, the NIHR will develop and implement jointly with INVOLVE a set of **national standards and indicators for public involvement in research** that can be used by organisations, research projects and individuals. It will also continue to develop web-based systems that retain the

information required to manage health and social care research in England (including the Health Data Finder and UKCTG websites) in a bid to continue to improve information about, and access to, clinical trials that may be suitable for clinicians and their patients.

In 2017/18, the NIHR will establish a new flagship initiative – the NIHR Bioresource for Translational Research in Common and Rare Diseases, which is described in the case study below.

Case Study – Facilitating Research into Rare Diseases through the NIHR

In 2016 the Secretary of State for Health announced a **£816 million investment in the NIHR Biomedical Research Centres**, over 5 years commencing 1 April 2017. This investment has been awarded to 20 leading NHS and university partnerships across England. Each of the 20 NIHR Biomedical Research Centres hosts the development of new, ground-breaking treatments, diagnostics, prevention and care for patients in a wide range of diseases and has considerable expertise, capacity and activity in research for rare diseases.

The NIHR BioResource – Rare Diseases was established to **identify the genetic causes** of rare diseases, **improve rates of diagnosis** to enable studies that **develop and validate treatments** and **improve care for patients and their families**. The NIHR BioResource – Rare Diseases is enrolling rare disease patients to the BioResource using a national consent model across 60 NHS Trusts. In partnership with Genomics England, this programme led the pilot for the rare diseases element of the 100,000 Genomes Project, and has delivered the sequencing of whole genomes of over 12,000 NIHR BioResource rare disease participants.

During the 2017 to 2018 period, the NIHR BioResource, NIHR BioResource - Rare Diseases and the NIHR RD-TRC, which share common aims and infrastructure, are being integrated. This will result in a newly formed **NIHR BioResource for Translational Research for Common and Rare Diseases**. This newly formed NIHR BioResource for Translational Research for Common and Rare Diseases will **provide a nationally accessible resource of volunteers** from the general population and patients with common and rare diseases. It will aim to expand the number of rare disease patients, their families and volunteers from the general population who are recallable for experimental medicine research thereby increasing the number of rare diseases covered by identifying up to 100 for initial national recruitment. It will facilitate recall by investing in genomic and phenotypic characterisation of participants, providing investigators with unprecedented access to highly characterised patients with common and rare diseases, and volunteers from the general population. In addition, it will provide rare disease patients and their families with increased opportunities to become involved in research, and shape how it evolves within the framework of rapid technological advances.

The **UK Clinical Trials Gateway (UKCTG)** contains all experimental medicine trials registered on ISRCTN (the UK clinical trials registry) and ClinicalTrials.gov, including those trials focussed on rare diseases. The UKCTG has been exploring ways to maximise its potential to be used by patients to identify opportunities to participate in clinical trials.

The NIHR Clinical Research Network Coordinating Centre (NIHR CRNCC) has recently taken oversight of the UKCTG and is now updating the system to improve the usability and flexibility for volunteers and researchers.

Research is also of **fundamental importance to the NHS**. This is emphasised in the NHS mandate for 2017/18 (the process by which direction is set for the NHS) which focusses on supporting research, innovation and growth. This is further augmented through the

implementation of the NHSE research plan. In addition, NHSE aims to develop and implement over the next two years a process for recognising Rare Disease Collaborative Networks (RDCNs, see case study below). The NHSE Board recently agreed '12 Actions to Support and Apply Research in the NHS', which also formed the basis of a recent consultation on measures to simplify and strengthen arrangements for research in the NHS (The consultation ran to 1 February 2018, see here for details:

<https://www.engage.england.nhs.uk/consultation/simplifying-research-arrangements/>).

Finally, the successful 100 000 Genomes Project has, as a research project, already provided **tangible benefits for rare disease patients** – around 25% of rare disease patients participating in the project have received a diagnosis for the first time – and so led the way to the establishment of the aforementioned Genomics Medicine Service in the NHS in 2018/19 to facilitate faster and better diagnosis and treatment especially for patients with rare diseases and cancer.

Please see annex 1 for specific actions DHSC and its partner organisations will take to meet the commitments under the research theme of the Strategy. Actions by NHSE are described in the NHSE implementation plan.

The case study below summarises some of the major rare diseases initiatives mentioned throughout this document.

Case Study – Major Rare Disease initiatives

European Reference Networks

European Reference Networks are centres of knowledge, skills and expertise in the field of rare diseases and complex conditions. ERNs function as virtual networks that provide a formal platform to create partnerships between healthcare providers. They encompass the principles of better access for patients to highly specialised services and support European co-operation on highly specialised healthcare, knowledge sharing and improved diagnosis and care in medical domains where expertise is limited. ERNs can also be focal points for medical training and research.

NIHR Bioresource for Translational Research in Common and Rare Diseases

In 2017/18 the NIHR BioResource, NIHR BioResource - Rare Diseases and the NIHR RD-TRC, which share common aims and infrastructure, are being integrated. (*For more information, please see previous NIHR Case Study p.23*).

NHS England's Rare Disease Research Networks

Rare Disease Research Networks are being formed by groups of providers who have a demonstrable research-active interest in a rare/very rare disease, the aim of the network being to improve patient outcomes. More detail on these research networks can be found in NHSE implementation plan.

Genomics Medicine Centres (GMCs)/ Genomic Laboratory Hubs (GLHs)

A part of the 100,000 Genomes Project, a nationwide network of 13 NHS Genomic Medicine Centres (GMCs) was set-up. GMCs provide equitable access to populations of 3-5 million and involve over 85 hospital trusts. Within the 100,000 Genomes Project they are responsible for the clinical care, consenting patients and providing clinical data and appropriate samples from participants.

NHSE is now in the process of procuring a Genomic Medicine Service (GMS) that will include a

national network of up to seven Genomic Laboratory Hubs (GLH). The GLHs will create a world class resource for the NHS and underpin the GMS and the broader research and innovation agenda, working via Genomics England to deliver a Whole Genome Sequencing service that will build upon the 100,000 Genomes Project.

The National Congenital Anomaly and rare Disease Registration Service

The National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) was launched in 2015. It currently collects data from 567 NHS providers across the country.

A national register and information collection is really important and provides:

- a resource for clinicians to support high quality clinical practice
- empowerment for patients and their carers (by providing information relevant to their disease or disorder)
- epidemiology and monitoring of the frequency, nature, cause and outcomes of these disorders
- support to all research into congenital anomalies, rare diseases and precision medicine including basic science, cause, prevention, diagnostics, treatment and management
- information for planning and commissioning of public health and health and social care provision
- a resource to monitor, evaluate and audit health and social care services, including the efficacy and outcomes of screening programmes.

Annex 1: Actions to implement the 51 commitments

The Table below lists the specific actions DHSC and its partner organisations will take in the coming year to implement the commitments across the 5 themes of the Strategy. For a full list of the 51 commitments, please see: <https://www.gov.uk/government/publications/rare-diseases-strategy>.

This should be read alongside [NHSE's implementation plan](#) which covers complementary actions for which NHSE has taking lead responsibility for.

Table 2. Specific actions from DHSC and its partner organisations to implement the commitments across the 5 themes of the Strategy.

Theme 1: Empowering Those Affected by Rare Diseases

Action	Lead organisation	Commitment
Engage patients through the Rare Diseases UK's Patient Empowerment Group as well as the Rare Diseases Forum.	DHSC	C1; C8
As part of continued engagement work, hold for the UK Rare Diseases Policy Board an annual Rare Disease Forum conference as well as continue to improve on feedback the recently launched online platform for Forum members to engage with the Policy Board.	DHSC	C1; C8
Ensure that patient representatives, among others, can contribute and take part in the annual implementation plan review meeting to ensure its continued relevance.		C1; C8
Work collaboratively with OLS on relevant elements in the Life Sciences Industrial Strategy and Sector Deal, for example in relation to proposals in the LSIS for Digital Innovation Hubs and patient registries.	DHSC	C1; C8
NCARDS will produce a workplan outlining the rare disease expansion work until 2020. This plan is	PHE	C7; C8

Action	Lead organisation	Commitment
<p>currently in development but will include the following workstreams:</p> <ul style="list-style-type: none"> • Infrastructure: <p>Further development of our data management system to ensure systems to collect, process, quality assure, analyse and report on rare disease data and to ensure robust coding and classification of rare diseases, standard core data set agreed and standard operating procedures in place.</p> <ul style="list-style-type: none"> • Clinical data liaison: <p>Establish new data feeds with rare disease specialist clinics, laboratories and other relevant NHS services. Ensuring all information governance procedures are in place and strong engagement from notifiers.</p> <ul style="list-style-type: none"> • Multi source approach: <p>Secure access to routine data feeds e.g. HES, ONS, develop methodology for accurate case ascertainment through these data sets and data linkage.</p> <ul style="list-style-type: none"> • Patient portal: <p>Explore feasibility of a patient portal to enable patients to self-register; to include function, validation and information governance issues.</p> <ul style="list-style-type: none"> • Data outputs: <p>Continue patient and stakeholder engagement regarding NCARDRS content, function and output.</p> <p>‘Awareness raising phase’ of NCARDRS: PHE will work to ensure the initiative is compatible with and collaborating with major developments in rare disease healthcare, such as the implementation of the 100,000 Genomes Project into mainstream NHS practice, registers of treatment use mandated by European Medicines Agency licences and NICE Managed Access Agreements.</p> <p>Position NCARDRS as the obvious collaborator with research studies for data storage and linkage.</p>		
<p>Our actions regarding the research elements of C7 and C8 are covered below under Theme 5 - The Role of Research in Rare Diseases.</p>		

Theme 2: Identifying and preventing rare diseases

Action	Lead organisation	Commitment
<p>Run an open call for new screening proposals (at the time of writing this is open from September 2017 to December 2017);</p> <p>Work with stakeholders to understand and communicate about informed choices;</p> <p>Regularly assess whether the existing screening programmes should be maintained or ceased;</p> <p>Accept and consider changes to the existing programmes (e.g. change in tests or test modalities); and in line with recommendation 6 (see annex 2) of '<u>Generation Genome</u>':</p> <ul style="list-style-type: none"> • Work with PHE and NHS England to see where newer technologies like genomics can replace current confirmatory tests looking for genetic errors. • Discuss with expert stakeholders about a more general summary of Whole Genome Sequencing (WGS) in newborns. 	UKNSC	C9
<p>Consider the outcome of any UKNSC recommendation and work to ensure that an appropriate NHS service (where it is the responsible commissioner for that service) is available to treat patients with the identified condition.</p> <p>In line with recommendation 7 (see annex 2) of '<u>Generation Genome</u>':</p> <ul style="list-style-type: none"> • An evaluative roll out of contingent Non-invasive Prenatal Testing (NIPT) is underway and will examine costs, acceptability, informed choices and feasibility. • Together with UKNSC review the evidence to consider reflex testing within Down's screening as a major programme modification in accordance to its published evidence review process. 	NHSE	C9
<p>Set standards, monitor progress;</p> <p>Continue to publish data on all antenatal and newborn screening programmes on a quarterly and annual basis.</p>	PHE	C9

Action	Lead organisation	Commitment
<p>Provide public and patient information;</p> <p>Quality-assure the existing programmes;</p> <p>Be responsible for pilots and evaluations where recommended by the UKNSC and ministers.</p>		

Theme 3: Diagnosis and early intervention

Action	Lead organisation	Commitment
<p>Continue to deliver the GEP, ensuring knowledge, skill and expertise of NHS staff in genomics and precision medicine – this will increasingly become a vital skill through the routine commissioning of WGS for diagnostic purposes. This aligns with the implementation of recommendation 22 of the CMO's 'Generation Genome' report.</p>	HEE	C15
<p>Work with PHE to deliver commitment C19.</p> <p>Support the work of the Diagnostic Odyssey Task and Finish Group with data release in line with appropriate governance procedures and approvals.</p>	NHS Digital	C19
<p>Explore the option of using NHSE's commissioning levers to drive sharing of data with NCARDRS to further improve its impact and support the link between data bases and health records, PHE will.</p> <p>Note that the development of NCARDRS is covered under commitment C7 in 'Theme 1'</p>	PHE	C19
<p>Work with delivery partners and representatives from industry and patient groups to develop the Accelerated Access Pathway (AAP) for breakthrough products. This expedited route to market will bring breakthrough products to patients as quickly as possible by streamlining regulatory and market access decisions.</p>	MHRA	C13
<p>Further actions by NIHR are covered under Theme 5 below.</p>		

Theme 4: Coordination of Care

Action	Lead organisation	Commitment
<p>Receive and take action as appropriate the report from the task and finish group on diagnostic odyssey</p> <p>Support the development of a post-EU Exit relationship in line with its stated principle that patients should not be disadvantaged.</p> <p>The Government's policy paper, 'Collaboration on Science and Innovation: A Future Partnership Paper' stresses the importance of continued collaboration with European partners to ensure that the UK remains one of the best places in the world for science and innovation. European Reference Networks (ERNs) for rare diseases patients were cited in the paper as an example of collaboration that the UK and EU need to discuss [in the negotiations], given the mutual benefits.</p> <p>Set up and provide the secretariat to the new National Genomics Board (NGB) to deliver its vision to make sure that the UK remains the world's leading centre for genomic medical research, and to leverage this position to deliver quantifiable benefits for NHS patients</p>	DHSC	All relevant commitments; C25
<p>Continue to work with the life sciences industry, stakeholder groups and across Government negotiate a Sector Deal for Life Sciences.</p>	OLS	C25
<p>Support the work of the Diagnostic Odyssey task and finish group with data release in line with appropriate governance procedures and approvals.</p> <p>Work with other interested parties, such as PHE's NCARDRS and Genomics England, to improve systems to record genetic and other relevant information accurately to detail the incidence and prevalence of disease.</p>	NHS Digital	C25; C29
<p>NIHR's actions against commitment C25 are covered under Theme 5.</p>		

Theme 5: The role of research

Action	Lead organisation	Commitment
<p>Continue to support rare disease research through its Research Programmes and through the provision of research infrastructure which facilitates world-class research in the NHS as well as supporting clinical trials. This will include supporting the integration of the NIHR BioResource, NIHR BioResource - Rare Diseases and the NIHR Rare Disease – Translational Research Collaboration to establish the NIHR BioResource for Translational Research for Common and Rare Diseases.</p> <p>Through the NIHR research infrastructure, with support from the NIHR Office for Clinical Research Infrastructure (NOCRI), continue to enable and support collaboration with the life sciences industry, research charities and other public funders of research.</p> <p>Continue to promote and advance public involvement in research, ensuring all research projects, programmes and infrastructure supported by the NIHR have active patient/ public engagement and involvement in their design and conduct. Working with INVOLVE to develop and roll out a set of national standards and indicators for public involvement in research that can be used by organisations, research projects and individuals.</p> <p>Continue to develop web-based systems that retain the information required to manage health and social care research in England. Including the Health Data Finder and the UK Clinical Trials Gateway (UKCTG) website to provide the public and clinicians with information about trials that may be suitable for them or their patients.</p>	NIHR	C25; C40; 49; C50
<p>Consideration of progress that has been made to support rare disease research (before the end of 2018).</p>	OSCHR	C50
<p>Continue to participate in rare disease events to emphasise the importance of research and collaborative working between patients/carer organisations, health professionals and regulators. These informal networking events bring together patients and carers, healthcare professionals, researchers and regulators to inform future strategies.</p> <p>Continue to support the Paediatric Regulation with a focus on paediatric-only drug development programmes. This is of particular importance due to the methodological challenges and limitations and the small number of patients available for participation in studies of paediatric rare diseases.</p>	MHRA	C36; C39

Action	Lead organisation	Commitment
<p>Further support initiatives related to the exchange of good practices and development of new scientific guidelines such as modelling and simulation strategies and extrapolation concepts to facilitate the conduct of paediatric studies and reduce the number of necessary study participants.</p> <p>Further develop the understanding of the underlying mechanisms for some areas of rare diseases and support additional basic research in rare diseases to inform appropriate drug development.</p>		
<p>Pilot a 'just in time' research site activation approach, in which instead of opening multiple research sites prospectively in the hope that one or more will see a patient meeting the rare disease inclusion criteria of the study, the sponsor will be able to notify a number of potential sites, but only activate each one as such a patient presents.</p> <p>This can deliver clear efficiencies and transform the delivery of research in rare disease areas but will also require significant changes to the way in which research sites are set up to ensure that centre activation (including any necessary cost and contract negotiation) can be concluded in the short timeframes envisaged.</p> <p>Continue to work with the research community, regulators, providers of NHS services and research funders to promote good practice and facilitate consistent and streamlined processes.</p> <p>As part of the proportionality workstream component of its Service Improvement Project, HRA will consider developing more risk-proportionate regulation using a risk stratified approach.</p> <p>Provide HRA endorsement of recruitment registers / databases to streamline approval by reassuring Research Ethics Committees and others that appropriate standards and safeguards are in place for the registry to be used as a recruitment method.</p>	HRA	C39; C41
<p>Continue to deliver and develop the Genomics Education Programme which is described in Theme 3.</p>	HEE	C45
<p>Help to support work to look at how the 4 UK countries develop, change or expand information systems to capture, connect and analyse data about clinical and social care pathways.</p>	NHS Digital	C31
<p>Work with the UK Rare Diseases Policy Board and devolved administrations to facilitate UK-wide</p>	DHSC	C31

Action	Lead organisation	Commitment
<p>collaboration and learning across the four Nations.</p> <p>In response to Recommendation 11 of 'Generation Genome':</p> <ul style="list-style-type: none"> • Consider the establishment of regional Digital Innovation Hubs to facilitate the use of NHS data for research purposes. • Work with partners in NHSE to consider how we might pursue this recommendation. 	DHSC and OLS	
<p>Work with NHSE to deliver recommendation 9 of 'Generation Genome':</p> <ul style="list-style-type: none"> • Convene the 'Patient Consent in Mainstreaming Genomic Medicine Working Group'. The Working Group is co-chaired by NHSE and Genomics England and is made up of representatives from key stakeholder bodies that include: Genetic Alliance UK, National Cancer Research Institute (NCRI), NHS Digital, PHG Foundation and Wellcome Trust/Understanding Patient Data. • Engage with key stakeholders to develop an agreed NHS consent model. • Review the need for any changes to the 100,000 Genomes Project's consent materials and/or approach to support the transition to routine genomic testing in the NHS. • Share the proposed model with a wider group of stakeholders, including: patient advocacy groups, charities; healthcare professional organisations; Government and NHS organisations; and research bodies. <p>Work with other bodies to deliver recommendation 10 of 'Generation Genome':</p> <ul style="list-style-type: none"> • Actively reach out to other trials and cohorts – where appropriate consents are in place – to access additional sample data. • Work to increase the size of the dataset by: <ul style="list-style-type: none"> ○ Harnessing samples commissioned by the NHS annually ○ Accessing additional cohorts of patients through partnerships with other projects (subject to appropriate participant consent) such as UK Biobank, East London Genes 	Genomics England	C37; C47; C48

Action	Lead organisation	Commitment
<p style="text-align: center;">and Health and NIHR Bioresource</p> <p>Work with all relevant regulatory bodies to explore the feasibility of accessing the stored tissue of those individuals with consent who might, for example, have signed forms of consent other than that used in the 100,000 Genomes Project and have passed away – but whose inclusion would add substantial understanding of the disease or treatments.</p>		

Annex 2: Measuring Tangible Progress

In 2017 the UK Rare Diseases Policy Board set up a task and finish group to recommend a set of metrics by which progress can be measured against meeting the commitments of the Strategy.

This work is now underway and metrics for some of the commitments will be further developed as this work progresses. We will publish updated metrics, alongside new activities to meet the commitments on an annual basis. Table 3 sets out metrics we have identified so far.

Table 3 – Progress Metrics

Measure as per the actions in this implementation plan (Q = quarterly, A = annually, O = ongoing)	Commitment(s) being measured
<ul style="list-style-type: none"> • Deliver Rare Diseases Forum conference to enable attendee-led discussions on highlights, limitations, key challenges and forward view to inform Rare Diseases Policy Board discussions. (A) • Number of Forum members active on the Rare Diseases Forum platform. (A) • Number of Forum suggestions discussed by Policy Board and published on Forum Platform. (A) • Publication of minutes from the Rare Diseases Policy Board meetings. (Q) • Number of engagements with the Rare Diseases UK's Patient Empowerment Group in the review of implementation plan and progress report. (A) • Number of engagements with the Rare Disease UK's Patient Empowerment Group in the NCARDRS work plan (O) • Number of patients involved in MHRA and HRA groups and committees. (A) 	C1; C36
<ul style="list-style-type: none"> • Total number of rare disease patient samples returned to GMCs (A) • Total number of rare diseases patients recruited to 100,000 Genomes project (A) • Number of Master's in Genomic Medicine completed • Total number of NHS and HE staff involved in 100, 000 Genome Project (A) 	C1; C15; C25; C42 (completed); C45
<ul style="list-style-type: none"> • Development of a secure electronic method to enable patients to self-register to NCARDRS (O; A) - Number of patients self-registered to NCARDS. (A) • Population coverage of NCARDRS across England. (O) • Clinicians treating rare diseases to have access to information collected by NCARDRS (O by 2020; A) – Number of access requests to data held in NCARDRS. (A; from 2020) • Number of response and advice requests to the Rare Diseases Policy Board; Forum and Rare Diseases UK. (A) 	C1; C7; C9; C29
<ul style="list-style-type: none"> • Number of providers endorsed as members/leads of European Reference Networks. (O) 	C28; C1; C8; C49

<ul style="list-style-type: none"> Guidance development on data records and inclusion in national data sets. (O) → Following guidance development, further metrics to be developed. (O) Number of guidance documents developed by HRA/HTA on consent for sharing patient data/ tissue. (O) 	C29; C40
<ul style="list-style-type: none"> Number of approaches/enquiries to data provider sites for access to data presented via 'Health Data Finder'. (A) 	C35
<ul style="list-style-type: none"> Risk-proportionate regulation <ul style="list-style-type: none"> Time line for overall approval including both ethical review and assessment for proportionate review studies Number of amendments for adaptive trials. Development of a streamlined process to local NHS permissions with a view to reducing timescales. MHRA to ensure risk proportionality remain a principle in UK clinical trials, marketing authorisations and risk-based inspections after UK's exit from the EU. (O) Monitor the impact of the Joint Statement on the Application of Good Clinical Practice to Training for Researchers issued with other regulators, royal colleges and industry in October 2017. (O) 	C39; C41
<ul style="list-style-type: none"> Industry income and number of studies from contract and collaborative studies through the NIHR infrastructure. (A) Number of participants recruited through NIHR infrastructure. (A) Numbers of grants received / publications in peer reviewed journals. (A) Funding for NIHR BioResource. (A) Number of researchers and clinicians links through GeCIPS. (A) Number of industry partners taking part in the Discovery Forum. (A) 	C45; C46; C47; C48; C49; C51
<ul style="list-style-type: none"> Progress on rare diseases to be considered by OSCHR in 2018.(O; A) 	C50
Metrics without a quantitative measure	
<ul style="list-style-type: none"> This is in development or the commitments do not lend themselves to a quantitative measure Please note that the NHSE implementation plan lists metrics for the commitments NHSE has taken lead responsibility for. 	C19; C20; C31; C37 and C38.