



UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES EUROPEAN UNION OF MEDICAL SPECIALISTS

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International non-profit organisation

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Syllabus for residents and trainees in Rare and Undiagnosed Diseases

This is a usual syllabus, an outlined summary of major and specific topics to be covered in a training course of a trainee. The goal of the syllabus is to ensure a fair and impartial working material as a connection between the instructor and the trainee. The syllabus is not a road map of the course, nor an organization/direction relaying the instructors' teaching policy to the trainees, so the syllabus is not a learning guide. Instead, the syllabus is a supporting reference material with priorities of training. However, it should be taken as a flexible material. It can differ between training institutions. Since the major pillars of the rare disease ETR rely primarily on internal medicine, neurology, pediatrics and medical genetics, it is strongly recommended to use the UEMS approved ETRs for these specialties as additional training material.

Domain 1: Basics

1.1 Rare disease terms, items, definitions

- 1.1.1 Rare disease definitions and rare disease basics in medical specialties
- 1.1.2 Causes of rare diseases
- 1.1.3 Rare disease clinical research networks
- 1.1.4 ORPHANET/ORPHACODE
- 1.1.5 EURODIS (Voice of rare disease patients)
- 1.1.6 National rare disease policies
- 1.1.7 International rare disease policies
- 1.1.8 Living with rare diseases
- 1.1.9 Rare disease helplines
- 1.1.10 Specialized social servers
- 1.1.11 Therapeutic recreational programs
- 1.1.12 Adapted housing and research centres

Domain 2: Clinical knowledge

2.1 Medical Records in Rare Diseases

- 2.1.1 Review medical records and identify information sources including databases and literature searches

2.2 Taking a detailed medical and family history and pedigree construction and interpretation

- 2.2.1 To analyse a clinical history in a relevant, succinct and logical manner
- 2.2.2 Use interpreters and advocates appropriately
- 2.2.3 Manages alternative and conflicting views from family, carers, friends and members of the multi-professional team
- 2.2.4 Assimilates history from the available information from patient and other sources including members of the multi-professional team
- 2.2.5 Recognises and interprets appropriately the use of nonverbal communication from patients and carers

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2.3 Diagnosis, investigation and management of individuals with rare inherited diseases and their families

2.3.1 Examination

- 2.3.1.1 Perform a reliable and appropriate examination to elicit relevant signs of genetic disease
- 2.3.1.2 Perform examination appropriately in situations involving cultural sensitivity
- 2.3.1.3 Understand when additional specialist examination is required
- 2.3.1.4 Recognises the possibility of deliberate harm (both self-harm and harm by others) in vulnerable patients and report to appropriate agencies

2.3.2 Involvement of non-family members in process

- 2.3.2.1 Role of patient advocacy groups
- 2.3.2.2 Role of networks (scientific, patient oriented)

2.3.3 Diagnosis and Management

- 2.3.3.1 Present disease information to a patient in a sensitive and understanding manner
- 2.3.3.2 Use computerized genetic databases and registers for information retrieval
- 2.3.3.3 Present undiagnosed cases to colleagues, including dysmorphology club meetings
- 2.3.3.4 Clearly and openly explain management options
- 2.3.3.5 Record concisely, accurately, confidentially and legibly the appropriate elements of the history, examination, results of investigations, differential diagnosis and management plan

2.3.4 European Reference Networks (ERNs)

- 2.3.4.1 ERNs, structure, function, mission
- 2.3.4.2 CPMS as a diagnostic tool

2.3.5 Decision Making

- 2.3.5.1 Interpret clinical features, their reliability and relevance to clinical scenarios including recognition of the breadth of presentation of common disorders
- 2.3.5.2 Incorporates an understanding of the psychological and social elements of clinical scenarios into decision making
- 2.3.5.3 Construct a concise and applicable problem list using available information
- 2.3.5.4 Construct an appropriate management plan in conjunction with the patient, carers and other members of the clinical team and communicate this effectively to the patient, parents and carers securing their agreement to the course of action
- 2.3.5.5 Define the relevance of an estimated risk of a future event to an individual patient
- 2.3.5.6 Use risk calculators appropriately
- 2.3.5.7 Apply quantitative data of risks and benefits of screening and therapeutic intervention to an individual patient
- 2.3.5.8 Search and comprehend medical literature to guide reasoning
- 2.3.5.9 Generate hypothesis within context of clinical likelihood
- 2.3.5.10 Test, refine and verify hypotheses
- 2.3.5.11 Develop problem list and action plan

2.3.6 Ability to take samples for genetic analysis

- 2.3.6.1 Phlebotomy from adults and children, including those with special needs
- 2.3.6.2 Hair Root Extraction
- 2.3.6.3 Skin biopsy
- 2.3.6.4 Collection of other samples, such as buccal smears, urine samples, etc.

2.3.7 Clinical Photography

- 2.3.7.1 Demonstrate ability to take photographs of sufficient quality for clinical use
- 2.3.7.2 Use of digital photography and storage of data

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2.4 Therapeutic aspects and emerging therapies of genetic diseases

- 2.4.1 Prescribe and oversee enzyme replacement therapies for applicable disorders, including lysosomal storage disorders within a multidisciplinary clinical team consensus
- 2.4.2 Prescribe other repurposed drugs to specific genetic condition (e.g., losartan) within a multidisciplinary clinical team consensus
- 2.4.3 Develop a management strategy, including preventative surgery, for men and women with hereditary cancer

2.5 Risk assessment and role in genetic testing

- 2.5.1 Calculate genetic risk in single gene disorders by hand
- 2.5.2 Calculate genetic risk by use of a computer programme

2.6 Paediatric genetics including training in Dysmorphology (knowledge of common dysmorphic syndromes, their aetiology and the use of dysmorphology databases) and investigation of learning and intellectual disability in children

- 2.6.1 Be able to take a relevant history, and perform an appropriate examination, obtain illustrative photographs
- 2.6.2 Have a rational approach to investigation of children with delayed development and/or dysmorphic syndromes
- 2.6.3 Formulate differential diagnoses of unknown syndromes. Utilise journals and databases used in syndrome identification
- 2.6.4 Cultivate critical assessment of database information and case reports to identify uncertainty and subjectivity in syndrome diagnosis
- 2.6.5 Be able to provide a diagnostic service within a multidisciplinary clinical team
- 2.6.6 Present and discuss cases with colleagues

2.7 Adult genetics to include knowledge of late onset disorders and disorders with a significant genetic component presenting in adult life (including predictive testing)

- 2.7.1 Be able to take a relevant history, perform an appropriate examination and formulate clinical diagnoses
- 2.7.2 Be able to assess patients and families affected by genetic conditions
- 2.7.3 Judge when it is necessary to sustain supportive relationships with patients with chronic disease
- 2.7.4 Be able to discuss reproductive options (AID, ICSI, IVF, pre-implantation diagnosis) with the patient and their partner in a sensitive manner
- 2.7.5 Be able to discuss and formulate integrated care pathways and management plans with individuals/families
- 2.7.6 Verify diagnoses from old hospital records

2.8 Prenatal Genetics and knowledge about effects of teratogens in foetal development

- 2.8.1 Interpret family history data
- 2.8.2 Provide genetic advice and organize testing for women who may undergo preimplantation or prenatal diagnosis
- 2.8.3 Formulate differential diagnoses and assess prognosis in collaboration with the foetal medicine team
- 2.8.4 Assess risk to foetus when pregnancies are exposed to hazards such as congenital infections, alcohol, ionising irradiation or drugs
- 2.8.5 Assess clinical significance of chromosome, DNA and foetal imaging in the context of foetal abnormality
- 2.8.6 Evaluate foetal post-mortem findings
- 2.8.7 Interpret the reports of non-invasive prenatal testing (NIPT)

2.9 Genetic screening programmes

- 2.9.1 Team-working with database managers, genetic associates and nurse specialists in:
 - 2.9.1.1 ‘Cascade screening’ and provision of genetic services for extended families with common single gene disorders (cystic fibrosis, Xp21 muscular dystrophy, fragile X syndrome, Huntington’s disease)
 - 2.9.1.2 Family based screening for individuals at high risk of developing cancer
 - 2.9.1.3 Contribute to the maintenance of departmental genetic registry systems
 - 2.9.1.4 Be able to explain the benefits and consequences of screening programmes

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2.10 Examination of paediatric and adult patients, knowledge of dysmorphic signs, and main neurologic signs

2.10.1 Physical examination, body measurements and review of medical information

2.11 Gene therapy and its current and future applications

2.11.1 Be able to discuss the pros and cons of gene therapy in relation to a specific disorder and suggest clinical trials, if appropriate

2.12 Common diseases with a genetic component and oligo-/polygenic disorders

2.12.1 Distinguish between classical Mendelian and oligogenic inheritance and be able to calculate the appropriate recurrence risk

2.12.2 Be able to recognize and counsel patients with a strong genetic component

2.13 General knowledge base from UEMS specialities

Allergology
Anaesthesiology
Cardiology
Cardiothoracic Surgery
Connective Tissue Genetics
Dermatology and Venereology
Emergency Medicine
Endocrinology
Gastroenterology
Genetics of Craniofacial Anomalies and Ear Nose and Throat disorders
Genetics of Immunological and Auto-inflammatory Diseases
Geriatrics
Gynaecology and Obstetrics
Haematology
Hepatology
Hereditary metabolic disorders
Infectious Diseases
Internal Medicine
Laboratory Medicine / Medical Biopathology
Malformation, developmental anomalies and rare intellectual disabilities
Medical Genetics
Medical Microbiology
Medical Oncology
Multi-systemic vascular diseases
Nephrology
Neurogenetics
Neurology
Neurosurgery
Occupational Medicine
Oncology
Ophthalmology
Oro-Maxillo-Facial Surgery
Orthopaedics
Traumatology
Otorhinolaryngology
Paediatrics
Pneumology
Prenatal and Reproductive
Pulmonology
Psychiatry
Public Health Medicine
Radiology

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Radiation Oncology and Radiotherapy
Rheumatology
Skeletal Disorders
Surgery
Urology/ Urogenital

2.14 List¹ of comprehensive Entrustable Professional Activities (EPAs)²

- 2.14.1 Evaluate and manage a new medical condition in an ambulatory patient and coordinate care between healthcare providers across multiple care settings
- 2.14.2 Manage the care of patients with rare medical conditions across multiple care settings
- 2.14.3 Manage the care of patients with complex medical conditions, and/or comorbidities, across multiple care settings
- 2.14.4 Manage transition of care for adult patients transferring to another care setting
- 2.14.5 Manage transition of care for young patients transferring from pediatric to adult services
- 2.14.6 Provide medical consultation to nonmedical specialties
- 2.14.7 Lead a family meeting to discuss serious news (bad news, end of life care) with a patient and/or family and other health providers
- 2.14.8 Obtain initial history, perform physical examination, and formulate a management plan for a new ambulatory patient in continuing care
- 2.14.9 Manage the care of patients with chronic conditions across multiple care settings
- 2.14.10 Access medical information to provide evidence-based care
- 2.14.11 Facilitate the understanding of patients, their families, and members of the multidisciplinary team
- 2.14.12 Recognize and diagnose common nonmedical conditions (i.e., surgical, neurological, dermatologic, psychiatric etc.) and refer appropriately to other specialty care
- 2.14.13 Diagnose and comanage patients with complex conditions needing other specialty care (inpatient or outpatient)
- 2.14.14 Organize and maintain information and knowledge through medical practice to improve personal development when delivering care and educating others (journal club, etc.)
- 2.14.15 Recognize when palliative care is needed and liaise with palliative care specialists
- 2.14.16 Counsel patients appropriately
- 2.14.17 Advocate for individual patients by representing them, supporting them and working for them
- 2.14.18 Improve patient safety
- 2.14.19 Provide age appropriate screening and preventative care
- 2.14.20 Identify and address any need for quality improvement in a clinical setting
- 2.14.21 Improve the quality and safety of healthcare at both individual and systems levels
- 2.14.22 Provide telephone management for an ambulatory rare disease patient
- 2.14.23 Provide care to nonnative speakers in an inpatient or outpatient setting through the use of appropriate translation services
- 2.14.24 Develop and implement a management plan based on review of outcome data for ambulatory patient population
- 2.14.25 Provide inpatient and outpatient care for patients with difficulty in accessing appropriate healthcare; advocate for individual patients where needed
- 2.14.26 Participate in an in-hospital cardiopulmonary resuscitation
- 2.14.27 Perform common procedures in internal medicine (lumbar puncture, thoracentesis, central line insertion, joint aspiration)

¹ Adopted with revisions from Karen. E. Hauer, Jeffrey Kohlwes, Patricia Cornett, Harry Hollander, Olle ten Cate, Sumant R. Ranji, Krishan Soni, William Iobst, and Patricia O'Sullivan (2013) Identifying Entrustable Professional Activities in Internal Medicine Training. Journal of Graduate Medical Education: March 2013, Vol. 5, No. 1, pp. 54-59 and the Alliance for Academic Internal Medicine. Internal Medicine End of training EPAs, 2012

² Definition: An EPA is 'a critical part of professional work that can be identified as a **unit** to be **entrusted** to a trainee once sufficient competence has been reached'. An EPA goes a level higher than the traditional 4⁺ level of competence which is the 'independence competency'. The key factor is **Entrustment**. The trainee is not only capable of tackling the particular procedures or units independently, but he can be **trusted** to do this by his tutors.

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- 2.14.28 Undertake a research project (e.g., a degree or diploma, quality improvement, educational opportunity, other)
- 2.14.29 Develop the practice of lifelong learning
- 2.14.30 Demonstrate professional behavior at all time

Domain 3: Detailed and specific Topics

3.1 Detailed Topics

- 3.1.1 Applied pharmacology
 - 3.1.1.1 Drug side effects
 - 3.1.1.2 Pharmacovigilance activity
 - 3.1.1.3 Pharmacogenomics in drug action
 - 3.1.1.4 Pharmacotoxicology
 - 3.1.1.5 Side effects, adverse effects
- 3.1.2 Cancer
 - 3.1.2.1 Take a relevant history, perform an appropriate examination and undertake risk estimation using a variety of methods
 - 3.1.2.2 Use of cancer registers and other sources to verify diagnoses
 - 3.1.2.3 Use disease registers to support follow-up of affected and at-risk patients
 - 3.1.2.4 Assessment of screening protocols for at-risk relatives
 - 3.1.2.5 Identify at-risk patients and relatives who are eligible to participate in trials of cancer prevention strategies
 - 3.1.2.6 Rare cancers; differences and similarities with rare diseases. Types (classification: Pediatric cancers, Hematologic rare neoplasms; Sarcomas; Rare thoracic cancers; Neuroendocrine tumors; Head & neck cancers; Central nervous system tumors; Rare female genital cancers; Rare urological and male genital tumors; Endocrine gland tumors; Digestive rare cancers; Rare skin cancers & non-cutaneous melanoma)
- 3.1.3 Cardiovascular diseases
 - 3.1.3.1 Relevant history, perform an appropriate examination
 - 3.1.3.2 Work with bereaved families following sudden adult death
 - 3.1.3.3 Rare variants in common polygenic diseases
 - 3.1.3.4 Assessment of screening protocols for at-risk relatives
 - 3.1.3.5 Coordinate diagnostic and predictive genetic testing in ICC families
 - 3.1.3.6 Identify at-risk patients/trios eligible to participate in prevention strategies (e.g., therapeutic trials)
- 3.1.4 Communicable diseases
 - 3.1.4.1 Basics in microbiology
 - 3.1.4.2 Rare infectious diseases
 - 3.1.4.3 Travellers, migrants and their significance in the spread of communicable diseases
 - 3.1.4.4 Diagnostic features
- 3.1.5 Connective tissue diseases
 - 3.1.5.1 Conduct a physical examination appropriate for evaluation of an individual with a suspected connective tissue disorder, including appropriate body measurements (arm span, upper/lower segment ratios, Beighton score, arachnodactyly, hindfoot valgus, pes planus, pectoral abnormalities, etc.)
 - 3.1.5.2 Formulate a differential diagnosis for a patient with joint laxity
 - 3.1.5.3 Formulate a differential diagnosis for a patient with Marfanoid habitus
 - 3.1.5.4 Formulate a differential diagnosis for a patient with aortic dilatation using family history, medical history, and physical examination
 - 3.1.5.5 Apply diagnostic criteria to establish a diagnosis of Loeys-Dietz syndrome, including use of imaging (such as evidence of vascular tortuosity)
 - 3.1.5.6 Establish the specific type of EDS based on diagnostic criteria
 - 3.1.5.7 Apply clinical and laboratory criteria to establish a diagnosis of Stickler syndrome

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- 3.1.6 Craniofacial Anomalies and Ear, Nose and Throat disorders
 - 3.1.6.1 Differential diagnosis for craniofacial Anomalies and ear nose and throat disorders
 - 3.1.6.2 Differential diagnosis in new-borns identified with congenital deafness either through new-borns screening or clinically
 - 3.1.6.3 Interpret audiologic tests and distinguish different patterns of hearing impairment, including sensorineural and conductive
 - 3.1.6.4 Management plan for a child or an adult with congenital or progressive hearing impairment
- 3.1.7 Dermatological Diseases
 - 3.1.7.1 Formulate a differential diagnosis for a patient with an ichthyosiform disorder
 - 3.1.7.2 Recognize the features of skin fragility and blistering associated with epidermolysis bullosa
 - 3.1.7.3 Differential diagnosis for a patient with abnormal ectodermal structures (hair, teeth, nails, sweat glands)
 - 3.1.7.4 Differential diagnosis for a patient with premature aging, photosensitivity, vascular lesions or multiple cutaneous neoplasms or hamartomas
 - 3.1.7.5 Order appropriate genetic testing for suspected genodermatoses
 - 3.1.7.6 Cutaneous features that are associated with multisystem disorders
 - 3.1.7.7 Formulate a differential diagnosis for a patient with porphyria
 - 3.1.7.8 Formulate a differential diagnosis for a patient with Morphea
 - 3.1.7.9 Formulate a differential diagnosis for a patient with Incontinentia pigmenti
 - 3.1.7.10 Formulate a differential diagnosis for a patient with Ehlers-Danlos syndrome
 - 3.1.7.11 Formulate a differential diagnosis for a patient with Cutis laxa
 - 3.1.7.12 Formulate a differential diagnosis for a patient with Neurofibromatosis
 - 3.1.7.13 Formulate a differential diagnosis for a patient with Tuberous sclerosis
 - 3.1.7.14 Formulate a differential diagnosis for a patient with Autoinflammatory syndromes
 - 3.1.7.15 Formulate a differential diagnosis for a patient with Darier's disease
 - 3.1.7.16 Formulate a differential diagnosis for a patient with Hailey-Hailey disease
 - 3.1.7.17 Formulate a differential diagnosis for a patient with Xeroderma pigmentosum
 - 3.1.7.18 Formulate a differential diagnosis for a patient with Pseudoxanthoma elasticum
 - 3.1.7.19 Formulate a differential diagnosis for a patient with Cutaneous paraneoplastic disorders
 - 3.1.7.20 Formulate a differential diagnosis for a patient with Neurocutaneous melanosis and giant melanocytic naevi
- 3.1.8 Diseases of malformation, developmental anomalies and rare intellectual disabilities
 - 3.1.8.1 Determine if a congenital anomaly represents a malformation, deformation, disruption, or dysplasia
 - 3.1.8.2 Difference between a syndrome, sequence, and association
 - 3.1.8.3 Congenital anomalies in terms of dysfunction of normal development, both at the level of the embryo and at the level of cellular mechanisms of morphogenesis
 - 3.1.8.4 Explain how foetal exposures/environment can adversely affect foetal growth and/or development
 - 3.1.8.5 Explain how prenatal studies can facilitate diagnostic evaluation
 - 3.1.8.6 Developmental milestones and growth parameters and recognize patterns of abnormal development
 - 3.1.8.7 Differential diagnosis and testing strategy for a patient with one or more major anomalies
 - 3.1.8.8 Specific patterns of dysmorphic features that allow for clinical diagnosis of recognizable genetic conditions
 - 3.1.8.9 Differential diagnosis for a patient with hypotonia and dysmorphic features
 - 3.1.8.10 Differential diagnosis for a patient with disordered growth
 - 3.1.8.11 Differential diagnosis for a patient with autism and dysmorphic features
 - 3.1.8.12 Apply diagnostic criteria to establish diagnosis of congenital anomaly syndromes
- 3.1.9 Endocrine diseases
 - 3.1.9.1 Formulate a differential for a child with short stature
 - 3.1.9.2 Evaluate a child with ambiguous genitalia, and formulate differential diagnosis
 - 3.1.9.3 Recognize Albright's hereditary osteodystrophy
 - 3.1.9.4 Counsel families with a child with 21-hydroxylase deficiency and adults with infertility, including Klinefelter syndrome, mosaic Turner syndrome, and androgen insensitivity syndrome.
 - 3.1.9.5 Formulate a differential diagnosis for sex reversal
 - 3.1.9.6 Counsel families with multiple endocrine neoplasia (MEN) I or II
 - 3.1.9.7 Evaluate the child with thyroid abnormalities and hearing loss

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- 3.1.10 Gastrointestinal diseases
 - 3.1.10.1 A differential diagnosis for congenital anomalies such as intestinal aganglionosis, pyloric stenosis, intestinal malrotation, etc.
 - 3.1.10.2 A differential diagnosis for patients with hereditary pancreatitis
 - 3.1.10.3 Recognize the need for a cancer control plan for extra intestinal cancers in polyposis syndromes (e.g., breast cancer in Peutz-Jeghers syndrome)
- 3.1.11 Gynaecological and Obstetric Diseases
 - 3.1.11.1 Stages of embryonic development and their relationship to teratogenic windows in the context of maternal teratogens such as alcohol, medications, or viral exposures
 - 3.1.11.2 Range of normal variation in foetal ultrasound images, the associations of normal variants with and the limitations of ultrasound as a screening modality
 - 3.1.11.3 Counsel and initiate the appropriate prenatal genetic tests when a structural malformation and/or growth abnormality is identified by foetal ultrasound
- 3.1.12 Hematological diseases
 - 3.1.12.1 Fanconi anemia
 - 3.1.12.2 Genetic causes of familial neutropenia syndromes (e.g., cyclic or severe congenital neutropenia, and Shwachman-Diamond syndrome), and disorders of neutrophil function (e.g., chronic granulomatous disease)
 - 3.1.12.3 Differential diagnosis for genetic red cell membrane disorders such as hereditary spherocytosis
 - 3.1.12.4 Diagnose and counsel patients with sickle cell trait, beta thalassemia trait, and the various forms of alpha thalassemia trait
 - 3.1.12.5 Plan laboratory assessments for pregnant women with microcytic anemia
 - 3.1.12.6 Counsel families with hemoglobinopathy
- 3.1.13 Hepatic diseases
 - 3.1.13.1 Differential diagnosis for patients with biliary atresia or arteriohepatic dysplasia
 - 3.1.13.2 Families with hepatic disorders
- 3.1.14 Immunological and auto-inflammatory diseases
 - 3.1.14.1 A differential diagnosis for a child with severe combined immune deficiency
 - 3.1.14.2 A differential diagnosis for a patient with hypogammaglobulinemia
 - 3.1.14.3 A differential diagnosis for a patient with chronic granulomatous disease
 - 3.1.14.4 Signs of hereditary angioedema
 - 3.1.14.5 Diagnosis for an adult with auto-inflammatory disease
- 3.1.15 Inherited metabolic diseases
 - 3.1.15.1 Family history data that suggest familial metabolic disease
 - 3.1.15.2 Clinical signs in affected individuals
 - 3.1.15.3 Be able to draw up a differential diagnosis and institute appropriate genetic testing
 - 3.1.15.4 Assessment of symptoms and signs in patients at risk of metabolic disorders
 - 3.1.15.5 Make timely, appropriate referrals to other specialists
 - 3.1.15.6 Identify at-risk patients and relatives who are eligible to therapeutic and preventional strategies
- 3.1.16 Multi-systemic vascular diseases
 - 3.1.16.1 Formulate a differential diagnosis for multi-systemic vascular diseases
- 3.1.17 Nephrological diseases
 - 3.1.17.1 Provide genetic counselling for an individual who has or is at risk for infantile or adult polycystic kidney disease
 - 3.1.17.2 Genetic aetiologies that contribute to nephrotic and renal tubular disorders
 - 3.1.17.3 Differential diagnosis between Alport syndrome and other renal disorders
 - 3.1.17.4 Apply diagnostic criteria to establish diagnosis of disorders including Bardet-Biedl syndrome, tuberous sclerosis complex, von Hippel-Lindau syndrome, Meckel syndrome, Zellweger syndrome
- 3.1.18 Neurodiseases and neuromuscular diseases
 - 3.1.18.1 Recognise family history data that suggest familial neurological disease

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- 3.1.18.2 Clinical signs in affected individuals
- 3.1.18.3 Differential diagnosis and institute appropriate genetic testing
- 3.1.18.4 Assessment of symptoms and signs in patients at risk of adult-onset neurogenetic disease
- 3.1.18.5 Application of protocols for pre-symptomatic diagnosis of Huntington's disease and other neurodegenerative disorders
- 3.1.18.6 Make timely, appropriate referrals to other specialists such as neurologists, psychologists, psychiatrists, speech therapists

- 3.1.19 Ophthalmological disease
 - 3.1.19.1 Differential diagnosis for a child with microphthalmia/ anophthalmia/ coloboma with or without a congenital anomaly of the central nervous system
 - 3.1.19.2 Ocular form of oculocutaneous albinism
 - 3.1.19.3 Diagnostic criteria to establish the diagnosis of various genetic syndromes with supporting ophthalmologic features
 - 3.1.19.4 Clinical trials in gene-replacement treatment strategies for childhood heritable retinal dystrophies

- 3.1.20 Psychiatric diseases
 - 3.1.20.1 Genetic differential diagnosis based on DSM criteria
 - 3.1.20.2 Disorders, including Huntington disease, metachromatic leukodystrophy, some forms of porphyria, and Wilson disease may present with psychiatric symptomatology before other symptoms.
 - 3.1.20.3 Be able to diagnose, manage and counsel individuals with these disorders
 - 3.1.20.4 Inborn errors of metabolism, particularly syndromes elevating ammonia levels, may be associated with altered behaviours that are symptomatic of acute decompensation
 - 3.1.20.5 Knowledge of the features, consequences, and guidelines for management of foetal alcohol syndrome and foetal alcohol spectrum disorder (FASD)
 - 3.1.20.6 Syndromic aetiologies based on presentation, including sex and age of onset of symptomatology
 - 3.1.20.7 Cardinal features and implement management recommendations for microdeletion syndromes associated with behavioural psychopathology as a primary or major component
 - 3.1.20.8 Poorly controlled metabolic disorders often have prominent psychiatric consequences

- 3.1.21 Pulmonary diseases
 - 3.1.21.1 Differential diagnosis, for hereditary pulmonary emphysema
 - 3.1.21.2 Differential diagnosis, for idiopathic pulmonary hypertension
 - 3.1.21.3 Counsel patients with idiopathic pulmonary fibrosis
 - 3.1.21.4 Counsel families with or at risk for cystic fibrosis
 - 3.1.21.5 Counsel patients with alpha-1-antitrypsin deficiency

- 3.1.22 Reproductive system
 - 3.1.22.1 Preconceptional genetic counselling to couples with sub-/infertility and organize genetic testing
 - 3.1.22.2 Preconceptional genetic counselling to couples with genetic and inherited disorders for their reproductive choices including invasive diagnosis, non-invasive testing, and assisted reproductive technologies (ART)
 - 3.1.22.3 Different ART options according to the national legislation and European guidelines including preimplantation genetic testing

- 3.1.23 Skeletal diseases
 - 3.1.23.1 Differential diagnosis of a fetus suspected of having a skeletal dysplasia or dysostosis and assess whether the condition is compatible with postnatal survival
 - 3.1.23.2 Differential diagnosis for a child with a congenital limb, axial, and/or craniofacial malformation, including teratogenic causes, syndromic causes, and skeletal dysostoses/dysplasias
 - 3.1.23.3 Be able to evaluate radiographs and other imaging studies and know when to order further biochemical or molecular genetic tests, as well as which tests are appropriate for a given situation

- 3.1.24 Teratology
 - 3.1.24.1 Historical perspective on teratology

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- 3.1.24.2 Mechanisms of teratology
- 3.1.24.3 Epidemiology of congenital malformations
- 3.1.24.4 Types and classes of teratogens
- 3.1.24.5 Effects of teratogens (death, abortion, miscarriage, malformation, etc.)
- 3.1.24.6 Counselling for teratogen exposure
- 3.1.24.7 Genetic inbreeding

3.1.25 Toxicology

- 3.1.25.1 Reproductive toxicology
- 3.1.25.2 Basic toxicological principals
- 3.1.25.3 Organs in detoxification
- 3.1.25.4 Developmental toxicology
- 3.1.25.5 Toxic substances
- 3.1.25.6 Ionising radiation
- 3.1.25.7 Toxicology in society, environmental toxicology, food toxicology, clinical toxicology, risk assessment

3.1.26 Urogenital diseases

- 3.1.26.1 Differential diagnosis for a child with a congenital anomaly of the urogenital tract

Domain 4: Bioinformatics

4.1 Bioinformatics

- 4.1.1 Basic methods of medical statistics
- 4.1.2 Knowledge of the principles of Human Phenotype Ontology
- 4.1.3 Knowledge in the use of large data sets and “big data”
- 4.1.4 Array data analysis and interpretation
- 4.1.5 Next generation sequencing raw data, massive parallel sequencing file types
- 4.1.6 Next generation sequencing data analysis
- 4.1.7 Analysis of WCF files
- 4.1.8 Public sequence domains used for next generation sequence analysis

Domain 5: Rare disease and society

5.1 Rare disease and society

- 5.1.1 Families living with rare diseases
- 5.1.2 Patient advocacy groups
- 5.1.3 Patient advocacy networks (patient perspectives)
- 5.1.4 Medical education in patient families and advocacy groups
- 5.1.5 Awareness on healthcare policy and decision making
- 5.1.6 Specific legislation related to access and coverage for essential medical therapies, role in clinical trials
- 5.1.7 Genetic laws
- 5.1.8 ELSI in rare diseases
- 5.1.9 Rare Disease Day

Domain 6: Logbook Recommendations³

6.1 Logbook Recommendation:

- 6.1.1 Purpose: The purpose of the logbook is to document that the applicant has had direct and meaningful involvement in the rare disease evaluation, counseling and management of patients and/or families, and has received appropriate clinical supervision.
 - 6.1.1.1 The EPA is a Unit and units can be counted. The certified Logbook with a category for EPA included is the key. Because the emphasis and attitudes regarding the spectrum of competences and education within any Medical Specialty, including Cardiology, vary significantly in the

³ Based on the American Board of Medical Genetics “Certification in Clinical Genetics and Genomics Logbook Guidelines”
<http://www.abmgen.org/2019/2019%20Logbook%20Documents/2019%20Clinical%20genetics%20logbook%20FINAL.pdf>

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individual states, one cannot expect applicants to have attained EPA competency in each and every item listed in the Syllabus/Curriculum. In other words, one cannot expect Eligible Candidates to have attained must have attained 100% of the possible EPA Units in the Syllabus / Curriculum. The Eligibility Committee applies the correct degree of flexibility allowing for equivalence of some procedures. To give an example, the percentage of items in the Syllabus to be expected of an applicant attaining the EPA grade of competence, for the EBSQ General Surgery, is presently set at 65%. This is an arbitrary figure which was reached by evaluating the previous year's candidates' data, but will obviously vary with each particular Competency Assessment and possibly from year to year. Another important legal point, is that each Examination Board has to establish this threshold when the Exam Webpage goes online.

- 6.1.2 Requirements: Logbook of the 55 cases must be completed in accordance with the instructions provided in this summary, and anticipates ongoing review of cases between the trainee and their program director, the applicant should assure that all requirements have been fulfilled before submitting the final logbook for review.
- 6.1.3 Case Selection:
- 6.1.3.1 All cases must be obtained through accredited residency and/or training program.
- 6.1.3.2 Supervision for case encounters in genetics clinics must be provided by faculty who are certified.
- 6.1.3.3 All 55 cases must be obtained during the inclusive dates of the applicant's training. No more than 2 cases may be obtained in any one day.
- 6.1.3.4 Each logbook entry must document a face-to-face interaction between the applicant and an individual patient and/or family. Evaluation, management, or counseling performed via telephone or in group counseling sessions will not be accepted.
- 6.1.3.5 A given patient or family may appear only once in an applicant's logbook, regardless of the number of encounters with that patient or family.
- 6.1.4 Description of Logbook Headings/Columns:
- 6.1.4.1 Entry Number: The logbook spreadsheet allows a trainee to enter an unlimited number of cases while in training. For the final logbook that may be requested for audit, you must select 55 cases to submit that fulfill all of the defined requirements. The applicant must be able to identify each case by its entry number if questions arise about a logbook entry
- 6.1.4.2 Date: The date in month/day/year [MM/DD/YYYY] format identifies when the patient was seen
- 6.1.4.3 Patient Age Category: For each case, the patient's age must be defined as Infant (5 cases), Child and Adolescent (20 cases), or Adult (25 cases) or Undiagnosed of any age (5 cases). Age refers to age of the patient on the date of the clinic visit.
- 6.1.4.4 Diagnosis: No more than 5 cases may have the same specific diagnosis. Variations in genotype or phenotype of a specific diagnosis, such as age of onset or particular mutation, are not considered sufficient to count as separate diagnoses. It is the age at onset and not the age of diagnosis or the age at which the trainee saw the patient that should be taken into account in satisfying this requirement.
- For each case, enter the diagnosis using the guidelines below:
- 6.1.4.4.1 Enter the diagnosis using the OMIM name or an ORPHACODE alternative title. All cases representing the same condition should be entered using the same diagnosis name.
- 6.1.4.4.2 Do not use abbreviations unless an OMIM/ORPHACODE alternative title.
- 6.1.4.4.3 Primary diagnosis must be listed first.
- 6.1.4.4.4 Use the most specific diagnosis for each case when known.
- 6.1.4.4.5 Log only those cases for which the diagnostic evaluation is complete. For example, "5p deletion syndrome" not "Rule out chromosome anomaly." If making a specific diagnosis was the reason for the referral, for example, is this Marfan syndrome?, use "Marfan syndrome" if the diagnostic evaluation is complete and this is the diagnosis or "Marfan syndrome, excluded" if the diagnostic evaluation is complete and this diagnosis was excluded but a more specific diagnosis could not be made. If a more specific diagnosis could be made, such as Shprintzen-Goldberg syndrome, use the more specific diagnosis.
- 6.1.4.4.6 If more than one patient or family with the same genetic category, age category, diagnosis, visit date, trainee role(s), and supervisor are recorded, clearly indicate that entries are not duplicated records or members of the same family, as follows:

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Neurofibromatosis, patient or family 1; Neurofibromatosis, patient or family 2.

6.2 Trainee's Role:

- 6.2.1 Medical history: involves obtaining pertinent medical information, such as pregnancy history, developmental milestones, and environmental exposures, by patient interview and review of medical records.
- 6.2.2 Pedigree: includes eliciting information for the construction of a pedigree that includes at a minimum all first and second-degree relatives using standard symbols.
- 6.2.3 Physical examinations: entails performing a complete physical examination or, if more appropriate, a targeted examination, to assess the system(s) of concern or to look for manifestations of a Mendelian condition in individuals who present for evaluation of a common complex disorder.
- 6.2.4 Management/Evaluation plan: involves determining recommendations for appropriate tests and/or assessments of medical or psychosocial care for a patient/family.
- 6.2.5 Testing options/results: includes explaining the technical and medical aspects of diagnostic and screening methods and reproductive options, including associated risks, benefits, and limitations, as well as interpreting and communicating testing results.
- 6.2.6 Risk assessment: entails performing pedigree analysis and evaluation of medical and laboratory data to determine recurrence/occurrence risks.
- 6.2.7 Inheritance/risk counseling: involves educating the patient or family about recurrence/occurrence risks and modes of inheritance of the disorder.
- 6.2.8 Discussion of diagnosis/natural history: includes conveying genetic medical information about the diagnosis, etiology, natural history, prognosis, and treatment/management of the disorder(s) in question.
- 6.2.9 Psychosocial support/counseling: involves providing short-term, patient or family- centered counseling, psychosocial support, and anticipatory guidance to the family, as well as addressing patient concerns.
- 6.2.10 Information access: includes literature review and database searches, as well as identification of resources for the patient or family and referring healthcare provider.
- 6.2.11 Documentation and follow-up: involves writing a consultation report or letter to the family or healthcare provider and recording adequate follow-up notes.
- 6.2.12 Undiagnosed Case: Full description of what happened with the sequence analysis record of deposition of a network (ERN, UDNI, PhenomeCentral, CPMS).

6.3 **Supervisor:** Include the full name, degree(s), and type of certification of the supervisor who was present and was directly responsible for your activities regarding that case

Domain 7. Competencies

7.1 Knowledge

- 7.1.1 knows of
- 7.1.2 knows basic concepts
- 7.1.3 knows generally
- 7.1.4 knows specifically and broadly

7.2 Clinical Skills

- 7.2.1 Has observed – the trainee acts as an ‘Assistant’. From complete novice through to being a competent assistant. At end of level 1 the trainee:
 - 7.2.1.1 Has adequate knowledge of the steps through direct observation.
 - 7.2.1.2 Demonstrates that he/she can handle the apparatus relevant to the procedure appropriately and safely.
 - 7.2.1.3 Can perform some parts of the procedure with reasonable fluency
- 7.2.2 Can do with assistance - a trainee is able to carry out the procedure ‘Directly Supervised’. From being able to carry out parts of the procedure under direct supervision, through to being able to complete the whole procedure under lesser degrees of direct supervision (e.g. trainer immediately available). At the end of level 2 the trainee
 - 7.2.2.1 Knows all the steps - and the reasons that lie behind the methodology.
 - 7.2.2.2 Can carry out a straightforward procedure fluently from start to finish
 - 7.2.2.3 Knows and demonstrates when to call for assistance/advice from the supervisor (knows personal limitations).
- 7.2.3 Can do the whole procedure but may need assistance – a trainee is able to do the procedure ‘indirectly supervised’. From being able to carry out the whole procedure under direct supervision (trainer immediately available) through to being able to carry out the whole procedure without direct supervision i.e. trainer available but not in direct contact with the trainee. At the end of level 3 the trainee

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- 7.2.3.1 Can adapt to well-known variations in the procedure encountered, without direct input from the trainer.
- 7.2.3.2 Recognizes and makes a correct assessment of common problems that are encountered.
- 7.2.3.3 Is able to deal with most of the common problems.
- 7.2.3.4 Knows and demonstrates when he/she needs help.
- 7.2.3.5 Requires advice rather than help that requires the trainer to intervene
- 7.2.4 Competent to do without assistance, including complications. The trainee can deal with the majority of procedures, problems and complications, but may need occasional help or advice.
- 7.2.5 Can be **trusted** to carry out the procedure, independently, without assistance or need for advice. This concept would constitute one Entrustable Professional Activity (EPA). An EPA is ‘a critical part of professional work that can be identified as a unit to be entrusted to a trainee once sufficient competence has been reached’. This would indicate whether one could *trust* the individual to perform the job and not whether he is just competent to do it. At the end of level 5 the trainee:
 - 7.2.5.1 Can deal with straightforward and difficult cases to a satisfactory level and without the requirement for external input to the level at which one would expect a consultant to function.
 - 7.2.5.2 Is capable of instructing and supervising trainees.
- 7.3 Technical Skills
 - 7.3.1 Has observed.
 - 7.3.2 Can do with assistance.
 - 7.3.3 Can do whole but may need assistance.
 - 7.3.4 Competent to do without assistance, including complications, but may need advice or help.
 - 7.3.5 **Can be trusted to carry out the procedure, independently, without assistance or need for advice (EPA).** EPAs have been explained previously.

The above detailed classification of Competence Levels could be useful during the process of formative training, when it comes to deciding when an applicant is eligible to sit an eventual Specialist Exit examination, it is the evaluation of the EPAs which is essential. In this sense, the Eligibility Assessment Process is really the first part of the Examination and that explains the suggestion that the ‘5th level of Technical Skills competence’ should be included in a standardized Logbook Template for all trainees