Specific Operationnal Criteria - Cutaneous Diseases related to DNA Repair Disorders

The requested information will be used to define the specific criteria for our project proposal for a European Reference Network (ERN) for Rare and Undiagnosed Skin Disorders. Please note that, each health care provider member of our ERN will have to fulfil these criteria. These criteria have to be realistic/reasonable while ensuring a high level patient management. These criteria have to be based on the evidence and consensus of the scientific, technical and professional community.

NB: A sample of healthcare providers will be selected for on-site audits to validate the information.

Rare Diseases(s)	Short description of the rare disease	Code/ ICD/ Orphacode	Epidemiology	Incidence	Prevalence
1. xeroderma pigmentosum	genetically heterogenerous autosomal recessive disorder with increased sensitivity to ultraviolet (UV) irradiation and increased risk of skin cancer resulting from a defect in DNA repair. XPC is the most common form of XP in the white population, accounting for over a third of all cases in this group.		1/1000000 births in Europe	1:1000000	unknown

2.trichothiodystrophy	genetically heterogenerous autosomal recessive disorder in which patients have brittle, sulfur-deficient hair that displays a diagnostic alternating light and dark banding pattern, called 'tiger tail banding,' under polarizing microscopy. TTD patients display a wide variety of clinical features, including cutaneous, neurologic, and growth abnormalities. Common additional clinical features are ichthyosis, intellectual/developmental disabilities, decreased fertility, abnormal characteristics at birth, ocular abnormalities, short stature, and infections. There are both photosensitive and nonphotosensitive forms of the disorder. TTD patients have not been reported to have a predisposition to cancer		1/1000000 births in Europe	1/1000000	unknown
3. Cockayne syndrome	genetically heterogeneous autosomal recessive syndrome characterized by abnormal and slow growth and development that becomes evident within the first few years after birth, cutaneous photosensitivity, thin, dry hair, a progeroid appearance, progressive pigmentary retinopathy, sensorineural hearing loss, dental caries. Patients often show disproportionately long limbs with large hands and feet, and flexion contractures of joints, delayed neural development and severe progressive neurologic degeneration resulting in mental retardation. Death occurs usually before puberty, with however no significant increase in skin cancer or infection.		1/1000000 births in Europe	1/1000000	unknown

Rare Diseases(s)	Specific challenges associated with the recognition of the condition	Specific challenges associated with the diagnosis	Specific challenges associated with the treatment	Specific challenges associated with care of these patients over their
1.xeroderma pigmentosum	diagnosis easy in at risk families but more difficult until specific skin features appear in families without known risk	need of molecular diagnosis	no specific treatment except photoprotection and treatment of skin cancers	avoidance of UV, need specific equipment during daytime, major quality of life impact, difficulties in all age groups, better overall prognosis since implementation of strict photoprotection since infancy
2.trichothiodystrophy	difficult clinical diagnosis when hair symptoms not prominent in the context of a large number of presenting features in particular mental retardation	need of trichological screening, biochemistry of hair, and molecular diagnosis	supportive care, no treatment	dominated by mental retardation and specific care according to handicap (variable clinical presentation)
3.Cockayne syndrome	difficult clinical diagnosis of a delayed development and skin, eye, skelettal, neurological symptoms	need of molecular diagnosis	supportive care, no treatment	progressive neurodegeneration, mental and physical disabilities

Rare Diseases(s)	Key Diagnostic Tests	Key Treatment, Resources or Procedures
1.xeroderma pigmentosum	molecular diagnosis	photoprotective devices, dermatological treatment
2.trichothiodystrophy	hair examination, molecular diagnosis	supportive care and education
3.Cockayne syndrome	molecular diagnosis	supportive care and education

Please state the minimum/optimum thresholds that Healthcare Providers within the network will need to meet to maintain competence and expertise.					
Rare Diseases(s)	Minimum Number of patients treated per year at each HCP			Minimum Number of new	
	Adults	Paediatric*	Rationale for the threshold	Adults	Paediatric*
1.xeroderma pigmentosum	2 patient	3 patients	very rare disease	0	0 to 1

2.trichothiodystrophy	?	1 patients	very rare disease and management shared with other specialties. Outcome in adulthood variable	0	0 to 1
3. Cockayne syndrome	?	1 patient	very rare disease and management shared with other specialties. Early death	0	0 to 1

Please list the necessary human resources and the profesional qualifications essential to the quality of patient care within the Network's area of				
Rare Diseases(s)	**Health Care Professional (type)**	**Training & Qualifications**	**Minimun of number of procedures per patient per year**	**Rationale**
1.xeroderma pigmentosum	dermatologist/ pediatric dermatologist; ophthalmologist; specialised nurse	treatment of skin and OPH complications	not specific to XP	acceleration of skin cancer incidence, no specific care except for limiting large excisions
2.trichothiodystrophy	dermatologist/ pediatric dermatologist trained hair diagnosis	diagnosis of rare diseases	clinics with a specialization in rare skin disorders and clinical genetics	need to know a large repertoire of disorders to consider this diagnosis
3.Cockayne syndrome	pediatrician, pediatric dermatologist, clinical geneticist, or mixed clinics (best)	diagnosis of rare diseases	clinics with a specialization in rare skin disorders and clinical genetics	need to know a large repertoire of disorders to consider this diagnosis

Please list the specialised equipment, infrastructure, and information technology required to support the rare or complex disease(s), condition(s) or highly specialised intervention(s) and describe the importance of each					
Rare Diseases(s)	**Specialised equipment, infrastructure, and information technology**	**Threshold**	**Rationale**		
1. xeroderma pigmentosum	center with clinical expertise and access to molecular diagnosis; a room with no UV emitting lamp for examination and surgery; information about UV exposure (patient's advocacies very active to deliver in addition to clinical centres		UV protection at the centre of care		

2.trichothiodystrophy	center with clinical expertise and access to molecular diagnosis; hair diagnosis (microscope and polarised light); importance of multidisciplinary approach		patients rarely followed only for skin problems
3.Cockayne syndrome	center with clinical expertise and access to molecular diagnosis; importance of multidiciplinary approach		patients rarely followed only for skin problems

Please provide a summary explaining the approach or plans your group will undertake to produce good practice guidelines		
For XP, guidelines exist already at several national levels, and harmonization is necessary at the EU level. There is a need to standardize severity grading of skin lesions for future clinical trials. Ressources concerning molecular diagnosis need to be shared at the EU level. NGS is becoming available and will speed up diagnosis of difficult cases. Quality control needed for molecular diagnosis. 2. for TTD and CS, in addition to XP, a EU registry is the first step to implement, as well as an interdisciplinary board to produce good practice guidelines and implement outcome measures and quality controls. The NGS panels should be the same for all 3 diseases and non listed clinical variants.		