Department of Health & Social Care

The UK Strategy for Rare Diseases

2019 update to the Implementation Plan for England

Published: 27 February 2019

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Introduction

Document summary

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. Despite being described as ‘rare’, collectively rare diseases affect the lives of around 3 million people in the UK. 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 UK Strategy for Rare Diseases in 2013 (hereafter referred to as ‘the Strategy’), a high-level framework containing 51 commitments which sets out a strategic vision for 2013-2020 covering five key areas: empowering those affected by rare diseases; identifying and preventing rare diseases; diagnosis and early intervention; coordination of care; and the role of research.

To achieve the 51 commitments across the UK, implementation plans were published by England, Wales, Scotland and Northern Ireland. Implementation plans for England were co-published in January 2018 by the Department of Health and Social Care (DHSC) and NHS England. The two documents are designed to be read alongside one another and together cover actions to achieve the 51 commitments across England.

The DHSC 2018 Rare Disease Implementation Plan for England (hereafter referred to as ‘the implementation plan’) covers the 21 commitments in the Strategy for which DHSC have lead responsibility and where we work collaboratively with a range of partners to deliver them. **This document is an update to the DHSC-led implementation plan. It reviews progress over the last year and takes a forward look of actions for 2019/20.** The NHS England led implementation plan and its commitments are not considered in this document. NHS England, the lead organisation for 30 of the commitments, will publish an update on their implementation plan later in 2019.

The main body of this document provides an update on activity in the last year across the five themes of the Strategy. Annex 1 outlines forward looking actions for 2019/20 for DHSC and our partner organisations. Some of these actions are a continuation of those from the 2018 implementation plan and others are new. Annex 2 gives a measurement of progress over the last year, where it is possible to do so. In addition, relevant recommendations from England’s Chief Medical Officer 2016 ‘Generation Genome’ report are quoted throughout this document, and have been included for reference in Annex 3.

In producing this document, we have worked in close collaboration with our partner organisations to capture the work we have done collectively towards delivering actions

from the 2018 implementation plan. To this effect, we convened a workshop with delivery partners and patient representatives in November 2018 to discuss progress and actions for the coming year.

Partner organisations involved in writing this document include: Genomics England; Health Education England (HEE); Health Research Authority (HRA); Medicines and Healthcare products Regulatory Agency (MHRA); NHS Digital; NHS England; Office for Life Sciences (OLS); Public Health England (PHE); The National Institute for Health Research (NIHR); UK National Screening Committee (UK NSC).

Policy Context

The rare disease landscape has been much transformed in 2018. There have been significant breakthroughs, such as the completion of the sequencing phase of the 100,000 Genome Project in December 2018. The Project has delivered life-changing results for patients with one in four participants with rare diseases receiving a diagnosis for the first time, and providing potential clinically actionable findings in up to half of cancer patients.

DHSC have set up and provided the secretariat to the ministerially chaired National Genomics Board (NGB). The NGB's goal is to ensure the UK remains the world's leading centre for genomic medicine and research, and to use this position to deliver quantifiable benefits for NHS patients and the life sciences sector. The second Life Sciences Sector Deal was published in December 2018 and highlighted the importance of genomic healthcare. DHSC Secretary of State Matt Hancock set out an ambitious vision for genomics in October 2018, announcing a new goal to sequence 5 million genomes over the next 5 years, including 1 million whole genomes from NHS and UK Biobank participants. In January 2019 the NHS Long Term plan was published, which included the commitment that from 2019, all seriously ill children who are likely to have a rare genetic disorder, children with cancer, and adults suffering from certain rare conditions or specific cancers, will begin to be offered whole genome sequencing via the new NHS Genomic Medicine Service. These novel initiatives are just some examples of the government's commitment to improving healthcare for people living with rare diseases.

Some of the changes in the rare diseases landscape over the past year could not have been foreseen when the Strategy was published in 2013, most notably the UK's intention to leave the EU. We recognise that one of the areas of particular concern to the rare diseases community will be the impact on the UK's participation in European Reference Networks (ERNs). At the time of publication of this document, the outcome of the negotiations with the European Union on any future partnership are not known. In its July 2018 White Paper The Future Relationship Between The United Kingdom and the European Union, the government said:

“To support cooperation, the UK should seek to participate in specific policies and networks which benefit businesses, researchers, citizens and patients across the UK and the EU, including: a. the European Reference Networks, which support European cooperation and knowledge sharing related to clinical care and research on rare diseases […]”.

An update on progress in 2018/19

Theme 1- Empowering Those Affected by Rare Diseases

Patient empowerment is crucial to improving healthcare for rare diseases. A large amount of work took place during 2018/19 to improve knowledge and understanding of conditions; build skills and confidence in the use of health information; and to ensure that patients can be active partners in their care. Access to quality data has also been a focus for delivery partners. This is some of what we have achieved:

At **DHSC** we have engaged with patients through the **UK Rare Disease Forum** and its online platform, Rare Disease UK's Patient Empowerment Group, and our implementation plan working group which we convene annually to capture progress.

Following last year's successful annual conference, the second UK Rare Disease Forum conference was hosted by the Welsh government in Cardiff on 17 October 2018 and was jointly chaired by Drs Graham Shortland and Mark Walker. The conference provided updates to attendees of developments and case studies in rare diseases across the UK and offered opportunities for first hand feedback from rare disease clinicians, health service commissioners and government officials. The next UK Rare Disease Conference is scheduled for 2019.

Feedback from the rare diseases community included the wish to extend membership to the Rare Disease Forum and online platform. At its January 2019 meeting, the UK Rare Diseases Policy Board agreed that - although the Forum was not intended for individuals or disease specific organisations but their umbrella organisations - it would consider such proposals where there might be a particular gap in membership. In the coming months, DHSC will provide information on the online platform and look at ways to promote broader Forum membership.

Last year DHSC continued to run and maintain the online platform. We:

- Circulated agendas for UK Rare Diseases Policy Board meetings.
- Took questions from Forum members for the Policy Board and fed back responses.
- Published the Policy Board minutes. Following stakeholder feedback, we amended the procedure for sign-off of minutes to facilitate a timelier publication. This is a recent development at the request of patient representatives and was actioned for the first time in January 2019.

- Posted information on relevant publications or upcoming events of interest concerning rare diseases.

- Actively sought feedback from Forum members on how the platform could be improved.

As for the 2018 implementation plan, we shared a draft of this document with Rare Diseases UK's Patient Empowerment Group (PEG). PEG was established by the Rare Disease UK Campaign, run by Genetic Alliance UK, to help monitor the implementation of the Strategy. The purpose of the group is to ensure that the patient voice is properly informed and effectively represented in the implementation of the Strategy. We are grateful for PEG's comments which made this a better document.

At the **MHRA**, we have also made progress on patient engagement and empowerment through the continuation of our Patient Group Consultation Forum (PGCF). This group was established in 2014 and provides a framework for patient groups to get involved with the regulator and acts as an agency-wide resource that can be called upon to hear patients views and add value to decision making processes.

The PGCF currently has over one hundred individual members, representing a wide variety of health constituencies, including rare diseases. Genetic Alliance UK (the national charity representing over 180 rare disease patient organisations) is a member of the PGCF, alongside several groups that represent specific rare disease populations such as Muscular Dystrophy, including Duchenne, and some rarer forms of cancer. RareConnect, which promotes information and support for patients with rare diseases globally, is also represented. Topics for discussion can be put forward by the agency or members of the group. Past topics have included: the Accelerated Access Review; patient attitudes to the pathways to innovation in connection with Regenerative Medicine; patient views on promotion of the Early Access to Medicines Scheme to healthcare professionals and patient groups.

PHE's National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) developed a two year work plan outlining the rare diseases expansion work to run until 2020. There have been six main areas of progress over the last year:

1. Infrastructure

    - Orphanet coding has been introduced to the data management system, allowing more specific and standardised coding of rare diseases compared to the current International Classification of Diseases-10 (ICD-10) system.

    - A plan for Office for National Statistics (ONS) death registration data to flow into the NCARDRS data management system has been developed. This is expected to start in early 2019 and will strengthen understanding of patient outcomes.

- A data quality improvement plan has been developed, which will be implemented in 2019.

- NCARDRS' coding tool is used by all registration staff to ensure standardised coding. The tool has been developed to support the rare disease registration and will continue to be developed further in 2019.

2. Clinical data liaison

- NCARDRS obtained national data on newborn blood spot inherited metabolic conditions (Maple Syrup Urine Disease, Isovaleric acidaemia, Glutaric aciduria type 1, Medium-chain acyl-CoA dehydrogenase deficiency, Homocystinuria) to support research; and data collection of antenatally and postnatally diagnosed sickle cell disease and thalassemia to support the newborn blood spot national screening programme.

- NCARDRS is also seeking access to rare disease data, where available. For example, NCARDRS has implemented a prospective reporting system for Wilson's Disease with the Supra-Regional Assay Service and is agreeing a data sharing agreement with the genome-wide association study for Wilson's Disease (CROWD Study; UCL).

3. Multi source approach

- NCARDRS gained permission to access identifiable ONS mortality data, which could be combined with Hospital Episode Statistics (HES) to develop methods for identifying cases of rare disease and to describe morbidity and mortality outcomes for patients.

- Two medical doctors (externally funded) are providing clinical expertise to support work on rare rheumatic disease (Nottingham University) and Wilson's Disease (British Association of the Study of the Liver). This work includes developing methods for identifying ANCA-Associated Vasculitis cases in HES data. The resulting case lists will be used to improve patient treatment and outcomes.

- The HES and ONS mortality data have been used to undertake an internal NCARDRS quality assurance project. The results have led to improvements in the reporting of cases of congenital anomalies which are also rare diseases.

4. Patient portal

- Discussions have been held with existing registers, including a review of best practice, to understand the challenges of implementing patient self-reporting systems. This will inform the PHE plan going forwards.

5. Patient and stakeholder engagement regarding NCARDRS content, function and outputs

    - Engagement has increased through work with the Early Access Medicines Scheme, participation in National Institute for Health and Care Excellence (NICE) scoping exercises and ad hoc round table discussions.

    - NCARDRS have been working closely with the national Genomics Medicine Service with regard to cancer and rare disease.

    - Data has been provided to NHS England Specialised Services to support commissioning decisions.

    - NCARDRS have continued to be a member of the NIHR Bioresource group (discussed in Theme 5).

    - Patient groups are met with regularly, which improves NCARDRS understanding of patient perspectives. Presentations are given at conferences and NCARDRS are currently working with several patient groups on data sharing.

6. Research Strategy

    - There has been collaboration between NCARDRS and the British Paediatric Surveillance Unit studies including planning for long-term storage of study data and working with the Next Generation Sequencing Database Development for Newborn Screening Disorders (Sheffield). NCARDRS encourage discussion with any rare disease researchers who may wish to collaborate and share data.

The implementation of NCARDRS rare disease expansion work plan continues in 2019. See Annex 1 for details of actions going forward.

Theme 2 - Identifying and Preventing Rare Diseases

Identifying and preventing rare diseases is crucial for patients, families and the healthcare system. Progress made in this area over the last year is detailed in this section.

PHE's UK National Screening Committee (UK NSC) work to help diagnose patients earlier or identify those at higher risk of developing conditions in the future through screening programmes. These programmes can allow earlier intervention through healthcare or lifestyle, dramatically improving the health of the population.

UK NCS ran an annual open call for new screening proposals between September and December 2017. This open call saw four proposals, of which three were for rare diseases:

1. Screening for auditory neuropathy spectrum in new-borns: This proposal is currently under consideration as a potential modification to the new-born hearing screening programme, a decision on which will be made by 2020.

2. Screening for keratoconus in children and young adults with Down's syndrome: This proposal was outside the UK NSC's remit of population screening programmes, so is not being considered further.

3. Screening for increased risk of stroke in children with sickle cell disease: This is outside the remit of the UK NSC but part of the existing care pathway for children with sickle cell disease.

All three calls listed above either proposed a change to an existing programme or targeted high-risk groups. For proposals that do not meet the criteria, UK NSC strive to offer advice on where best to direct the proposal. To help with the process, UK NSC amended the proposal template for the 2018 call to better explain the assessment criteria.

The annual call for 2018/19 screening proposals was open between October and December 2018. Members of UK NSC met in January to discuss the submissions and aim to write to the proposers of the programmes with a decision about whether the proposal will be taken forward into evidence review by the end of February 2019. More information can be found on the PHE Screening website.

UK NSC have also run campaigns and published guides, leaflets and blogs to improve understanding and communication about informed choices. See the PHE Blog page for more information.

UK NSC review evidence for running screening programmes for a particular condition every 3 years to ensure the decision is up to date. UK NSC have reviewed the evidence for the following screening programmes this year: Biliary Atresia; Biotidinase deficiency; Congenital cytomegalovirus (CMV); Feto-maternal autoimmune thrombocytopenia (FMAIT); Group B streptococcus (GBS); Human T-cell lymphotropic virus (HTLV); Severe combined immunodeficiency (SCID); Thrombophilia; Tyrosinaemia; Vasa praevia.

Except for SCID, the above reviews concluded that there was insufficient evidence to introduce a population screening programme for the condition at this stage. DHSC have commissioned a piece of research into GBS screening to increase the evidence base. More information and the published reviews can be accessed via the UK NSC website.

The SCID evidence review recommended that screening for SCID should be evaluated in the NHS. An evaluation was carried out on the new SCID programme proposal and the government is considering UK NSC's advice.

UK NSC have been considering genomic opportunities for screening programmes in line with Recommendation 6 from 'Generation Genome' (see Annex 3). UK NSC are currently writing a report on what existing screening programmes have possibilities to use genomic technology as a primary screening test or confirmatory test. The report is due to be published in the middle of 2019. Alongside this, UK NSC is working with Genomics England on research activities relating to opportunities from whole genome sequencing in new-borns.

In 2018/19 the NHS and UK NSC have continued to set standards and monitor progress of screening programmes, information of which is publicly available through the NHS Screening Programme annual reports. The most recent report published was for 2016/17 and the 2017/18 report is due for publication in early 2019.

Over the last year, **NHS England,** have been working on fulfilling the actions in the NHS England Implementation plan, an update to which is planned for publication in 2019. We have also worked to implement Recommendation 7 of 'Generation Genome' (see Annex 3) to evaluate the roll out of contingent Non-invasive Prenatal Testing (NIPT) and review evidence and proposals for modifications to the Down's syndrome screening programme.

NHS England's Genomics Policy Unit has led on the procurement and roll out of the laboratory service as part of the wider Genomic Laboratory reconfiguration and procurement. This is part of the wider roll out of the Genomic Medicine Service, which will make whole genome sequencing available to all seriously ill children who are suspected to have an underlying genetic condition, and patients with hard to treat cancers.

Theme 3 - Diagnosis and Early Intervention

Diagnosis and early intervention are recognised as crucial to improving the lives of people living with rare diseases. This section describes the progress made over the last year, focussing in particular on what we have done to improve training; data to support diagnosis and treatment; and access to medicines.

HEE are transitioning the **Genomics Education Programme** (GEP) into business as usual, ensuring the continued and coordinated focus on genomics education and training for all NHS staff across all levels of skill and expertise. This will enable earlier diagnosis for patients, including those with rare diseases, through NHS staff harnessing the advances in genomic healthcare. This is in line with Recommendation 22 of 'Generation Genome' (see Annex 3), the implementation of the new Genomics Medicine Service and the National Genomics Test Directory.

In 2018/19 the Genomic Medicine Masters programme was recommissioned for a further three years and will continue to be delivered by seven Russell Group Universities, each closely aligned with a Genomic Medicine Centre. Such a multi professional programme

enables NHS staff to acquire underpinning knowledge across a broad range of genomic topics with options to undertake the learning as individual modules, Post Graduate Certificate, Diploma or full Master's degree.

We also developed additional educational resources including:

- A tool to develop competence in tumour assessment for whole genome sequencing for histopathologists and healthcare scientists.

- Further modules being added to HEE's Genomics 101 series, which is targeted at those with limited or no knowledge of genomics and its healthcare applications.

- A number of peer to peer medical specialty videos, which showcase the relevance of genomics in healthcare.

- A genomics board game for trainee midwives following the hugely popular board game HEE introduced for nurses.

The GEP have worked closely with professions over the last year and we have programmes of work with the Royal College of GPs and jointly with NHS England, the Academy of Medical Royal Colleges. The GEP have also continued their established Nurses Round Table, chaired by Lord Willis, and our work with healthcare scientist organisations.

One of the commitments in the Strategy is to "work to achieve reduced times for diagnosis of rare diseases". Under the **UK Rare Diseases Policy Board, DHSC** established a Task and Finish group in early 2017, chaired by Dr Trevor Cole (Consultant Clinical Geneticist at Birmingham Women's and Children's NHS Foundation Trust), with the aim to further explore and propose improvements to the collection of data to measure the time travelled in the diagnostic pathway for patients with rare diseases. These conditions are being used as exemplars to explore this: ANCA-related vasculitis, Bardet Biedl syndrome and tuberous sclerosis complex.

In 2018, the group continued their efforts in examining and defining the data for patients. The Task and Finish group convened eight times in 2018 either through full group meetings or smaller satellite meetings with clinical representatives. **NHS Digital** supported the group by collecting data and presenting information. The initial data collection of anonymised and aggregated data is concluded, outputs analysed and data presentation is being finalised. The report of the **Diagnostic Odyssey Task and Finish Group** will be published in 2019.

With the aim to improve diagnosis, PHE, in collaboration with NHS England, strive to drive sharing of data to improve the link between databases and health records. **NCARDRS** have had considerable success in obtaining data for rare diseases, but recognise that

NHS England's commissioning levers can provide an extra incentive for data sharing to drive the expansion of a national rare disease registry. This will form part of the forward planning for NCARDRS' rare disease expansion programme in 2019.

At **OLS** we are working to improve the prevention, detection and diagnosis of diseases through artificial intelligence (AI), digital and data. This includes the development of a pioneering programme on digital pathology and radiology using AI. In 2018, the government, working with UK Research and Innovation (UKRI), established a network of five centres of excellence in digital pathology and radiology with AI. This work was supported by £50m from the Industrial Strategy Challenge Fund and, in addition, it leveraged over £33m of investment from industry partners such as Philips, Roche Diagnostics, Canon, Siemens Healthineers, GE Healthcare and Leica. The work of the centres will enable earlier and improved diagnosis of diseases and lead to the development of new processes, practices and products that will benefit the NHS and patients as a whole. In addition, **Digital Innovation Hubs** are in the process of being developed, which will create a world leading data infrastructure to enable to safe and secure use of data, including for clinical trials. This work is led by Health Data Research UK (HDR UK), and is supported by £37.5 million of government funds from the Industrial Strategy Challenge Fund. By the end of 2018, HDR UK had reached the mid-point of the design phase for the Digital Innovation Hubs and opened applications for the first phase of innovative data projects which will inform the creation of the UK-wide data infrastructure and demonstrate how technology and data solutions can improve lives and speed up innovation in the NHS. These programmes are not specific to rare diseases but the work will ensure NHS patients can benefit from innovative treatments, including rare disease patients. Please see Annex 1 for details of future plans.

The government has also established the **Accelerated Access Collaborative**, bringing together CEO and Chair level representatives from the NHS, industry and patient groups to identify and support the most transformative health innovations. The support provided by partners to these products will provide an expedited route to bring cost-effective breakthrough products to patients, including those with rare diseases, as quickly as possible. The AAC has announced the first 12 products to be supported with each to be provided with dedicated support to increase their uptake in the NHS. More information on this can be found in the first Life Sciences Sector Deal (page 31) and in this document under Theme 5: The Role of Research in Rare Diseases.

Applications for the designation of **orphan medicines** are reviewed according to Regulation (European Commission) No 141/2000 by the European Medicines Agency (EMA), through the Committee for Orphan Medicinal Products (COMP). Via **MHRA**, the UK has continued to take a very active role in the decision-making process at the COMP. We ensure applications for Orphan Drug designation of potential drug candidates for rare diseases are appropriately recognised, encouraging companies to develop their products further.

The MHRA's (UK) member of COMP published three peer reviewed papers in 2018 in the rare disease field; 'Editor's foreword: evolving the rare cancer field'; 'Drug development in paediatric oncology – challenges and opportunities – reflections from European regulators' (Expert Opinion Orphan Drugs); 'Defining orphan conditions in the context of the European orphan regulation: challenges and evolution' (Nature Reviews Drug Discovery).

Orphan designation criteria are currently set at EU level, with UK participating in the European Medicines Agency Committee for Orphan medicinal products. In the event of a no deal Brexit outcome, where the UK does not continue to participate in the EU scheme, the UK will continue to support drug development in rare diseases and consider how current EU orphan incentives such as free scientific advice for small and medium sized enterprises, reduced application fees and a 10 year market exclusivity period could continue to be made available in the UK.

At the MHRA, we are responsible for two steps of the **UK Early Access to Medicines Scheme** (EAMS), which aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need. Under EAMS, a medicine for slowing the decline of respiratory function in patients with Duchenne Muscular Dystrophy (DMD) was approved in 2018. In a renewal procedure, a specific Patient Group Meeting was held ahead of a Commission on Human Medicines (CHM) review in order to gain a full understanding of the patient perspective. The patient meeting was attended by DMD patients, patient representatives, Commissioners and representatives from the MHRA. CHM advised that the EAMS scientific opinion should be upheld taking into account, amongst other issues, the high level of unmet need that was clearly described in the patient group meeting.

Finally, in 2018, we formed a cross agency 'Rare Disease Interest Group' which included members of the National Institute for Biological Standards and Control (NIBSC) and medicines regulator. The group is currently drafting a review paper highlighting the work of the MHRA in the field of rare diseases. The paper will be published in a rare diseases journal in 2019.

Theme 4 - Coordination of Care

A multidisciplinary and coordinated approach is imperative to provide high quality care to patients. This is particularly important for rare disease patients who often require several specialists and hospital departments to work in collaboration with their primary health care professional to provide timely diagnosis and care. This section describes some of our work in this area, noting however that the majority of actions to improve the co-ordination of care are covered in the implementation plan led by **NHS England**.

Over the last year, **DHSC** has facilitated the coordination of care through supporting the **Diagnostic Odyssey Task and Finish Group** (mentioned in Theme 3); supporting the

development of **European Reference Networks** at national and European levels; and have set up and provided the secretariat to the ministerially chaired **NGB.** The NGB met three times in 2018, with its inaugural meeting taking place in March 2018. Further information, including its membership, can be found on the NGB website.

In October 2018, Secretary of State for Health & Social Care Matt Hancock, MP, announced the NHS Genomic Medicine Service as the first national genomic healthcare service in the world. It will allow faster diagnosis and personalised care through consistent and equitable access to genomic medicine. Further details can be found on the Genomic Medicine Service website.

Theme 5 - The Role of Research in Rare Diseases

Rare disease research is essential for uncovering answers to the too many unknowns about the causes, indications, symptoms, and treatments for many rare diseases. Many organisations have been working on improving research, or the research environment, over the last year, and collaboration between them has been frequent. Here are some of the highlights:

The **NIHR**, has successfully integrated three previously separate entities: NIHR Bioresource, The NIHR BioResource Rare Diseases, and The NIHR Rare Disease Translational Research Collaboration (RD-TRC). The integration has established the **NIHR BioResource for Translational Research for Common and Rare Diseases**, which has bought in new individual centres, and with them new areas of expertise:

- The NIHR BioResource is led by 13 BioResource centres across England, hosted at NIHR Biomedical Research Centres (BRCs) and NIHR Clinical Research Facilities (CRFs). It aims to provide a nationally accessible resource of volunteers from the general population and patients with common and rare diseases who have consented to be recalled according to their genotype and/or phenotype for academic and industry led experimental medicine and clinical research studies. This resource will significantly improve the national capability to undertake and support studies that require access to national patient cohorts. It will continue to support in-depth phenotyping for rare diseases, and facilitate its linkage to genomic data, to provide greater understanding of the mechanisms underlying rare and common diseases, and to support the development of new treatments and diagnostics.

- During 2017/18 considerable progress was made to establish the new governance arrangements for the NIHR BioResource. An Oversight Board, chaired by Professor Sir John Savill, was established to oversee the overall direction. The Steering Committee has representation from the 13 NIHR BioResource centres and key stakeholders, including rare disease expertise, NCARDRS and rare disease patient

representatives. A Rare Disease Expert Working Group and Patient Advisory Group have also been set up.

- By the end of March 2018, 37 rare diseases had been adopted by the NIHR BioResource (of the up to 100 expected by the end of March 2022). At this time the NIHR BioResource had recruited over 15,600 patients with rare diseases from 50 NHS Trusts in England. Whole genome sequencing data is present for over 13,000 of these patients. The NIHR BioResource has also started actively recruiting for newly adopted rare diseases such as neurofibromatosis types 1 and 2.

- The NIHR BioReosurce hosted a successful ‘Think Research' Rare Diseases Patient Day in London in March 2018. The day was introduced by Vicky Ford MP and included a mixture of talks and break-out sessions to discuss how rare disease patients groups can engage through social media, work with industry, and gain information on how genomics data is used in research.

NIHR has continued to make progress on the implementation of the recommendations of ‘Going the Extra Mile’. Progress in 2018/19 includes:

- Development of Patient and Public Involvement Standards through a UK-wide partnership bringing together members of the public with representatives from the NIHR, the Chief Scientist Office (Scotland), Health and Care Research Wales and Public Health Agency (Northern Ireland). The standards, launched in March 2018, are designed to improve the quality and consistency of public involvement in research by providing clear benchmarks for effective public involvement alongside indicators against which improvement can be monitored. The standards are being piloted in 10 formal year-long testbeds and an additional 45 registered projects with an evaluation planned for spring 2019.

- Publication of co-production guidance and the development of a ‘Learning For Involvement’ website. This work continues to strengthen the relationships between health research, the general public, patient groups, charities and the wider voluntary sector, both nationally and internationally.

At **DHSC**, we have continued to develop web-based systems through the NIHR that retain the information required to manage health and social care research in England, including:

- **Health Data Finder** which helps direct researchers to high quality health research datasets. The Health Data Finder is a single point of access tool for browsing healthcare data sets from a wide variety of organisations that cover various conditions and data types, including primary and secondary care. There were 2057 visitors between December 2017 and December 2018.

- The **UK Clinical Trials Gateway** (UKCTG) website which provides the public and clinicians with information about trials that may be suitable for them or their patients. 51,000 people are registered with the UKCTG. The UKCTG service is managed by NIHR Clinical Research Network who have undertaken extensive work to identify a range of improvements to improve user experience, to increasingly empower the public to engage in research and to take account of the future developments in light of the 10 year NHS Long Term Plan.

- Work with NHS England, NHS Digital, NIHR, and Understanding Patient Data on developments to the **NHS App**. By 2021 the NHS App will allow people to find out more about research in the NHS, consent to their health and care data being used for research into improving disease prevention, diagnosis and treatment, and consent to be contacted to get involved in interventional research. The NHS App will also allow users to download their lifestyle data, swiftly, safely and securely, so that it can be linked to their wider health data for research into improving NHS patient care.

Genomics England has progressed its rare disease research work over the past year, announcing the sequencing of the 100,000th genome as part of the **100,000 Genomes Project** on 5 December 2018. Of the 100,000 whole genomes sequenced, 77,706 were for rare diseases. Work is ongoing to scope and agree the next phase of Genomic England's activity, informed by the Secretary of State for Health and Social Care's announcement on 2 October 2018 to sequence 5 million genomes within the next 5 years, of which 1 million genomes will be whole genome sequences.

Genomics England have also been working on Recommendation 9 from 'Generation Genome' (see Annex 3), regarding patient consent processes for genomic testing. This is being taken forward by NHS England, supported by Genomics England and others. Clinicians, patient groups and participants are working to develop a **patient choice model**, which covers two key aspects of choice when it comes to the NHS Genomic Medicine Service – clinical care and taking part in research. A working group was established in the autumn of 2018 to:

- understand and start to implement the revised patient choice model for genomic testing; and to build on the expertise developed during the 100,000 Genomes Project;

- build consensus and minimise variation across the country;

- provide feedback on patient choice and clinician consent materials; and

- work with each region to develop local implementation plans and identify support needed

The working group includes representatives from NHS Genomic Laboratory Hubs and Genomic Medicine Centre regions, Macmillan and Cancer Research UK, Clinical Nurse Specialists, and the NHS Clinical Reference Group.

Pursuing 'Generation Genome' Recommendation 10, Genomics England has brought in a small number of additional cohorts to be used as 'validation cohorts'. Participants for these were selected based on the available data and scientific merit. Analysis of the evidence from these cohorts will be used to establish if whole genome sequencing does or does not require additional validation – with the latter outcome reducing the costs of clinical implementation. The validation cohorts include a cohort of 1,000 individuals as part of the Epilepsy Society and a 300-600 sample cohort from National External Quality Assurance Scheme (NEQAS).

Genomics England's work is also progressing to access additional cohorts of patients through partnerships with other projects. A cohort of circa 300 from the NIHR Bioresource was re-consented and recruited to the 100,000 Genomes Project. Genomic and clinical data of patients sequenced through NIHR Bioresource is in the process of being copied into the 100,000 Genomes Project research environment. This cohort contributed to the total number of 100,000 genomes sequences which were announced on 5 December 2018.

The primary vehicle developed by Genomics England to engage with participants from the 100,000 Genomes Project is the **Genomics Conversation**. The Conversation's approach is one of partnership, and a key aim is to capture the opinions, aspirations and concerns of individuals with cancer and rare diseases regarding the implementation of genome sequencing into routine clinical service. A number of key engagements have taken place in 2018/19, such as:

- A survey conducted in collaboration with Genetic Alliance UK which was completed by rare disease patients and carers. The survey collected information on:
    - the experiences of participants in the 100,000 Genomes Project, including satisfaction with information, contact from Genomics England and outcomes, views about referral and results processes,
    - views about whole genome sequencing through the NHS, including attitudes to data sharing with third parties and data security.

The survey was completed by a self-selecting cohort. Awareness of the survey was raised through social media and e-newsletters through the following networks: Genetic Alliance UK (over 200 patient organisations), Rare Disease UK (over 2,500 supporters) and SWAN UK (over 1,000 families with children with an undiagnosed condition). Around 500 people responded to the survey.

- The **British Science Association** (BSA) Future Debates programme which comprised of 15 debates in 2018/19. They were held to stimulate public conversation on 'Personal Data' and capture attitudes and concerns across the UK. The debates explored issues such as the new NHS Genomic Medicine Service; the Cambridge Analytica scandal and its impact on attitudes to data sharing; attitudes to sharing and storing DNA sequence and health data; and whether we have a duty to share our DNA data to improve healthcare. Debates have been held in Aberdeen; Brighton; Cornwall; London; Nottingham; Portsmouth & Isle of Wight; Reading; and Tayside and Fife. In addition, and on advice from the BSA, debates were also held with different ethic and social groups traditionally under-represented in genomic medicine, including refugee, non-English speakers and economically disadvantaged groups. The future debate series will conclude with a flagship debate in London in early 2019.

- Progress Educational Trust (PET) Debates which have improved public understanding of science, law and ethics in fields that include human genetics. Working with Genomics England, PET held three debates which brought clinicians, researchers, ethicists and other experts in the genomics together with more than 300 members of the public. Discussion topics included: With Great Genomic Data Comes Great Responsibility; How Do We Make Genomics Everybody's Business?; and Whose Genome Is It Anyway?

- The **Sciencewise Public Dialogue** which focused on Recommendation 19 from 'Generation Genome' (see Annex 3) regarding a new social contract. It also captured the attitudes of people with rare diseases and their families. The project engaged stakeholder groups, including GAUK, and established a baseline understanding of and attitudes to genomic medicine, whole genome sequencing, the concept of a social contract and public 'redlines' in relation to genomic data, public ambitions/aspirations for genomic medicine, concerns the public identifies with genomic medicine, and the language the public understands and uses to talk about genomic medicine.

Beyond the Genomics Conversation, Genomics England has continued to engage with patients through their Participant Panel, made up of both rare disease and cancer participants. The Participant Panel, amongst other activities, facilitates the interchange of experiences and ideas between participants and other parts of the genomics community, including the research community.

To help coordinate **genetic data** including for research purposes, at **NHS Digital**, we have been working with Genomics England to improve the systems used to record genetic data and other relevant information. NHS Digital became Genomics England's software provider in April 2017, and we have since made a number of improvements to the specialist Data Acquisition Management System (DAMS), which supports the management of the participants in the 100,000 Genome Project. The first release of NHS Digital developed software took place in May 2017, and a regular monthly release cycle is

now in place. NHS Digital also provide technical support to Genomics England on the use of the DAMS software.

To further coordinate healthcare Information Technology (IT), we maintain Spine, which supports the IT infrastructure for health and Social Care in England. Spine is also used as part of the 100,000 Genome Project, where it ensures that participants' NHS number is recorded against the project data, meaning manual data entry is not required. This has helped to improve data quality and reduce the time taken for GMC's to register patients.

In addition, we produced a publication presenting the results and analysis of the national data collection from UK Genetic Testing Network (UKGTN) member laboratories of NHS molecular and cytogenetic test activity for inherited diseases in England and Scotland. This publication covered 2016/17 and was published in August 2018. We are also collaborating across the four UK nations to collect data for analysis and reporting to improve the rare disease research agenda. Data collection is mandated independently by each nation and progress requires all four countries to work together. For the genetic testing analysis report published in August 2018, only English and Scottish data was captured.

At the **HRA**, we met with the NIHR Coordinating Centres to discuss the "just in time" pilot for rare diseases (background can be found in the 2018 implementation plan). HRA then identified and met with a number of interested NHS Research & Development stakeholders to look at setting up studies based on the "just in time" approach.

HRA continued working with research communities throughout 2018/19 to provide a consistent and streamlined approach. Activities included:

- The development and phased roll-out of the pharmaceutical and radiation single technical assurance. These new arrangements started to roll out in the second half of 2018. They improve the quality of information to support NHS departments and reduce the duplication of reviews. The programme will continue to roll-out across the UK in a phased approach, with full implementation for all study types in 2019/20.

- Working across the four nations to develop a consistent approach to setting up research studies, including agreement and development of a UK wide local information pack.

- Piloting a 'combined ways of working' pilot in collaboration with the MHRA, in advance of the implementation of new European Union regulations for Clinical Trials of Investigational Medicinal Products (CTIMPs). The pilot streamlines processes to a single application and single decision from the regulator and research ethics committee.

- Development of a template that supports consistent attribution of costs related to non-commercial studies at the funding stage. This is part of a collaborative programme with NHS England and NIHR to reduce the burden and delays associated with agreeing Excess Treatment Costs for research studies. A related project within the programme is addressing delays associated with contract agreement for commercial studies, as the existing processes can sometimes disproportionately affect rare disease studies.

We have also endorsed 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. The work on standards is complete and guidance for researchers will be published later in 2019. Finally, HRA continues to promote the use of generic participant information leaflets through presentations, training and webinars supporting the research community.

As mentioned under Theme 3, at **HEE**, we have continued and expanded **their Genomics Education Programme** (GEP). Upskilling the NHS Workforce in Genomics aids the rare disease research agenda, as it increases healthcare professional awareness of the opportunities for enrolment of patients in genomic research and clinical trials, which might provide answers for patients or benefit others in the future. The GEP also allows healthcare professionals to acquire the knowledge base to enable the pursuit of academic careers in genomics.

As mentioned under Theme 2, at **MHRA** we have continued to work with the European Union (EU) and international partners within the framework of EU Paediatric Regulation to support **paediatric drug development**, particularly in areas of unmet therapeutic needs such as rare childhood diseases. The MHRA has maintained a leading role in the assessment of Paediatric investigation plans, supporting companies through national and EU scientific advice meetings. The MHRA supports research initiatives in the UK and internationally under the European Network of Paediatric Research at the EMA (Enpr-EMA). The Enpr-EMA is a network of research networks, investigators and centres with recognised expertise in performing clinical studies in children. There is also ongoing collaboration with the Food and Drug Administration (FDA) and other regulators to ensure that the proposed clinical trials are aligned globally. Finally, we have emphasised the importance of research through its continued collaboration with the Royal College of Paediatrics and Child Health (RCPCH), supporting events and initiatives that promote meaningful interactions between various stakeholders in this field. MHRA representatives participate in disease specific events such as psychiatry and neurology, to ensure experts' views on needs and development plans are incorporated into regulatory decisions.

Finally, **OLS** and government, in collaboration with the life sciences sector and industry, is making strong progress in implementing the first Life Sciences Sector Deal. The first sector deal included an investment of £85m in our already world-leading genomics assets at UK Biobank as part of our ground-breaking project to sequence 1 million whole

genomes in the next five years; £50m for five new centres of excellence in digital pathology and radiology which will apply AI tools to enable easier and more accurate detection of diseases. A £146m commitment to medicines manufacturing is building an end-to-end national infrastructure for advanced therapies including doubling capacity at the Cell and Gene Therapy Catapult manufacturing centre; three new advanced therapies treatment centres; and two new innovation centres for vaccines and medicines manufacturing. Supported by £86m of government funding, the government, the NHS and its partners are delivering on their clear commitment to implement the Accelerated Access Review, establishing the Accelerated Access Collaborative under the chairmanship of Lord Darzi and announcing the selection of the first products for support (see also Theme 3).

The second Life Sciences Sector Deal, was published in December 2018 and set out further plans to secure a global lead in those areas that represent the greatest opportunities for the UK and deliver on the mission to transform the prevention, diagnosis and treatment of chronic diseases by 2030. It strengthens government partnership with industry, universities and charities and demonstrates the important role of the NHS as a key delivery partner.

While the measures in both life sciences sector deals are not specific to rare diseases, they work to ensure the UK is an excellent place for life sciences research and development and that NHS patients, including those with rare diseases, can benefit from innovative treatments.

Annex 1: 2019/20 actions to implement the 51 commitments

The Tables below list the specific actions DHSC and its partner organisations will take in the coming year to implement the Strategy commitments across the 5 Themes. For a full list of the 51 commitments, please see the UK Rare Disease Strategy.

The political landscape has transformed since January 2018, especially regarding the UK leaving the EU. It's important to note whilst reading the table that some actions are subject to EU Exit developments.

Theme 1 - Empowering Those Affected by Rare Diseases

Actions	Lead organisation	Commitment
Continue to engage patients through the Rare Diseases Forum as well as Rare Diseases UK's Patient Empowerment Group. Work through the UK Rare Diseases Policy Board and with the Devolved Administrations on advice to government ministers on the future of the Strategy post 2020. Continue to convene, through the UK Rare Diseases Policy Board, an annual Rare Disease Forum conference. Aim to expand the membership of the Rare Disease forum and platform usage by: identifying suitable ways to promote broader forum membership through consideration of current gaps; publishing draft UK Rare Diseases Policy Board minutes on the forum platform ahead of formal sign-off; and responding to forum questions to the Board in a timely fashion.	DHSC	C1; C8
Work together on relevant elements in the Life Sciences Industrial Strategy and Sector Deals.	DHSC, OLS	C1; C8
Lead on the implementation of the second sector deal, which includes commitments to improve patient access to innovative health tech, diagnostics, treatments and self-management tools through a boosted Accelerated Access Collaborative, making it the umbrella organisation	OLS	

across the innovation landscape, overseeing and co-ordinating health funding and support, and increasing the number of high potential products, including for rare diseases, it can support.		
NCARDRS will continue their work plan (2018-2020) for rare disease expansion. This includes: • Infrastructure: Continue ongoing 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. • Clinical data liaison: Continue to 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 notifers. • Multi source approach: Continue to secure access to routine data feeds e.g. HES, ONS, develop a methodology for accurate case ascertainment through these data sets and data linkage. • Patient portal: Progress exploration of the feasibility of a patient portal to enable patients to self-register; to include function, validation and information governance issues. • Data outputs: Continue patient and stakeholder engagement regarding NCARDRS content, function and output. Continue ‘Awareness raising phase’ of NCARDRS: Continue work to ensure objectives and outputs are compatible with and in collaboration 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. • Research Strategy: Continue to position NCARDRS as the obvious collaborator with	PHE	C7; C8

research studies for data storage and linkage.		
Continue engaging with rare disease patients and representatives through the Patient Group Consultation Forum (PGCF).	MHRA	C1; C8
Our actions regarding the research elements of C7 and C8 are covered below under Theme 5 - The Role of Research in Rare Diseases.		

Theme 2 - Identifying and Preventing Rare Diseases

Actions	**Lead organisation**	**Commitment**
Continue with actions from the 2018 implementation plan. Continue to review the screening proposals submitted from the open call which ran from October – December 2018, and run an open call for new screening proposals in 2019/20. Continue work on the tyrosinaemia screening cost effectiveness report and the vasa praevia model, with reports on both to be published in 2019. Develop work to set up the SCID evaluation (subject to resources). Regularly assess whether existing screening programmes should be maintained or ceased. Continue to work with PHE, NHS England and Genomics England to see where genomic technology can be used as a primary screening test, or as a confirmation test (in line with Recommendation 6 of ‘Generation Genome’, see Annex 3). Report to be published on this in the middle of 2019. Consult and examine new methods of non-invasive prenatal testing using genomic technology.	PHE, UK NSC	C9

Actions	Lead organisation	Commitment
Evaluate the use of Next Generation Sequencing technology for confirmatory diagnosis in Cystic Fibrosis. Continue discussions with Genomics England on research activities relating to whole genome sequencing in newborns.		
Continue to consider the outcome of any UK NSC 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. Continue working in line with Recommendation 7 (see Annex 3) of 'Generation Genome' on: An evaluative roll out of contingent Non-invasive Prenatal Testing (NIPT) is underway and will examine costs, acceptability, informed choices and feasibility. Together with UK NSC review the evidence to consider reflex testing within Down's screening as a major programme modification in accordance to its published evidence review process.	NHS England	C9

Theme 3 - Diagnosis and Early Intervention

Actions	Lead organisation	Commitment
Continue to deliver the GEP to meet the needs of the whole NHS workforce to support the implementation of the Genomic Medicine Service and the new Genomic Test Directory in the NHS. This includes the development of a workforce plan and responding to relevant areas of new health policy and strategy (eg. NHS Long Term Plan) as well as the independent Topol review.	HEE	C15

Actions	Lead organisation	Commitment
Consider the benefits of analysing GP Extraction Service (GPES) data for the Diagnostic Odyssey Task & Finish report. This work is subject to obtaining required funding and a slot in the GPES extraction calendar.	NHS Digital	C19
Continue to be involved in working group discussions between all partners (including MHRA, NICE, NHS England/I and NIHE) on the development of the Accelerated Access Pathway (AAP).	OLS	C13
Begin to implement the government commitment to the 'Accelerating detection of disease' challenge, announced in the second Life Sciences Sector Deal and backed up by up to £79m (subject to business case approval) from the Industrial Strategy Challenge Fund to detect and diagnose diseases earlier. To build on work done to develop new centres of excellence in digital pathology and radiology using AI, which will enable earlier and improved diagnosis of diseases. Government have committed a further £50 million investment to scale up the programme, which is a first step in making the UK's digital pathology & radiology programme a truly national opportunity.	OLS	C11
Further actions by OLS and NIHR are covered under Theme 5 below.		

Theme 4 - Coordination of Care

Actions	Lead organisation	Commitment
Support the publication of the Diagnostic Odyssey Task and Finish Group report in 2019 and discuss any next steps with the Rare Diseases Policy Board. Continue to engage and support UK ERN Health Care Providers (HCPs) at national and international levels.	DHSC	All relevant commitments; C25

Actions	Lead organisation	Commitment
Support the genomics science strand to the NGB.		
Work with the UK Rare Diseases Policy Board and devolved administrations to facilitate UK-wide collaboration and learning across the four Nations.	DHSC	C31
Continue to work with the life sciences industry, stakeholder groups and across government to implement the second Life Sciences Sector Deal.	OLS	C25
Work with PHE and other interested parties to formulate a plan for improving data quality.	NHS Digital	C25; C29
NIHR's actions against commitment C25 are covered under Theme 5.		

Theme 5 - The Role of Research

Actions	Lead organisation	Commitment
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 the further development of the NIHR BioResource for Translational Research for Common and Rare Diseases as a national resource of individuals who have volunteered to be recalled for research based on their genotype and phenotype. Increasingly this is to include patients and their families across up to 100 rare diseases. 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. Continue to promote and advance public involvement in research, ensuring all research projects, programmes and infrastructure supported by the NIHR have active patient/ public	NIHR	C25; C40; 49; C50

Actions	Lead organisation	Commitment
engagement and involvement in their design and conduct. Working with INVOLVE to roll out a set of national standards and indicators for public involvement in research that can be used by organisations, research projects and individuals.		
Facilitate OSCHR Board discussion at the earliest opportunity in 2019 on the progress that has been made to support rare disease research.	OSCHR	C50
Following EU Exit, MHRA will ensure that the leading role of the UK in paediatric drug development continues by supporting companies and researchers, utilising UK research networks and the input of patient disease groups. The cross-agency 'Rare Disease Interest Group' plans to draft a review paper to publish in 2019 in a rare disease journal, highlighting the work of the agency in this field. Continue to develop its Patient Group Consultative Forum (PGCF).	MHRA	C36; C39
Roll out of the combined ways of working pilot for Clinical Trials of Investigational Medicinal Products (CTIMPs) to streamline and speed up approval of clinical trials. Scope out the 'just in time' pilot following the initial preparation work completed this year. This should include a clear definition of the types of scenarios that would be considered within the 'just in time' programme. Work with NHS stakeholders to consider local risk proportionate processes for setting up studies. Complete the full implementation for all study types in the roll out of the pharmaceutical and radiation single technical assurance. Continue to develop integrated processes within the HRA that support Research Ethics Committees, particularly in novel or complex areas. Publish guidance for researchers in 2019 in relation to recruitment registries/databases that	HRA	C39; C41; C40

Actions	Lead organisation	Commitment
have been endorsed by HRA and have met appropriate standards. Develop a new Integrated Research Application System (IRAS) and roll out across all study types, providing a simpler application system that supports study set-up. Develop and roll-out a revised Local Information pack and template. Dependencies and constraints on these actions are: • Implementation of NHS England Consultation on costs and contracts. It was noted by stakeholders to enable just in time activation, unmodified contracts must be in place, and fully costed. • The roll-out of the technical assurance programme, which will support just in time activation		
Develop and implement a training programme for the new hybrid (service and research) patient choice model so that healthcare professionals involved in consenting patients for genomic testing have the knowledge and the skills to guide their patients through this new process.	HEE	C45
Work with colleagues in DHSC and the 4 UK countries to encourage collaboration and data sharing. Work with colleagues who published data in 2018 to understand the challenges they faced.	NHS Digital	C31
Continue with the establishment of regional Digital Innovation Hubs to facilitate the use of NHS data for research purposes, as outlined in the second Life Science Sector Deal (Recommendation 11 of 'Generation Genome (see Annex 3)). HDR UK will complete the design phase for the Digital Innovation Hubs by April 2019 before moving to the delivery and implementation phase. A small number of exemplar data projects have now been announced and will take place throughout 2019 to inform the creation of the	OLS	C31

Actions	Lead organisation	Commitment
UK-wide infrastructure for health data research and innovation. Lead on the implementation of the governments ambition for genomics of sequencing 5 million genomes in the next 5 years to ensure the UK continues to lead the world in genomics research. One million of these will be whole genomes. Support Genomics England in their work to scope the development of a first-of-its-kind service to enable genomic volunteers to pay for a personalised report on their unique genetic make-up. With permission, the genetic data will be made available to researchers and scientists.		
Scope and agree the next phase of activity for Genomics England, informed by the Secretary of State for Health & Social Care's announcement on 2 October 2018 on the move to 1 million whole genomes within the next five years. Provisional actions that are subject to agreement of a Genomics England Business Plan. • Continue to progress Generation Genome Recommendation 9: work with NHS England to engage clinicians, patient groups and participants to develop a 'patient choice model' which encompasses clinical care and taking part in research. • Continue to work towards Generation Genome Recommendation 10: identify additional cohorts, selected both on their scientific merit and the available data that allows them to be used as validation cohorts. Work is also ongoing to harness samples commissioned through the NHS via the new NHS Genomic Medicine Service.	Genomics England	C37; C47; C48

Annex 2: Measuring Tangible Progress

The table below shows metrics to measure the progress between January 2018 – January 2019. We will continue to collect data and aim to improve measurement of progress going forward.

Measure as per the actions in the 2018 implementation plan (Q = quarterly, A = annually, O = ongoing)	**Lead**	**Measurement from Jan 18 - Jan '19**	**Commitment(s) being measured**
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)	DHSC	Achieved: The Rare Disease Forum conference was held in October 2018 in Cardiff Wales.	C1; C36
Number of Forum members active on the Rare Diseases Forum platform. (A)	DHSC	As of November 2018, we have 33 members on the Rare Disease Forum online platform.	
Number of Forum suggestions discussed by Policy Board and published on Forum Platform. (A)	DHSC	As of November 2018, the Rare Disease Policy Board discussed five forum suggestions.	
Publication of minutes from the Rare Diseases Policy Board meetings. (Q)	DHSC	As of November 2018, the Rare Disease Policy Board published the Minutes of each Board meeting (N=4) following sign-off. To facilitate faster publication, draft minutes will be published within a six weeks time frame following RDPB Board meetings.	
Number of engagements with the Rare Diseases UK's Patient Empowerment Group in the review of implementation plan and progress	DHSC	Workshop to review the 2018 plan attended by patient representatives. Engaged PEG in December 2018 to on reviewing this document.	

Measure as per the actions in the 2018 implementation plan (Q = quarterly, A = annually, O = ongoing)	Lead	Measurement from Jan 18 - Jan '19	Commitment(s) being measured
report. (A)			
Number of engagements with the Rare Disease UK's Patient Empowerment Group in the NCARDRS work plan (O)	PHE	NCARDRS attended two PEG meetings, including the PEG Industry Meeting.	
Number of patients involved in MHRA and HRA groups and committees. (A)	MHRA/ HRA	MHRA examples include: The Patient Group Consultative Forum – 108 patient representatives; Valproate Stakeholders' Network – 12 patient representatives; Lay Members' Forum – 13 lay members, 4 of whom are patient representatives; Safer Medicines in Pregnancy Consortium – 3 groups that represent women who are pregnant or breast feeding. HRA examples include: The Public Involvement Network - 80 people registered.	
Total number of rare disease patient results returned to GMCs (A)	GEL	As of 12 December 2018, 47,501 results have been returned to NHS GMCs – 35,914 of which are for rare disease.	C1; C15; C25; C42 (completed); C45
Total number of rare diseases patients recruited to 100,000 Genomes project (A)	GEL	As of 12 December 2018, the 100,000 Genomes Project has sequenced 100,249 genomes in total, with 77,706 of these for rare disease participants.	
Number of Master's in Genomic Medicine completed	HEE	Figures from the last census in June 2018 show that in total 1563 individuals have undertaken various elements of the Genomic Medicine Master's programme,	
Total number of NHS and HE staff involved in 100, 000 Genome Project	HEE/NHS England	Total number of NHS staff involved in the 100,000 Genomes Project is estimated to be 50,000.	

Measure as per the actions in the 2018 implementation plan (Q = quarterly, A = annually, O = ongoing)	Lead	Measurement from Jan 18 - Jan '19	Commitment(s) being measured
(A)		Within HEE those directly involved in the 100,000 Genomes Project via the GEP is 13.	
Development of a secure electronic method to enable patients to self-register to NCARDRS (O; A) - Number of patients self-registered to NCADRS. (A)	PHE	NCARDRS is currently in the scoping phase of developing a patient self -reporting interface, so the number of patients self-registered is currently zero.	C1; C7; C9; C29
Population coverage of NCARDRS across England. (O)	PHE	NCARDRS has 100% population coverage for conditions diagnosed in an antenatal or postnatal pathway, increasing coverage from 49% in 2017/18.	
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)	PHE	In 2018 a total of 36 data requests were made to NCARDRS, including those from clinicians.	
Number of response and advice requests to the Rare Diseases Policy Board; Forum and Rare Diseases UK. (A)	DHSC	In 2018 there were a total of 9 questions asked of the Rare Disease Policy Board via the forum platform. DHSC posted a total of 15 times, this includes responses to questions and information on minutes, agendas and events of the UK Rare Disease Policy Board. At the 2018 Forum conference DHSC presented on the online forum platform. Feedback from forum members present was for membership to be widened, questions to be responded more promptly and for Policy Board minutes to be circulated more quickly. We are looking to implement these requests.	
Number of providers endorsed as members/leads of European	DHSC/ NHS	There were no calls from the European Commission to increase membership of ERNs.	C28; C1; C8; C49

Measure as per the actions in the 2018 implementation plan (Q = quarterly, A = annually, O = ongoing)	Lead	Measurement from Jan 18 - Jan '19	Commitment(s) being measured
Reference Networks. (O)	England	DHSC and NHS England ran an application process for 'Affiliated Partners' to ReCONNET (ERN on Rare and Complex Connective Tissue and Musculoskeletal Diseases) where the UK does not have a full member. No application was received.	
Number of guidance documents developed by HRA/HTA on consent for sharing patient data/ tissue. (O)	HRA	HRA has worked with NHS Digital, Medical Research Council, PHE and others through NHS Digital's Research Advisory Group to develop guidance relating to use of patient data for research. Monitoring is undertaken by NHS Digital. HRA/HTA have published guidance on consent.	C40
Number of approaches/enquiries to data provider sites for access to data presented via 'Health Data Finder'. (A)	NIHR	2057 visitors to the Health Data Finder between December 2017 and December 2018	C35
Risk-proportionate regulation 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.	HRA	Proportionate review studies (i.e. non-trials) timelines have decreased significantly since 2016 and remain stable at median of less than 40 days end to end including applicant response time. Numbers of amendments for adaptive designs cannot currently be measured separately from other trials, but currently continue to have many amendments. HRA have worked with Cancer Research UK and MHRA to advise the cancer research community on best practices to reduce regulatory burden. Local NHS permission processes were abolished in 2016 with the implementation of HRA Approval, and a number of actions are underway to reduce site set-up times. HRA are working with NIHR and NHS England to streamline contracting and costing aspects of site set-up that are the major causes of delay	C39; C41

Measure as per the actions in the 2018 implementation plan (Q = quarterly, A = annually, O = ongoing)	Lead	Measurement from Jan 18 - Jan '19	Commitment(s) being measured
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)	MHRA	MHRA supports risk proportionate regulation and encourages trial sponsors to follow UK guidelines on risk-adapted approaches to the management of clinical trials of investigational medicinal products. MHRA also provide a notification scheme for certain lower-risk trials, defined as 'Type A' trials. In these cases the risk to the patient from the Investigative Medicinal Product (IMP) is converted to be no greater than that of standard medical care. Trials under the notification scheme have simplified requirements for conducting the trial. The approach is endorsed by Good Clinical Practice (GCP) Inspectorate and supported through inspections. This has included blog publication issuing guidance on the risk adapted approach in practice.	
Monitor the impact of the Joint Statement on the Application of Good Clinical Practice (GCP) to Training for Researchers issued with other regulators, royal colleges and industry in October 2017. (O)	MHRA and HRA	Training in accordance with the GCP legislation and associated guidance (which includes the joint guidance statement) is an integral part of GCP inspections and will continue to be going forwards. HRA have supported NIHR Coordination Research Network's delivery of training to staff groups such as pharmacists. Feedback on Good Clinical Practice training across the NHS given through HRA collaborative Learning Reference Group.	
Industry income and number of studies from contract and collaborative studies through the NIHR infrastructure. (A)	NIHR	In 2017/18: industry income - £347.6 million (up 172% on 2016/17) number of industry studies – 4,688 (up 33% on 2016/17)	C45; C46; C47; C48; C49; C51
Number of participants recruited through NIHR infrastructure. (A)	NIHR	Number of participants recruited to studies supported by the NIHR was 835,904 in 2017/18 (up 6% on 2016/17)	

Measure as per the actions in the 2018 implementation plan (Q = quarterly, A = annually, O = ongoing)	Lead	Measurement from Jan 18 - Jan '19	Commitment(s) being measured
Numbers of grants received / publications in peer reviewed journals. (A)	NIHR	Total publications by NIHR in 2017/18 was 13,573	
Funding for NIHR BioResource. (A)	NIHR	£37.5 million over 5 years from 1 April 2017 to 31 March 2022	
Number of researchers and clinicians links through GeCIPS. (A)	GEL	As of 12 December 2018, there are 3,164 GeCIP members.	
Number of industry partners taking part in the Discovery Forum. (A)	GEL	As of 18 December 2018, the Discovery Forum industry network has grown to 105 companies. Of these, 12 have subscribed to Full Membership which provides access to the Main Programme dataset within our Research Environment.	
Progress on rare diseases to be considered by OSCHR in 2018.(O; A)	OSCHR	OSCHR only met once in 2018 and did not consider rare diseases at that meeting. No further updates at the time of writing (January 2019).	C50

Annex 3: Generation Genome recommendations

Table 3 references the recommendations made from CMO's 'Generation Genome' paper.

Table 3 References to 'Generation Genome' recommendations.

Recommendation		Organisation
1	I recommend that DH establishes a new National Genomics Board, chaired by a minister. This would facilitate collaboration and ensure effective delivery of appropriate actions, with key priorities including: • Patient and Public Interest; • Genomic Research Coordination; • Industrial Development; • NHS England and Genomics England Partnership; • Regulation Development.	DHSC
6	I recommend that the National Screening Committee conducts a systematic evaluation of the opportunities offered by genomics for present and potential screening practices. These may be national, population-based programmes as well as cascade or individual. This should include evaluation of: • cost-effectiveness; • feasibility; • acceptability; • impact on uptake.	NSC
7	I recommend that NHS England, working with the National Screening Committee, ensures that the implementation of contingent NIPT is accompanied by an evaluation of the cost-effectiveness of universal NIPT testing for Down's syndrome and other indications. This should consider different assumptions of sequencing costs, including research on its uptake and cost savings from fetal anomaly screening elements that a NIPT programme would replace.	NHS England; NSC
9	I recommend that DH, building on the learning from the 100,000 Genomes Project, convenes a group to agree a national, simple, two-stage routine consent model, acceptable to patients, that allows re-contact for invitation to enrol in research studies and clinical trials. This group should include Genomics England, NHS	DHSC

Recommendation		Organisation
	England, Health Research Authority, academia, and civil society.	
10	I recommend that Genomics England, NHS England, and the Human Tissue Authority explore the feasibility of offering the opportunity to be enrolled in the 100,000 Genomes project to existing NHS patients, in relevant clinical trials, with stored tissue samples.	Genomics England; NHS England; HTA
11	I recommend that DH should ensure any future government Life Sciences Strategy provides funding for the digital infrastructure necessary to make the UK a great place to carry out clinical trials that embed genomics, maximising the potential for learning through reanalysis and appropriate pooling of genomic information.	DHSC
19	I recommend that Genomics England and NHS England should engage in an extensive public dialogue on the shared social contract between patient, public, clinicians and academics in relation to genomic medicine. This needs to be a collaborative exercise and build on the experiences of the 100,000 Genomes Project and NHS expertise in clinical genetics.	Genomics England; NHS England
22	Health Education England should continue the work of the Genomics Education Programme, developed as part of the 100,000 Genomes Project, and ensure that this continues to provide staff with relevant data science expertise for the NHS.	HEE