

SCHEDULE 2 – THE SERVICES

A. Service Specifications

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| Service Specification No: | 1648 |
| Service | DNA Nucleotide Excision Repair Disorders Service (all ages) |
| Commissioner Lead | |
| Provider Lead | The service specification is for adoption following completion of a provider selection process by April 2019 |

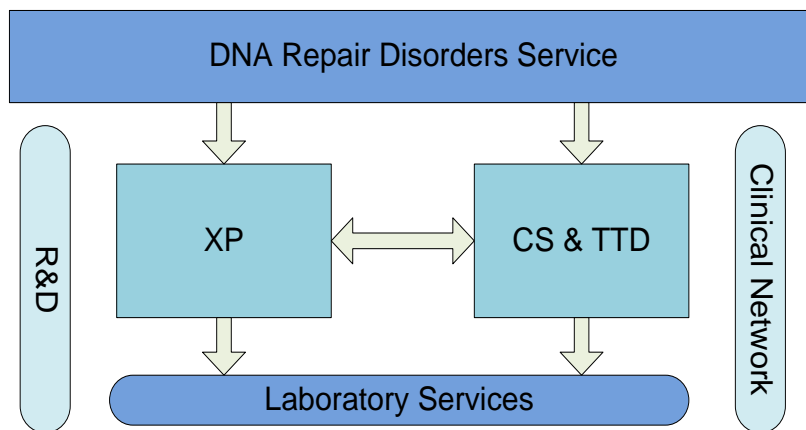
1. Scope

1.1 Prescribed specialised service

This service specification covers the provision of a DNA nucleotide excision repair disorders service.

1.2 Description

This service specification outlines the provision of a single, nationally integrated, multidisciplinary clinical and molecular diagnostic service to co-ordinate the care and management of patients with DNA nucleotide excision repair disorders. This highly specialist service, provided by a rare disease centre, will include provision for adults, children, and patients in transitioning between paediatric and adult services with Xeroderma Pigmentosa (XP), Cockayne Syndrome (CS) and Trichothiodystrophy (TTD).



1.3 How the service is differentiated from services falling within the responsibilities of other commissioners

Clinical Commissioning Groups (CCGs) commission the local care recommended in the management plans developed by the highly specialist DNA repair disorders service.

2. Care pathway and clinical dependencies

2.1 Care pathway

Please note that access to treatment will be guided by any applicable NHS England national clinical commissioning policies.

Aims and objectives of the service:

The objective of this service is to provide a high quality, multidisciplinary team service to patients with DNA repair disorders. This unique clinical service will establish a forum for translational research opportunities that would not otherwise exist and provide a vital mechanism for seamless transitional care for patients moving from paediatric into adult services.

The objectives are to:

- achieve uniformly high standards of care wherever patients are treated within a clinical network
- create a group of clinicians from key specialties with expertise and experience in treating patients with DNA repair disorders working together as a team to agree patient management
- provide a one-stop multidisciplinary team (MDT) clinic, reducing the cost and inconvenience of multiple attendances
- develop the experience, knowledge and skills of the MDT to ensure high quality sustainable service provision
- provide genotyping and DNA repair assay in all patients
- improve management of symptoms and pre-symptomatic surveillance of potential complications
- provide an exemplary and comprehensive service for all eligible referred patients with DNA repair disorders
- operate a rolling programme of clinical audit to test current practice and inform the evolution of care in DNA repair disorders
- provide care with a patient and family-centred focus to maximise the patient experience of care within the national service
- be seen as the leading clinical service and a source of expert advice for the diagnosis and management of DNA repair disorders within the NHS
- act as a beacon internationally of high standards and cutting edge care in DNA repair disorders
- contribute to raising standards of care outside the UK as well as in the NHS in the UK by collaborating with DNA repair disorder services and/or health professionals in other countries
- support local healthcare providers to manage patients with DNA repair disorders whenever it is clinically appropriate and safe to do so
- work with local hospitals to provide shared care for patients when appropriate to do so
- provide high quality information for patients, families and carers in appropriate and accessible formats
- have a Paediatric/Adult Clinical Nurse Specialist providing an outreach service (a) to support patients in their homes and (b) to coordinate care with patients' local specialists
- develop a high quality research programme in DNA repair disorders in translational research with demonstrable patient benefit as the sole objective.

The aims and objectives will be met by establishing the following service model

Comprehensive multidisciplinary clinics:

One-stop multidisciplinary clinics will take place over a one or two day period. Patients will be offered an annual review, tailored to their diagnosis and specific needs. The provider will aim to reduce non-attendance to below 5% at each clinic.

- A patient-centred model will be utilised; the patient remains in the consulting room and the specialists will go to the patient in rotation. This system helps to relax the patient and provides convenience for all parties. This is particularly helpful for patients with visual, cognitive and physical disabilities. The specialists will reconvene to discuss issues as they arise and form a management plan.
- If a patient chooses not to travel to be seen in the multidisciplinary clinic, or is unable to do so, advice and a detailed management plan will be developed in consultation with the local specialists. As part of the outreach service, the clinical nurse specialist will be able to visit the patient at home and provide appropriate input and advice.
- If necessary, patients may wish to travel on the day prior to the clinic and stay overnight in appropriate accommodation.
- The provider has a duty to cooperate with the commissioner in undertaking Equality Impact Assessments as a requirement of race, gender, sexual orientation, and religion and disability equality legislation. Providers require staff to attend mandatory training on equality and diversity and the facilities provided offer appropriate disabled access for patients, family and carers. When required the providers will use translators and printed information is available in multiple languages.

Patients will have access to several specialists at each visit. If a named specialist consultant is on leave, the department will provide cover if required. The specific diagnosis will determine which specialists are appropriate. These specialists will include:

| XP | CS & TTD | Extended MDT membership |
|---|---|--|
| <ul style="list-style-type: none"> • Consultant Dermatologist • Dermatological Surgeon • Consultant Paediatrician with a special interest in Neurology • Adult Consultant Neurologist • Consultant Ophthalmologist • Clinical Neuropsychologist • Consultant Clinical Geneticist • Clinical Nurse Specialists | <ul style="list-style-type: none"> • Consultant Clinical Geneticist • Consultant Dermatologist • Consultant Paediatric Neurologist • Consultant Paediatric Dentist • Ophthalmologist • Clinical Psychologist • Clinical Nurse Specialist | <ul style="list-style-type: none"> • Dietician • Consultant Endocrinologist • Optometrist • Medical Photography • Consultant Audiologist • Palliative Care |

- Care will be delivered working with the patient support groups (e.g. Amy and Friends for CS, and the XP Support Group for XP patients). They will play a pivotal role in providing a comprehensive service, providing an opportunity to deliver a unique blend of clinical and pastoral

care to patients. A patient liaison officer from the relevant support group will be present as far as is possible at clinic to provide support.

- Clinic Coordinators will have responsibility for coordinating the clinics, updating the patient database, inviting the patients to clinic, arranging their transport and overnight accommodation.
- At every multidisciplinary XP Clinic, Dermatology, Adult Neurology, Dermatological Surgery, Neuropsychology, Ophthalmology must be present: if the named consultant is on leave, their department must provide cover. The Clinical Geneticist arranges which XP clinics to attend with the Clinical Lead. The Paediatrician attends a minimum of 80% of the Paediatric XP clinics (counted over a 2 year period). All these named individuals must have job plans with sufficient time allocated to fulfil their roles.

Follow-up and planning: Part of the multidisciplinary assessment for DNA repair disorder patients will be to establish the nature of the neurological, dermatological, eye, and neuropsychological involvement and arrange a clinically appropriate follow-up plan, with the balance between local and specialist care depending on the type and severity of disease in each organ.

- Following attendance at the national centre a comprehensive, multidisciplinary letter of advice will be sent to the patient, General Practitioner (GP) and local paediatrician/consultant. The summary letter will provide details of the assessment by each speciality, the results of any investigations undertaken and a tailored management and follow-up plan.
- Liaison with local services will be paramount and an integral part of the patient's care pathway. The clinical nurse specialist will act as the key liaison between the national centre and the local teams, ensuring maintenance of minimum standards of care outlined in the disease management protocols and acting as a point of contact for the patients/families.
- Patients will be invited for annual review at the national service. However, if clinically appropriate they may access the required sub-speciality expertise locally to manage their condition with oversight from the national centre as required.

Transition: The provider will be responsible for both paediatric and adult services for DNA nucleotide excision repair disorders in order to ensure that transition from paediatric to adult services is seamless for patients. Dedicated transition clinics will be held in an appropriate environment and transition protocols developed to address the patients' changing needs.

End of life care: DNA nucleotide excision repair disorders are debilitating and life-limiting. They are associated with multi-system co-morbidities. As a national service, communication between the centre and local services is vital to ensure that patients are able to access appropriate palliative care services. The clinical nurse specialist liaison nursing team will provide regular support to the patient and their family during this period in conjunction with local services.

End of life care protocols will be developed by the service.

Laboratory diagnostic service:

A dedicated and UK Accreditation Service accredited molecular genetic laboratory will support the clinical service, providing the capability to molecularly confirm diagnoses, carrier test relatives and offer option of prenatal diagnosis when requested.

The laboratory service will provide:

- a Next Generation Sequencing (NGS) approach; thereby offering a comprehensive and robust

molecular service for all DNA nucleotide excision repair disorders

- complementation group analysis in XP, enabling disease sub-typing for prognostication
- antenatal testing including pre-implantation genetic diagnosis (PGD) where applicable including discussion about the availability of reproductive options as appropriate
- DNA repair assay on all patients
- opportunities for members of the laboratory staff to increase their knowledge and expertise in this area to enable succession planning and ensure a sustainable service with dedicated laboratory personnel.

Clinical network:

A network for this service will be developed by the national service to provide outreach support for patients at their local hospitals and in their home, school and work environments. The clinical nurse specialists will play a key role in managing the network and smoothing the transition between local and specialist care.

Support:

- The centre should have access to adequate continuous secretarial support and information technology systems to allow multidisciplinary clinic reports containing all reports and all results to be sent within an absolute maximum of 20 working days, and other clinic letters within 5 working days of the clinic.
- Administrative support should have sufficient time allocated in the job plan to fulfil the duties of the role. There should be adequate cover provided for any absence of the post holder. Each named Consultant/Specialist in each specialty area in the XP Service is responsible for maintaining an up-to-date data collection sheet and for completing the data collection sheet on each patient at each clinic review.
- Adequate and appropriate clinic facilities and space offering protection from ultraviolet (UV) light are available to allow all parts of the multidisciplinary service (adult and paediatric services and clinics) to run smoothly.
- Adequate and appropriate office facilities and space must be available in order that all administrative functions can be carried out, that the Nurse Outreach Service can run efficiently with all necessary estates infrastructure, and to support team members who are part of the extended MDT including Patient Support Group representatives when working in the clinic and with the service. There will be adequate office facilities to host any other meetings required for the smooth running of the service, and to host foreign and other patient representatives and health professionals visiting the clinic/service.

Research strategy:

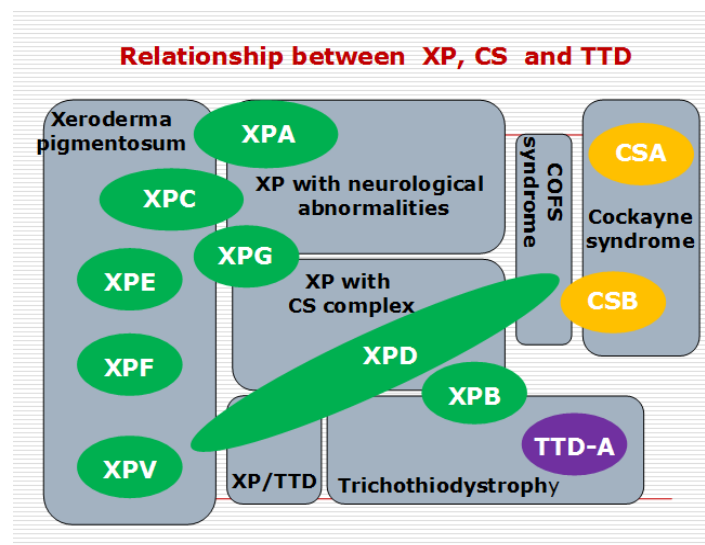
Clinicians with specialist expertise in DNA nucleotide excision repair disorders will be able to collate knowledge about the long-term natural history of these conditions in a systematic manner to aid in the comprehensive management of patients. Detailed knowledge of patient's clinical manifestations and their genetic mutations will be essential for tailoring emerging therapies.

Specialists participating in these clinics have established links with other research groups who are at the frontline of developing therapeutics strategies for DNA nucleotide excision repair disorders e.g. in Europe and the National Institute of Health in the USA. Patients will therefore have access to new therapeutic strategies being developed.

2.2 Interdependence with other services

- The DNA nucleotide excision repair disorder service providers, as leaders in the NHS for patient care in this area, will provide a direct source of advice and support to other clinicians looking after patients in the local setting.

- The national service will also provide education within the NHS to raise and maintain diagnostic awareness of DNA repair disorders and their management.
- Patients with DNA nucleotide excision repair disorders require input from many services including paediatrics, genetics, dermatology, ophthalmology, nephrology, neurology, audiology, endocrinology and paediatric dentistry. Experienced and specialised dermatology input is required to address the skin problems (increased photosensitivity), which cause significant morbidity especially in XP. Inefficient management of UV exposure protection from lack of expertise leads to unnecessary and avoidable complications. If skin and eye tumours are diagnosed late in XP the prognosis is worse and instigation of UV protection has a dramatic effect on reducing the incidence of tumours.
- A combined DNA nucleotide excision repair disorders service will benefit from economies of scale; resources and staffing can be shared because some of the needs of patients with XP, CS and TTD are the same. For example, there is considerable overlap in laboratory diagnostic services and investigations for these disorders and the development of a progressive neurological picture.
- Collating expertise will enable a streamlined approach to a comprehensive and tailored care pathway that will ensure sustainability of the service.
- The need for social worker support for families so they have access to local schemes is recognised and would need to be considered and signposted by the trust as far as possible.



3. Population covered and population needs

3.1 Population covered by this specification

NHS England commissions the service for the population of England. Commissioning on behalf of other devolved administrations is reviewed annually and a current list is available from NHS England commissioners.

Patients seen in the service will have laboratory proven diagnosis of a DNA nucleotide excision repair disorder or, if laboratory data is not available, a referral from a hospital consultant where the clinical diagnosis of a DNA nucleotide excision repair disorder needs to be excluded. Standard international diagnostic clinical criteria will apply. Patients who fall outside the spectrum of these disorders will not be seen.

The NHS England Standard Contract includes provision for the service to treat eligible patients from overseas under S2 and aligned referral arrangements. Providers are reimbursed for appropriately referred and recorded activity as part of this contract. Trusts performing procedures on patients outside of S2 arrangements and aligned referral arrangements will need to continue to make the financial arrangements directly with the governments involved, separately from their contract with NHS England.

3.2 Population needs

The three main disorders of DNA repair in this service are Xeroderma Pigmentosum (XP), Cockayne Syndrome (CS) and Trichothiodystrophy (TTD). All three conditions are very rare.

3.3 Expected significant future demographic changes

There are no significant changes to the patient group expected and the service would incorporate small activity growth year on year.

3.4 Evidence base

The service will provide a nationally integrated, cost effective, multidisciplinary clinical and molecular diagnostic service to co-ordinate care and management of patients with DNA nucleotide excision repair disorders. This is a cohort of patients with specific, complex and specialised needs who will benefit from a comprehensive, expert and patient focussed service. The underlying diseases are not curable and therefore the objective of this service and potential for improving health and quality of life is accurate, prompt diagnosis and good multidisciplinary care for the many different organ systems affected by the diseases.

NHS England has commissioned a service for XP since 2010 which is a disorder of DNA repair [previously A12/S (HSS)/b]. This service specification overwrites and expands this XP service specification and encompasses the other two DNA nucleotide excision repair disorders.

Xeroderma Pigmentosum (XP) is a rare, life-threatening, inherited multi-organ disorder. There are currently 80-100 patients in the UK with this condition. Inherited defects in the process of repairing ultraviolet-induced DNA damage result in severe sunburn-type reactions to daylight, skin cancers in exposed skin from early childhood, eye disease (keratitis, conjunctivitis, corneal scarring, eye tumours), and progressive neurological degeneration in 20-30% of patients. 45% of patients develop skin cancers (mean age of onset eight years), and 40% of patients develop eye problems (11% develop eye cancers: mean age of onset six years). Previously the mean lifespan was 32 years ([Bradford PT, et al. J Med Genet. 2011; 48:168-76](#)) however, with improved medical care most patients now survive beyond the age of 40 years. Most patients need long term medical care. In the coming years we expect to see a steady increase in the prevalence, as a result of better recognition of the disorder.

The disease is diagnosed with an enzyme assay. Molecular testing of DNA repair genes is having an increasing value for diagnosis as next generation technologies develop.

Cockayne syndrome (CS) is a rare inherited (autosomal recessive) disorder with an estimated prevalence of ~1 in 500,000 (<http://ghr.nlm.nih.gov/condition/cockayne-syndrome>). There are currently 86 known affected persons with CS located throughout the British Isles, with the majority living in England. The majority of patients are children.

CS is a debilitating and life-limiting multi-system neuroprogressive disorder. It is associated with severe intra-uterine and postnatal growth retardation, microcephaly, learning difficulties, sensorineural hearing loss, visual disability (retinopathy and cataracts), hypersensitivity to sunlight (photosensitivity), dental and renal problems, hypertension and neurological difficulties (joint contractures, poor balance, neuropathy). Progressive deterioration of vision, hearing and neurology leads to severe disability. The average age of

survival in affected children is 12 years, with some surviving into the second decade. The clinical picture in CS can be extremely variable, from a congenital onset at birth to a later onset, which makes the diagnosis and an accurate prognosis difficult.

Trichothiodystrophy (TTD) is a rare inherited (autosomal recessive) disorders with an estimated prevalence of 1 in a million in Europe (<http://ghr.nlm.nih.gov/condition/trichothiodystrophy>).. TTD is an ectodermal disorder associated with multi-system involvement. The clinical manifestations are variably seen and include sparse, sulphur-deficient hair, intellectual impairment, eye and dental abnormalities ichthyotic skin, small stature, bone anomalies and hypogonadism. Recurrent infections with a high mortality (a 20 fold increase below the age of 10 years) and maternal pregnancy complications are well recognised. Many patients exhibit photosensitivity.

Wilson B et al (2016): The Cockayne Syndrome Natural History (CoSyNH) study: clinical finding in 102 individuals and recommendations for care. *Genetics in Medicine* 18, (5) pp. 483-493

Nance MA, Berry SA. Cockayne syndrome: review of 140 cases. *Am J Med Genet.* 1992;42:68–84. [http://www.ncbi.nlm.nih.gov/books/NBK1342/Cockayne syndrome](http://www.ncbi.nlm.nih.gov/books/NBK1342/Cockayne_syndrome), Edward G Neilan <http://ghr.nlm.nih.gov/condition/trichothiodystrophy>

Faghri S, et al (2009). Trichothiodystrophy: a systematic review of 112 published cases characterises a wide spectrum of clinical manifestations. *J Med Genet.* 2008 Oct;45(10):609-21. doi: 10.1136/jmg.2008.058743. Epub 2008 Jun 25.

Moslehi R et al (2009). Adverse effects of trichothiodystrophy DNA repair and transcription gene disorder on human fetal development. *Clin Genet.* 2010 Apr;77(4):365-73. doi: 10.1111/j.1399-0004.2009.01336.x. Epub 2009 Dec 10.

4. Outcomes and applicable quality standards

4.1 Quality statement – aim of service

The aim is to provide a nationally integrated, cost effective, multidisciplinary clinical and molecular diagnostic service to co-ordinate care and management of patients with DNA nucleotide excision repair disorders. This is a cohort of patients with specific, complex and specialised needs, who will benefit from a comprehensive, expert and patient focussed service.

The service needs to be all-encompassing, of high quality and meet the criteria set out in the NHS Outcomes Framework Domains. Detailed outcomes for the service are provided in 4.2. Utilisation and development of existing laboratory services, information technology (IT) systems and clinical expertise will provide an economy of scale. The clinical service should establish a forum for translational research opportunities and be a mechanism for seamless transitional care for patients moving from paediatric into adult services.

NHS Outcomes Framework domains

| | | |
|----------|---|---|
| Domain 1 | Preventing people from dying prematurely | ✓ |
| Domain 2 | Enhancing quality of life for people with long-term conditions | ✓ |
| Domain 3 | Helping people to recover from episodes of ill-health or following injury | ✓ |

| | | |
|-----------------|---|---|
| Domain 4 | Ensuring people have a positive experience of care | ✓ |
| Domain 5 | Treating and caring for people in safe environment and protecting them from avoidable harm | ✓ |

4.2 Clinical outcomes:

| Number | Indicator | Data source | Outcome Framework domain | CQC key question |
|------------------------------|--|------------------|--------------------------|-----------------------------|
| Clinical outcomes | | | | |
| 101 | % of XP patients receiving support within 10 working days | DNA database | 1, 3, 4 | safe, effective, responsive |
| 102 | % of XP patients with UV filter films fitted to home, work, school and car windows | DNA database | 2, 3, 4, 5 | effective, caring |
| 103 | % of XP patients using visors, gloves, hats, eye cover when outside | DNA database | 2, 3, 4, 5 | effective, caring |
| 104 | % of XP patients using a UV meter | DNA database | 2, 3, 4, 5 | effective, caring |
| 105 | Mean annual number of sunburn episodes reported for XP patients | DNA database | 2, 3, 4 | effective, caring |
| 106 | skin cancer staging for XP patients | DNA database | 1 | safe effective, caring |
| 107 | eye cancer staging for XP patients | DNA database | 1 | safe effective, caring |
| 108 | skin cancer stage 1 for XP patients | DNA database | 1 | safe effective, caring |
| 109 | skin cancer stage 2 for XP patients | DNA database | 1 | safe effective, caring |
| 110 | skin cancer stage 3 for XP patients | DNA database | 1 | safe effective, caring |
| 111 | eye cancer stage 1 for XP patients | DNA database | 1 | safe effective, caring |
| 112 | eye cancer stage 2 for XP patients | DNA database | 1 | safe effective, caring |
| 113 | eye cancer stage 3 for XP patients | DNA database | 1 | safe effective, caring |
| 114 | Clinical trials | DNA database | 2, 3 | safe, effective |
| Patient experience | | | | |
| 201 | Patient feedback | Patient forum | 4 | caring, responsive |
| 202 | Positive patient feedback | Patient forum | 4 | caring, responsive |
| 203 | Patient information | DNA database | 4 | caring, responsive |
| Structure and process | | | | |
| 301 | Lead clinician | Self declaration | 2,3,5 | well-led |

| | | | | |
|-----|---------------------|------------------|------------|-------------------------------------|
| 302 | DNA service MDT | Self declaration | 1, 2, 3, 4 | safe, effective, caring |
| 303 | Laboratory services | Self declaration | 1, 3 | safe, effective |
| 304 | One stop clinics | Self declaration | 1, 3 | safe, effective |
| 306 | Transition clinics | Self declaration | 1, 2, 3, 4 | safe, effective, responsive |
| 307 | Clinical guidelines | Self declaration | 2, 4 | safe, effective, responsive |
| 308 | Clinical audit | Self declaration | 1, 2, 3, 4 | safe, effective, caring, responsive |

4.3 Commissioned providers are required to participate in annual quality assurance and collect and submit data to support the assessment of compliance with the service specification as set out in Schedule 4A-C

4.4 Applicable CQUIN goals are set out in Schedule 4D

To be agreed with the commissioner.

5. Applicable service standards

5.1 Applicable obligatory national standards

The following sets of guidance are followed:

- NICE guidance on Skin tumours including melanoma (issued 2010)
- Royal College of Physicians Guidance on long term neurological conditions (2008)

The service will be fully integrated into the trust's corporate and clinical governance arrangements and will comply fully with the clinical negligence scheme for trusts and Care Quality Commission (CQC) requirements in terms of quality and governance.

The service will ensure that:

- regular meetings take place with patient representatives
- all practitioners participate in continuous professional development and networking
- patient outcome data is recorded and audited across the service.

The commissioners and service will conduct a formal Joint Service Review annually. All centres must participate in the national audit commissioned by NHS England. Audit meetings should address:

- clinical performance and outcome
- process-related indicators, e.g. efficiency of the assessment process, prescribing policy, bed provision and occupancy, outpatient follow up etc.
- stakeholder satisfaction, including feedback from patients, their families, referring surgeon and GPs

5.2 Other applicable national standards to be met by commissioned providers

- NICE guidance on skin tumours including melanoma (issued 2010)
- Royal College of Physicians guidance on long term neurological conditions (2008)

5.3 Other applicable local standards

(none)

6. Designated providers (if applicable)

It is expected that there will be a single service provider.

7. Abbreviations and acronyms explained

The following abbreviations and acronyms have been used in this document:

CCGs - Clinical Commissioning Groups

CQC - Care Quality Commission

CQUIN - Commissioning for Quality and Innovation

CS - Cockayne syndrome

GP - General practitioner

IT - Information technology

MDT - Multidisciplinary team

NGS - Next generation sequencing

PGD - Pre-implantation genetic diagnosis

TTD - Trichothiodystrophy

UV - Ultraviolet (light)

XP - Xeroderma Pigmentosa

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