UNION EUROPÉENNE DES MÉDECINS SPÉCIALISTES
EUROPEAN UNION OF MEDICAL SPECIALISTS
Association internationale sans but lucratif /International non-profit organization

European Training Requirements for competency in Paediatric Haematology and Oncology

Syllabus completed June 2024

European Society for Paediatric Oncology

European Hematology Association

European Academy of Paediatrics

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PREAMBLE

The UEMS (Union Européenne des Médecins Spécialistes, or European Union of Medical Specialists) is a non-governmental organisation representing national associations of medical specialists at the European level. With its current membership of 40 national associations and operating through 43 Specialist Sections and their European Boards, 17 Multidisciplinary Joint Committees and 4 Thematic Federations the UEMS is committed to promote the free movement of medical specialists across Europe while ensuring the professional consensus on the framework for the highest possible level of their training which will pave the way to the improvement of quality of care for the benefit of all European citizens and beyond.

UEMS and its Postgraduate Medical Specialists Training programmes. In 1994, the UEMS adopted its Charter on Postgraduate Training aiming at providing the recommendations at the European level for high quality training. This Charter set the basis for the European approach in the field of harmonisation of Postgraduate Specialist Medical Training, most importantly with the ongoing dissemination of its periodically updated Chapter 6's, specific to each specialty. After the most recent version of the EU Directive on the recognition of Professional Qualifications was introduced in 2011, the UEMS Specialist Sections and other UEMS Bodies have continued working on developing the documents on European Training Requirement(s) (ETRs). They reflect modern medical practice and current scientific findings in each of the specialty fields and particular competencies covered and being represented within the UEMS. In 2012 the UEMS Council adopted the document Template Structure for ETR.

The linkage between the quality of medical care and quality of training of medical professionals. It is the UEMS' conviction that the quality of medical care and expertise are directly linked to the quality of training, achieved competencies and their continuous update and development provided to the medical professionals. No matter where doctors are trained, they should have the same core competencies. The UEMS ETRs reflect many years (or even decades) of experience on the ground of the UEMS Sections/ Multidisciplinary Joint Committees (MJCs) and Boards developing in close collaboration with the relevant European Scientific Societies training requirements coupled with European Medical Assessments. It is one among the clear aims of the UEMS ETRs to raise standards of training to make sure that European patients find high quality standards of safe specialist care. While professional activity is regulated by national laws in EU Member States, it is the UEMS understanding that it has basically to comply with international treaties and UN declarations on Human Rights as well as the WMA International

Code of Medical Ethics.

UEMS and European legislation facilitating the mobility of medical professionals. The UEMS Council and its Specialist Sections, first created in 1962, have regularly provided advice and expert opinion to the European Commission. This helped create the framework that informed the drawing up of the Doctors Directives in 1975, which provided for the mutual recognition of medical diplomas and the free movement of doctors throughout the EU. The revised EU Directive on the recognition of Professional Qualifications (2013/55/EU) allows member states to decide on a common set of minimum knowledge, skills and competencies that are needed to pursue a given profession through a Common Training Framework (CTF) which represents the third mechanism that could be used to ensure mobility within the EU. This directive states that "professional qualifications obtained under common training frameworks should automatically be recognised by Member States. Professional organisations which are representative at Union level and, under certain circumstances, national professional organisations or competent authorities should be able to submit suggestions for common training principles to the Commission, in order to allow for an assessment with the national coordinators of the possible consequences of such principles for the national education and training systems, as well as for the national rules governing access to regulated professions". The UEMS supported CTFs since they encompass the key elements developed in modern educational and training models, i.e. knowledge, skills, professionalism. In addition, the Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare introduced a strong incentive for harmonisation of medical training and achieved competencies among EU/EEA Countries through the requirements to assure good and comparable quality of care to increasingly mobile European citizens.

The UEMS ETR documents aim to provide for each specialty the basic training requirements as well as optional elements, and should be regularly updated by UEMS Specialist Sections and European Boards to reflect scientific and medical progress. The three-part structure of these documents reflects the UEMS approach to have a coherent pragmatic document for each individual specialty, not only for medical specialists but also for decision-makers at the national and European level interested in knowing more about medical specialist training. To foster harmonisation of the ETR by adopting more specific guidelines, the CanMEDS competency framework is recommended which defines the entire set of roles of the professionals which are common across both medicine and surgery. UEMS has an agreement to use an abbreviated version of the competencies within those roles.

Importance of making a distinction between Knowledge and Competency in ETR documents. Competency-based education is not oriented towards the period of clinical rotations, but towards trainee, and trainee's progress in the acquisition of competencies. Having a clear distinction within an ETR's contents between competencies and knowledge helps define both how that training should be delivered and how it should be assessed. The UEMS considers that the appropriate use of different methods of assessment of knowledge and acquired skills, emphasising the workplace-based assessment, is an essential component of quality postgraduate training, focused on high standards of specialist medical practice. To improve the methods of assessment it is also recommended to use the so-called Entrustable Professional Activities (EPAs) in all specialties ETRs. In order to recognise common and harmonised standards on the quality assurance in specialist training and specialist practice at a European level some UEMS Specialist Sections and Boards also have, for a long time, organised European examinations (supported and appraised by the UEMS CESMA - Council of European Specialist Medical Assessments).

Overlapping of learning outcomes and competencies. Each of the UEMS ETRs defines a syllabus or knowledge base and describes learning outcomes defined for given competencies. Some of these curricula encompass a whole specialty, other focus on areas within or across specialties and define content of the training requirements for specific areas of expertise. By recognising the potential overlapping it creates the opportunity for those writing ETRs to draft overlapping or common goals for learning outcomes. Similar measurement does not necessarily equate to the same targets. Rather, across different specialties the final goal may differ, i.e. there may be clearly defined individual goals for trainees with different expectations.

UEMS ETRs and national curricula. The UEMS strongly encourages the National Medical Competent Authorities (NMCAs) to adopt such requirements and believes that this is the most efficient way of implementation of good standards in postgraduate training. We clearly respect and support the vital role of the NMCAs in setting high standards of training and care in their respective Countries and checking through robust quality control mechanisms the qualifications of medical specialists moving across Europe. The UEMS ETRs are developed by professionals for professionals and this adds unique value to them. UEMS aim is to indicate the knowledge and competencies that should be achieved by trainees in EU/EEA countries and also competencies and organisation of the training centres. The training environment and results described in UEMS ETRs may be achieved in adapted ways, depending on local traditions, organisation of healthcare

system and of medical specialist training. Adaptation of UEMS ETRs to local conditions assures the highest quality of specialist training and each state may include additional requirements, depending on local needs.

Importance of collaboration with other representative European medical bodies. The UEMS always wishes to work with all Colleagues, NMAs, professional and scientific organisations across Europe. In the process of ETRs development, the UEMS recognises the importance of meaningful collaboration with the other European medical representative bodies, the European Junior Doctors (EJD representing doctors in training), the European Union of General Practitioners (UEMO – Union Européenne des Médecins Omnipraticiens), the Standing Committee of European Doctors (CPME - Comité Permanent des Médecins Européens), the Federation of European Salaried Doctors (FEMS) and the European Association of Senior Hospital Doctors (AEMH - Association Européenne des Médecins Hospitaliers). In addition, UEMS continues to develop closer links with the many European specialist societies. UEMS, in collaboration with its fellow European representative bodies, has constantly been highlighting the importance of coordinated postgraduate specialist medical training programmes always accepting the differing needs of different specialties. In this way quality medical care is delivered by highly qualified medical specialists - essential to ensuring consumer confidence and protection all over Europe.

Conclusions. UEMS is very proud for all the hard work that has been done until now in developing the UEMS ETRs as well as that they are increasingly implemented as national curricula. However, we also recognise the need for constant improvement, and we are always open to further suggestions. The UEMS insists that the medical profession remains the driver in defining its own specialist training and continuous professional development needs. On this basis, we sincerely look forward to working with the key European Union responsible bodies, as well as the national stakeholders in implementing the basic common strategies and requirements outlined with this initiative. We are confident that the priorities detailed in UEMS ETR documents developed for individual specialties (and/or competencies) will become evident in national strategies and programmes, as well as action plans for postgraduate medical education and training.

PREFACE

Paediatrics is an independent medical specialty based on the knowledge and skills required for the prevention, diagnosis and management of all aspects of illness and injury affecting children of all age groups from birth to the end of adolescence, up to the age of 18 years. It also encompasses child health, which covers all aspects of growth and development and the prevention of disease. The influence of the family and other environmental factors also plays a significant role in the development of the child, and many conditions require life-long management and follow-up before a smooth transition of care to adult services.

For these reasons we believe that all physicians whose practice involves to a large part the medical care of children require a solid basic training in General Paediatrics, as set out by many National Training Authorities (NTAs), and in the recommended European Common Trunk Syllabus, approved by the EAP-UEMS. This training, which should be of 3 years minimum duration, should act as a prelude to higher training, and will underpin many of the principles set out in this document.

This document sets out the minimum requirements for training in Paediatric Haematology and Oncology. The latter historically constitutes a branch of pediatrics and is formally recognized as such by the European Academy of Paediatrics (EAP), itself a section of the Union of European Medical Specialists (*Union Européenne des Médecins Specialistes - UEMS*) through the European Board of Paediatrics (EBP).

COMPOSITION OF THE SYLLABUS SUBCOMMITTEE

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ACKNOWLEDGEMENTS

We are grateful to all listed below who have provided constructive comments and contributed significantly to this ETR:

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List of Abbreviations

ADA testing	adenosine deaminase testing
ALL	acute lymphoblastic leukemia
ALPS	autoimmune lymphoproliferative syndrome
AML	acute myeloid leukemia
aPPT	activated partial thromboplastin time
AYA	adolescents and young adults
BM	bone marrow
BMF	bone marrow failure
CAMT	congenital amegakaryocytic thrombocytopenia
CAR	chimeric antigen receptor
CBC	cell blood count
CDA	congenital dyserythropoietic anemias
CGD	chronic granulomatous disease
CID	combined Immunodeficiency
CIK	cytokine-induced killer cells
CML	chronic myeloid leukemia
CMV	cytomegalovirus
CNS	central nervous system
CSF	cerebrospinal fluid
CT	computed tomography
CTA/ CTV	computed tomography angiography/ venography
CVC	central venous catheter
CVID	common variable immune deficiency
DBA	Diamond Blackfan anaemia
DEB test	diepoxybutane test
EAP	European Academy of Paediatrics
EBP	European Board of Paediatrics
EBV	Epstein-Barr virus
EDA-ID	anhidrotic ectodermodysplasia with immunodeficiency
EHA	European Hematology Association
EPO	erythropoietin
ERN PaedCan	European Reference Network for Paediatric Cancer
ESMO	European Society of Medical Oncology
ETR	European Training Requirements
FDG-PET	fluorodeoxyglucose positron emission tomography
FHL	familial haemophagocytic lymphohistiocytosis
FISH	fluorescence in situ hybridization
FNAIT	fetal/neonatal alloimmune thrombocytopenia
GCSF	granulocyte colony-stimulating factor
GCT	germ cell tumours
GIT	gastrointestinal tract
GU	genitourinary
GvHD	graft-versus-host disease
HE	hereditary elliptocytosis
HIES	hyper IgE syndromes
HIT	heparin-induced thrombocytopenia

HLA	human leukocyte antigen
HLH	hemophagocytic lymphohistiocytosis
HPFH	hereditary persistence of fetal hemoglobin
HPP	hereditary pyropoikilocytosis
HPV	epidermodysplasia verruciformis
HSC-GT	gene therapy
HSCT	haematopoietic stem cell transplantation
HSE	Herpes simplex encephalitis
Igs	immunoglobulins
INR	international normalized ratio
IRS	Intergroup Rhabdomyosarcoma Study Group
ITP	immune thrombocytopenia
iv	intravenous
JMML	juvenile myelomonocytic leukemia
LCH	Langerhans cell histiocytosis
MAC	myeloablative conditioning
MCV	mean corpuscular volume
MDS	myelodysplastic syndrome
MECOM	*MDS1* and *EVI1* complex locus
MLD	metachromatic leukodystrophy
MMC test	mitomycin C test
MPSIH/ MPSIIIA	mucopolysaccharidosis I Hurler/ IIIA
MRA/ MRV	magnetic resonance angiography/ venography
MRI	magnetic resonance imaging
MSMD	mendelian susceptibility to mycobacterial disease
NAIT	neonatal alloimmune thrombocytopenia
NaPHOS	National Paediatric Haematology-Oncology Societies
NGS	next generation sequencing
NHL	non-Hodgkin lymphoma
NK	natural killer cells
NRT	non replacement therapy
OS	Omenn syndrome
PAN	polyarteritis nodosa
PC	platelet concentrates
PE	pulmonary embolism
PID	primary immunodeficiency
PJP	Pneumocystis jirovecii
PTLD	post-transplant lymphoproliferative disease
RBC	red blood cell
RIC	reduced intensity conditioning
RMS	rhabdomyosarcoma
RTC	reduced toxicity conditioning
RUS	radius, ulna and short bones
SAA	severe aplastic anaemia
SBDS	Schwachman-Bodian-Diamond syndrome
sc	subcutaneous
SCID	severe combined immune deficiency
SCN	severe congenital neutropenia

SCT	stem cell transplantation
SIOPE	European Society for Pediatric Oncology
STS	soft tissue sarcoma
TANEC	transfusion associated necrotizing enterocolitis
TAR	thrombocytopenia (low blood platelets) and aplasia (absence) of the radius
TEC	transient erythroblastopenia of childhood
TLR	Toll-like receptor
TNF	tumour necrosis factor
t-PA	tissue plasminogen activator
TPO	thrombopoietin
TPO-RA	thrombopoietin Receptor Agonists
TTP	thrombocytopenic purpura
UEMS	Union Européenne des Médecins Specialistes
US	ultrasound
VACTER-L	vertebral anomalies, anorectal anomalies (anal atresia), cardiac anomalies, tracheoesophageal fistula or atresia, renal anomalies, and limb anomalies
VTE	venous thromboembolism
VWD	von Willebrand Disease
WAS	Wiskott-Aldrich-Syndrome
WES	whole exome sequencing
X-ALD	X-linked adrenoleukodystrophy

INTRODUCTION AND BACKGROUND

The following syllabus is a comprehensive update to the former European Training Requirements (ETR) document dated 2013 regarding the recommended training programme in paediatric haematology and oncology. The present document is a joint effort between the European Society for Paediatric Oncology (SIOP-E) and the European Haematology Association (EHA), comprising training in both malignant and non-malignant haematology and oncology in children and adolescents. It provides recommendations toward essential training requirements for training centers, trainers and trainees in paediatric haematology/oncology.

This training program with a duration of two years has been designed in a modular fashion. The modules contain core knowledge and practical aspects per disease related to the diagnostic and therapeutic approach of patients, which are essential for specialized paediatric haemato-oncologists. Expertise in practical procedures is also required, specifically concerning lumbar punctures, bone marrow aspirations, bone marrow biopsies and skin biopsies. More specific aspects concerning supportive care, follow-up and palliative care are also described within the programme. In addition, the trainee is also expected to be familiar with research methodologies and ethical issues pertaining to research and clinical management.

Finally, based on final career intentions of the trainees, it may be advisable to spend one additional year for more specific training in haematological malignancies, solid tumours, central nervous system (CNS) tumours, non-malignant haematological conditions, or stem cell transplantation and gene therapy.

The main goal is to ensure a standard training program throughout Europe, to achieve high quality education for future specialists in paediatric haematology and oncology, and to allow them to learn, acquire and exercise skills to manage their patients in a specialized tertiary care unit.

AIM OF HIGHER TRAINING

Significant advances in paediatric haematology-oncology throughout the last decades at diagnostic, therapeutic and supportive care level, resulted in improvement of outcome for paediatric patients with non-malignant and malignant haematological and oncological diseases. At the same time, new technological methods, novel agents and innovative modalities and concepts for treatment have been developed which led to an exponential increase of the knowledge in this field. The implementation of high-quality standard of care and recent advances at the management of the patient, requires high-skilled and specialized health care providers, and thus a standardized and updated training programme for paediatric haematology-oncology. This programme should not only provide the basics knowledge to specialists for the care of their patients, but also the skills to continuously learn, implement and further boost advances in the field.

TRAINING REQUIREMENTS FOR TRAINEES

1. CONTENT OF TRAINING AND LEARNING OUTCOME

A medical doctor who has successfully completed at least 3 years of training in General Paediatrics will be eligible for further specialist training in Paediatric Haematology and Oncology. The key areas of general professional competencies required of a Paediatric Haematology and Oncology specialist are the same as those for all physicians. A Paediatric Haematologist/Oncologist should be:

- An expert in the medical domain: The Paediatric Haematologist/Oncologist is equipped with the requisite knowledge and expertise to effectively address the needs of children and adolescents with non-malignant and malignant disease. Recognizing the multidimensional and interdisciplinary nature of Paediatric Haematology and Oncology, the specialist possesses a comprehensive understanding and proficiency that surpasses the confines of individual bodily systems and specific age demographics. This expertise is seamlessly integrated into daily clinical practice. The Paediatric Haematologist/Oncologist demonstrates adept clinical reasoning, ensuring that diagnostic and therapeutic approaches align with the principles of evidence-based medical care. They exercise caution to avoid unnecessary or detrimental procedures or treatments. Adhering to both national and international standards, the specialist acknowledges their strengths while remaining cognizant of the limitations

inherent in their knowledge and skills, thereby facilitating appropriate referrals to other specialists when warranted. Continual updating of knowledge and skills is a priority for the Paediatric Haematologist/Oncologist. A health advocate: The Paediatric Haematologist/Oncologist actively advocates for the well-being of patients dealing with haematological non-malignant and malignant conditions, both within their clinical practice and beyond. This advocacy may take place individually or through involvement with scientific and professional organizations specializing in Haematology and Oncology. By pinpointing key health determinants, the Paediatric Haematologist/Oncologist crafts comprehensive management and prevention strategies, ensuring that patients can access appropriate healthcare and social services.

- A committed professional: The Paediatric Haematologist/Oncologist is unwavering in their commitment to delivering top-tier care to patients. This commitment extends to adhering to the highest ethical standards in medicine, encompassing informed consent, advanced directives, research ethics, and upholding patient autonomy with utmost respect.

A. Theoretical knowledge

By the end of their training, trainees are expected to have acquired knowledge of clinical, laboratory and competences related to regulations and principles according to the specificity of the clinical condition. A summary of the anticipated knowledge of a paediatric haematologist/oncologist upon completion of training is outlined below. Further information on theoretical knowledge is available in section 2.B. Curriculum of training.

General key subjects

- Epidemiology of childhood cancer and other non-malignant haematological diseases
- Genetic and environmental predisposing factors
- Clinical presentations, diagnostic workup and differential diagnosis
- Prognostic factors and therapeutic implications
- Emergencies at diagnosis and during treatment, including spinal cord

compression, intracranial hypertension, tumour lysis syndrome, abdominal occlusion, septic shock, mediastinal acute compressive syndrome, arterial hypertension

- Principles of chemotherapy and new agents: pharmacokinetics, pharmacodynamics, mechanism of drug resistance, side effects and complications related to chemotherapy
- Interactions between chemotherapy and concomitantly administered drugs
- Treatment for haematological malignancies and solid tumours according to current national/international protocols at diagnosis and relapses
- Supportive care, including infection management, pain control and blood products transfusion
- Imaging, including functional Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) in lymphoma and in other selected tumours; functional MRI in brain tumours; MIBG scintigraphy in neuroblastoma, and other new radiological procedures that may be important for the assessment of response and treatment strategies.
- Role of radiotherapy in different tumours
- Principles of paediatric oncologic surgery and tissue collection for diagnosis and biological studies
- Molecular markers as diagnostic and prognostic tools and treatment implications
- Fertility preservation
- Management and follow-up of germline syndromes predisposing to cancer

<u>Specific subjects</u>

- Solid tumours
    - Renal tumours
    - Neuroblastoma
    - Bone tumours

    - Soft tissue sarcoma
    - Retinoblastoma
    - Hepatic tumours
    - Non-intracranial germ-cell tumours
    - Central nervous system tumours
- Malignant Haematology
    - Paediatric myeloid leukemias
    - Paediatric lymphoid leukemias
- Non-malignant Haematology
    - Red blood cell disorders
    - Bone marrow failure syndromes
    - Isolated neutropenia
    - Primary immunodeficiencies
- Platelet disorders, thrombosis and haemostasis
- Haematopoietic stem cell transplantation and gene therapy
- Special aspects of paediatric transfusion management

B. Practical activities and General Skills/Entrusted Professional Activities

Diagnostic and therapeutic approach

- Clinical, laboratory and radiological investigations for appropriate staging of different tumours
- Basic knowledge of pediatric radiology (imaging methods and result interpretation)
- Interpretation of investigations and laboratory findings
- Treatment planning at diagnosis or relapse, according to current national/international protocols
- Recognition and treatment of the main emergencies at diagnosis and during treatment
- Treatment of infectious diseases according to current guidelines
- Accurate pain evaluation and adequate treatment
- Intrathecal drug administration and safety issues according to good clinical practice
- Management of acute reactions to drugs and extravasation of chemotherapy agents

- Autologous haematopoietic stem cells transfusion procedure and treatment related complications
- Tumour and treatment-related follow up plan
- Communication to parents, children and adolescents
- Interaction and coordination with other professionals involved in the care of children and adolescents with cancer (i.e. nurses, psychologists, physiotherapists, dietitians…)
- Specific needs for ethnically and socially diverse families

Palliative Care:

- Principles of palliative care in pediatric oncology (integration, indications and multidisciplinary collaboration)
- Symptom management
- Advance care planning and shared decision-making.
- Communication with children and their family throughout the disease trajectory and at end-of-life
- Discussion of complex cases/situation (for example withdrawing or withholding treatment), self-care and team-care supervision

Adolescents and young adults with cancer (AYA):

- Behavior, biology and treatment of hematological and oncological disorders in AYAs
- Addressing specific psychological needs and mental health issues in AYSs with hematological and oncological disorders
- Communication skills to engage with AYAs with hematological and oncological disorders
- Consent, legal and ethical aspects in AYAs with hematological and oncological disorders Topics of sexual and reproductive health
- Facilitating transitions from pediatric/adolescent to adult healthcare systems
- Multidisciplinary (tumour boards):
    - Coordination and moderation of a multidisciplinary boards (i.e., tumor board, molecular board, hematology board, etc.)
- Effective communication, proper documentation and reporting

- Interdisciplinary education and collaborative care planning
- Patient and family engagement

Late effects/Survivorship

- Late effects and morbidity in survivors
- Implementation of follow-up careNeurological, endocrinological, cardiovascular, cognitive, behavioural and social sequelae of different conditions, and respective treatment regimens

Recommended minimum number of procedures to be performed:

- 15 Lumbar punctures with/out intrathecal drug administration
- 5-10 intraventricular punctures with/out intrathecal drug administration
- 15 Bone marrow aspirations
- 10 Bone marrow biopsies
- 3-5 Skin biopsies

Recommended minimum number of patients to be evaluated (at least 3 out of 4 following patients' groups):

- 15 patients with haematological malignancies
- 15 patients with non-haematological malignancies
- 10 patients with brain tumours
- 15 patients with other solid tumours

C. Competences

Formative competence assessment

Formative assessments focus on the trainee's development and are used to identify how they are learning, their strengths and weaknesses, and tailor training/learning activities to meet their needs. Competences should be evaluated throughout the training period. There are several tools available for this purpose that describe different aspects of training. Some of these are shown in *table 1*. Formal and informal reflections on these assessments and the feedback received are important features for a trainee's professional development. Regular meetings between the trainer and the trainee should be arranged at least every six months to discuss the results of the assessment,

the trainee's strengths and areas for improvement, followed by the development of a targeted action plan.

Table 1. Examples of formative competence assessment tools*

Assessment	Purpose	Method
MiniCeX (Mini clinical examination)	Provides feedback on skills needed in clinical care	Trainer observes a trainee examining a patient, sharing information and explaining the management plan to the parents/guardians.
CbD (Case-based discussion)	Assesses clinical reasoning or decision making	Trainee presents a more complex case to the trainer and discusses the evidence or basis for diagnosis or treatment
LEADER	Focuses on leadership skills	A trainee is observed with a team and in a leadership capacity
HAT (Handover assessment tool)	Evaluates handover skills	Handover episodes are supervised and discussed
DOC (Discussion of correspondence)	Assesses letter writing skills	Clinic letters or discharges are reviewed and discussed
MSF (Multi-source feedback)	Provides wider feedback on performance	Confidential comments from a wide range of colleagues, patients and the trainee are sought

**Adapted from* www.rcpch.ac.uk/resources/assessment-guide

Additionally, non-technical skills that involve cognitive and social skills are paramount for safe and effective healthcare. These skills are depicted as follows:

Professionalism (attitudes)

- Towards patients and parents/carers
    - Respect their autonomy
    - Elicit and acknowledge their concerns
    - Share information and support them
    - Treat all fairly and irrespective of age, gender, race, disability, religion, social or financial status
    - Deliver best quality care in a compassionate and caring way
- Towards colleagues and junior staff
    - Respect and treat all individuals fairly and without prejudice

    - Communicate and collaborate in a productive manner
    - Acknowledge the multidisciplinary character of the specialism and expertise of all health care professionals
    - Behave in a responsible, reliable and dependable way
- Towards society
    - Appropriate communication to society about paediatric haematology and oncology conditions
    - Improve care by evaluating processes and outcomes
    - Make effective use of resources
- Towards themselves
    - Abide by the values of honesty, confidentiality and altruist
    - Acknowledge personal health, capacities, emotional reactions, and limitations in knowledge, skills, and attitude and take appropriate measures to correct these
    - Participate in educational programmes
    - Maintain competence and dedicated approach throughout professional career
    - Undergo regular supervisions

Communication

- Create and sustain a relationship that is therapeutic for patients and supportive of their families/carers
    - Communicate with family honestly and supportively
    - Determine extent to which patient and parents/carers want to participate
    - Be present, pay attention to patient
    - Care and work collaboratively
    - Accept and explore patients feelings
    - Provide a sustainable relationship that allows for repair when mistakes are made
    - Be authentic, honest, admit and apologise for mistakes
- Use effective listening, language and communication skills to facilitate the relationship
    - Recognise and select preferred and most effective mode of communication

    - Elicit, verify and provide information using effective nonverbal, verbal (questioning, explanatory) and writing skills
    - Use nonverbal cues, e.g eye contact, nodding, pausing
    - Use verbal skills, e.g. sign-posting, back tracking, reflecting, mirroring
    - Tailor information for patient's/family's needs and check understanding
    - Understand their perspective
- Create an atmosphere of mutuality and respect through patient and parents'/carers' participation and involvement in decision making
    - Collaboratively set agenda for encounter
    - Include them in choices and decisions to the extent they desire
    - Explain the role of different healthcare professionals to the patients and parents/carers
    - Negotiate mutually acceptable plans in partnership with patients/carers and professionals
- Work effectively with others as a member or leader of the health care team
    - Demonstrate respect, collaboration and cooperation
    - Ensure communication is adequate and clearly understood
    - Resolve conflict

Situational awareness

- Understand situations, anticipate and identify problems, and recognize need for action
- Integrate information from multiple sources
- Prioritise actions, ensure patient safety and prevent errors

Decision-making

- Synthesise information, evaluate options and propose best solutions for:
    - Individual case plans, long-term scheduling plans
    - under normal conditions and time pressure crisis situations
- Deal with uncertainty, and information which may be incomplete and conflicting
- Manage risk and re-evaluate

Safeguarding

- Understand children's rights and statutory context within which we work and legislation including the UN Convention on the Rights of the Child and Human Rights Act
- Recognise potential indicators of child maltreatment and make an appropriate referral. Document appropriately when a child is not brought to an appointment, identify patterns of nonattendance and act appropriately to ensure the child's health needs are met.
- Recognise that particular groups of children are more vulnerable. Have an understanding of the impact of adverse childhood experiences (ACEs).
- Proactively engage vulnerable young people to identify and address additional health needs.
- Understand the impact of parents'/carers' mental/physical health on the wellbeing of children.
- Understanding what to do about concerns about children including how and when to share information according to Caldicott principles and how to escalate concerns when the response is not appropriate.
- Understanding what to do about concerns about children including how and when to share information according to Caldicott principles and how to escalate concerns when the response is not appropriate.
    - Identify and act appropriately and proactively on safeguarding concerns including:
    - keep appropriate records, and differentiating fact from opinion
    - communicate safeguarding/child protection concerns both verbally and in a written report to a variety of multi-disciplinary for and within court proceedings. This will be supervised by the consultant in charge of the child's care.
    - intervene early and proactively to reduce risk, including contributing to risk assessments.
    - share information (in person, by phone and in writing)
    - seek further advice and help when necessary
    - make appropriate referrals
    - contribute to multi-disciplinary assessments and effective management plans
    - escalate concerns if concerns are not taken seriously
- Be aware of professional abuse and how to raise concerns.

- Act on concerns or suspicions about colleagues in relation to their actions or behaviours with children.
- Reflects on own safeguarding practice as appropriate to experience through audit, case discussion, peer review and supervision.
- Able to apply lessons learnt from serious case reviews, and other reviews.
- Understand and contribute to the child death process with guidance from consultant in charge of child's care.

Leadership

- Lead with integrity, responsibility and accountability
- Have a vision and clear sense of purpose, provide direction and be proactive to achieve this. Create climate of trust, inspire, show concern and advocate for followers
- Harness collective creativity and followers' contributions to problem solving
- Persevere and overcome challenges to achieve results

Teamwork

- Value the roles, expertise and limitations of all team members
- Contribute actively to team efforts. Share information and responsibility.
- Resolve misunderstandings and conflicts with and between members of the team

Time and Task management

- Prioritise and plan according to urgency and importance
- Prepare, review and update 'To do' lists
- Organise work productively, complete in a timely manner and be punctual
- Identifying and utilise available resources to provide and maintain standards. Delegate appropriately

Self-directed learning

- Take responsibility for active learning throughout training period
- Use patients and experiences encountered during training as triggers to explore new concepts, and continuously apply these to new situations
- Use the contents of this ETR, reflection from formative assessments/constructive

feedback and self-evaluation to

  - identify gaps in own knowledge and abilities
  - make plans to address these
  - monitor progress

- Find and use credible and varied sources for learning, including health care experts for tacit knowledge, standard textbooks, peer reviewed journals and evidence-based guidelines

Generic teaching and Educational skills

- Communicate clearly in the role of a teacher
  - Assess the educational needs of learners
  - Define aims of learning activity to meet these needs
- Apply principles of adult learning and facilitate learning from work-based experiences and formal educational sessions
- Prepare teaching materials and learning resources
- Use range of teaching and learning methods including online and blended learning
- Offer, seek and accept honest, constructive and timely feedback

Summative competence assessment

Summative assessments have important purposes in selection, certification and institutional accountability. Currently, satisfactory completion of the training programme in Paediatric Haematology (non-malignant and malignant) and/or Oncology (including all non-haematological malignancies = solid tumours) is undertaken according to the national representative body in each country (i.e., NaPHOS, National Paediatric Haematology-Oncology Societies and/or National societies of Paediatrics and Adolescent Medicine). Moreover, considering that not all countries follow the training pathway as described above, programmes should be reviewed by the respective national representative bodies before approval and certification.

2. ORGANISATION OF TRAINING

A. Schedule Of Training

The suggested 2-year (with 1 extra optional year) training programme includes knowledge at different levels of differentiation from the following topics:

1. Solid tumours (including Central Nervous System)
2. Malignant haematology
3. Non-malignant haematology
4. Haematopoieticc stem cell transplantation and gene therapy
5. Transfusion management

Research training of at least 6 months, within the spectrum of paediatric haematology/oncology, is highly recommended during the 2-year training programme. The research may be at clinical or laboratory level. In addition, the trainee should become familiar with the conduction of clinical trials including:

- Clinical trial methodology and study design,
- Basic principles of epidemiology and biostatistics,
- International regulations that should be applied according to General Data Protection Regulation, Good Clinical Practice, Declaration of Helsinki and European Directive 2001/20 on clinical trials, etc.
- Data and safety reporting
- Regulatory and drug development process.

B. Curriculum Of Training

The curriculum aims to cover training of future paediatric haematologists/oncologists for general competencies and haematology/oncology-specific competencies. It should allow flexibility for personal development according to the needs of the individual, the Centre, and the country where the candidate is training. Certain countries may already have their curriculums for training in paediatric haematology/oncology. European curriculum should take into account diverse health systems and clinical settings of different countries, as well as different spectrum of skills required by national curriculums. SIOPE and EHA have suggested the level descriptors in *table 2* to classify the requirements of trainees.

Table 2. Classification of expected training requirements' knowledge

Level	Type of skill	Level descriptors
1	Clinical skills	● Describe the clinical features and epidemiology of a condition OR indications for a specific treatment/procedure OR appropriateness/utility of a test. ● Recognize a patient who may have this condition OR require this treatment OR benefit from this test.
	Laboratory skills	● Recognize the appropriateness and utility of a specific test for diagnosing and follow-up of specific haematological conditions
	Regulation competences	● Identify applicable regulations OR principles
2	Clinical skills	● Describe the pathogenesis ● Identify clinical features and investigations required to diagnose a condition and interpret test results correctly ● Describe prognosis ● Identify correct referral routes OR initiate appropriate treatment (according to established protocol) ● Identify the need for and establish urgent consultation with subspecialist (particularly if the condition has potentially life-threatening debut symptoms)
	Laboratory skills	● Choose/order appropriate test(s) for a specific patient, considering: o Indications o Accuracy and limitations o What is entailed for the patient in performing the test o Interpret results for a specific patient
	Regulation competences	● Apply this regulation/principle relevantly and appropriately within my own clinical work
3	Clinical skills	● Decide and manage first line treatment ● Identify treatment failure and need for second-line management ● Identify when there is a need for, and deliver, genetic counselling ● Seek out and integrate new knowledge and concepts in relation to condition/treatment
	Laboratory skills	● Create/issue an interpretative report of test results ● Select/justify tests according to their cost-effectiveness
	Regulation competences	● Explain regulation/principle in appropriate language to a non-specialist audience ● Seek out and integrate new knowledge and concepts in relation to regulation/principle ● Recognize and plan how to improve own limitations, and demonstrate improvement

The following syllabus is divided into sections that comprise the expected level of knowledge in the several fields of paediatric haematology/oncology. Each section provides information regarding diagnosis, treatment and follow-up.

Section 1: Oncology - Solid Tumours

Solid Tumours	Learning Points	Level
1A **Renal Tumours**	• Epidemiology, etiology and congenital anomalies associated with Wilms' tumour and current screening strategy • Symptoms and differential diagnosis of a renal mass • Pathology and molecular biology of renal tumours • Nephroblastomatosis and Wilms' tumour • Principles of treatment of unilateral, bilateral and metastatic Wilms' tumours • Management of tumour or treatment related symptoms/ complications (hypertension, rupture, V. cava thrombus, VOD) • Molecular and pathological risk factors of Wilms' tumour related to outcome • Principles of treatment of non-Wilms' renal tumours • Late effects and long-term follow-up of renal tumours • Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling	**3**
1B **Neuroblastoma**	• Updated neuroblastoma classification • Genetics in neuroblastoma • Stage Ms Neuroblastoma • Knowledge of paraneoplastic syndrome (opsoclonus-myoclonus-ataxia and secretory diarrhea) • Management of clinical tumour-related problems, i.e., hypertension, spinal cord compression • Laboratory findings: urinary catecholamines, neuron specific enolase, ferritin and lactate dehydrogenase • Treatment and prognosis according to age, stage, histology and molecular-genetic aspects (such as MYCN amplification) • Role of MIBG scintigraphy for assessment of response • Immunotherapy (anti-GD2 therapy, retinoic acid) • Late effects and long-term follow-up • Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling	**3**

1C **Bone Tumours**	● Genetic (i.e., Rothmund-Thompson Syndrome/RECQL4, Li-Fraumeni/TP53, retinoblastoma/RB) and non-genetic predisposing factors (e.g., previous irradiation) and screening strategies in affected individuals. ● Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling ● Differential diagnosis of a suspected bone tumour, according to anatomic site (e.g., metaphyseal, diaphyseal or epiphyseal), patient's age and radiological aspects (e.g., Codman's triangle). Admission to a tumour orthopedic centre for biopsy and histopathological as well as genomic aspects, of osteosarcomas (e.g., high-grade vs. low-grade, genomic instability) and Ewing Tumours (EWS1-FLI1 fusion gene, MIC-99, epigenetics) ● Frequency and site of primary metastases (i.e., lung metastases, skip metastases) and staging investigations. ● Systemic therapy: Role of neoadjuvant chemotherapy to facilitate surgery and assess tumour response to treatment (good and poor response criteria). How to choose adjuvant chemotherapy. ● Local therapeutic approaches: Ablative (amputation and rotation plasties) vs. limbs salvage surgery (allo-, autografts or prostheses) and the role of radiotherapy (photon-, proton- or heavy ion therapy). ● Classification of resection margins and importance of completeness of surgical resection. ● Liquid biopsies in bone sarcomas ● Late effects and long-term follow-up after bone sarcoma therapy: Principles of rehabilitative and preventive care. ● Management of relapsed disease	**3**
1D **Soft Tissue Sarcoma**	● Diagnostic procedures, histological and biological subtypes of RMS, prognosis and inherent treatment stratification based on histology/molecular diagnosis, IRS-stage, size, site, and nodal stage. Importance of adequate local therapy, often including ● radiotherapy. Basic chemotherapy schedule for low, standard and high and very high-risk RMS ● Diagnostic procedures, main non-RMS STS subtypes, prognosis and inherent treatment stratification, based on histology/ molecular diagnosis, IRS-stage, grading (according to FNCLCC), size and localization ● Late effects and long-term follow-up ● Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling	**3**
1E **Retinoblastoma**	● Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling ● Staging of retinoblastoma according to tumour extent ● Indications for enucleation	**3**

	● Relationship between post-surgical tumour extension and treatment after enucleation ● Approach to bilateral retinoblastoma ● Role of conservative treatments, including new approaches ● Request of appropriate imaging examination for retinoblastoma ● Screening and follow up in siblings and descendants of a patient with retinoblastoma ● Secondary cancer after retinoblastoma ● Late effects and long-term follow-up	
1F **Hepatic Tumours**	● Differential diagnosis of right upper quadrant masses ● Congenital and acquired conditions associated with an increased risk of hepatoblastoma and hepatocellular carcinoma ● A basic understanding of the molecular biology of hepatoblastoma ● Role of serum α-fetoprotein in the diagnosis and monitoring of treatment in liver tumours ● PRETEXT staging system and associated annotation factors in hepatoblastoma ● Treatment of hepatoblastoma and hepatocellular carcinoma ● Prevention of cisplatin-induced ototoxicity ● Indications for liver transplantation in the management of hepatic tumours ● Late effects and long-term follow-up ● Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling ●	**2**
1G **Non-intracranial Germ Cell Tumours**	● Epidemiology and Biology ● Conditions predisposing to GCT ● Embryology and Histological classification ● Biomarkers and Molecular biology ● Diagnosis ● clinical presentation and investigations ● Treatment ● Surgery ● Chemotherapeutic strategies ● Current treatment approaches ● Follow-up and long-term effects ● Relapse treatment	**2**

1H Central Nervous System Tumours (CNS)	• Different biopathological types of brain tumours and related treatment (medulloblastoma, low grade glioma, high grade glioma, brainstem glioma, ependymoma, germ cell tumours, • craniopharyngioma, atypical teratoid/rhabdoid tumours and other rare brain tumours) • Accurate staging, including the use of RMI spine and CSF cytology in medulloblastoma, intracranial germ cell tumours and other selected tumours, serum and CSF tumour markers in intracranial germ cell tumours • Multimodal treatment concepts and role for targeted therapies • Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling • Impact of subgroups, variants, cytogenetics and other molecular abnormalities affecting prognosis and treatment (i.e. MYC family genes and β-catenin in medulloblastoma) • Complications and late effects arising from tumour, surgery, radiotherapy, and chemotherapy related to patient's age and stage of development (potential neurological, endocrinological, cognitive sequelae and behavioural changes) • Predisposition to CNS tumours Multiprofessional team approach (working in an interdisciplinary way) to rehabilitation aiming to improve functioning and reduce disability in long term survivors after a CNS tumor	**3**

Section 2: Malignant Haematology - Paediatric Myeloid Leukemia

Paediatric Myeloid Leukemia	Learning Points	Level
2A Acute Myeloid Leukemia (AML)	• Constitutional and genetic conditions predisposing to leukemia • Genetic classification • Management of the treatment-related complications, including tumour lysis, coagulopathy, thrombosis, infections, septic shock • Treatment according to different types of leukemia • Indications for bone marrow transplant • Current role of radiotherapy and associated complications • Cytogenetic and molecular aspects affecting prognosis and treatment in infants and children • Clinical, laboratory and molecular response to treatment for prognosis and treatment plan • Management of testicular, CNS and bone marrow relapse • Late effects and long-term follow-up	**3**

2B **MDS and JMML**	• Management of myelodysplastic syndrome and rarer forms of childhood leukemia (such as chronic myeloid leukemia and juvenile myelomonocytic leukemia) • Differential diagnoses of pancytopenia • Management options of low-grad MDS; observation, immunotherapy, HSCT • Management options of MDS with excess of blasts; limited effect of chemotherapy, HSCT • Diagnostics of JMML by clinical, haematological and genetic factors • Therapy depending on genetics varying from observation to HSCT • CML: knowledge of the initial therapy, cytoreductive therapy, and long-term therapy with tyrosine kinase inhibitors • Late effects and long-term follow-up	**3**
2C **Histiocytoses (LCH, rare non-LCH and HLH)**	• Classification of the histiocytosis • Diagnostic criteria • Staging and stratification of LCH • Prognostic factors in LCH • Standard treatment of multisystem LCH • Standard treatment of HLH • Late effects and long-term follow-up	**3**

Section 3: Malignant Haematology - Paediatric Lymphoid Malignancies

Paediatric Lymphoid Malignancies	**Learning Points**	**Level**
3A **Acute Lymphoblastic Leukemia (ALL)**	• Constitutional and genetic conditions predisposing to leukemia • Genetic classification • Management of the treatment-related complications, including tumour lysis, coagulopathy, thrombosis, infections, septic shock • Treatment according to different types of leukemia • Indications for bone marrow transplant • Current role of radiotherapy and associated complications • Cytogenetic and molecular aspects affecting prognosis and treatment in infants and children • Clinical, laboratory and molecular response to treatment for prognosis and treatment plan • Management of testicular, CNS and bone marrow relapse • Late effects and long-term follow-up	**3**

3B Hodgkin's disease	• Histological subtypes and influence on prognosis • Diagnostic procedures • Role of FDG-PET at diagnosis and in assessment of response and treatment intensity • Staging, stratification and therapy of patients according to international protocols • Potential late effects related to chemotherapy and radiotherapy: increased risk of second cancers mainly in patients receiving radiotherapy, cardiac and lung dysfunction, damage of reproductive function • Long-term follow-up	**3**
3C Non-Hodgkin's lymphoma	• Histological subtypes and influence on prognosis • Request of appropriate imaging examination at diagnosis and in assessment of response • Diagnostic procedures incl. possible diagnosis on tumour touch imprints and effusions (cytomorphology, immunophenotype, genetics) • Management of acute emergencies at diagnosis, including tumour lysis, mediastinal compressive syndrome, intestinal obstruction, airway compression and spinal cord compression • Staging, stratification and therapy of patients according to international protocols • Molecular-genetic characterization • Management of rare NHL subtypes • Late effects and long-term follow-up of NHL	**3**

Section 4: Non-Malignant Haematology - Red Blood Cell Disorders

Red Blood Cell Disorders	Learning Points	Level
4A Classification of anaemias	• Reticulocyte response (hypo/ non-hyporegenerative): evaluate COOMBS test and other hemolysis parameters • MCV values (normo-, micro-, macrocytic) • involvement other cells lines (isolated vs non isolated) • congenital (inherited/de novo) vs acquired: investigate family history/ past medical history/ drugs	**3**

Haemoglobinopathies **4B** **Sickle Cell Anaemia**	● Pathophysiology ● Genetic basis including variants in combination with thalassemia/other hemoglobinopathies ● Geographic distribution ● Clinical manifestation, age-related – multi-organ involvement including hematopoiesis, splenic function, pulmonary, CNS, liver, skeletal, renal ● Management of disease manifestations – acute events and chronic sequelae ● Approach to acute sickling events – anaemia (hemolysis vs aplastic crisis), pain crisis, acute chest, splenic sequestration, dactylitis, acute stroke, penile erection ● Approach to chronic sequalae – o indications for chronic transfusions (top-off vs exchange transfusions), management of these treatment protocols-complications (iron overload) o treatment of chronic pain o pulmonary hypertension ● Therapeutics – indications for hydroxyurea, newer therapies, stem cell transplantation ● Genetic counseling for affected persons and their families and family planning	**3**
4C **Thalassemia syndromes and other haemoglobinopathies**	● Pathophysiology ● Spectrum of thalassemia syndromes ● Clinical manifestation ● Diagnosis ● Treatment ● blood transfusion: transfusion dependent, non-transfusion dependent ● splenectomy ● fetal hemoglobin induction ● Stem cell transplantation ● Gene therapy ● Management of disease manifestations and chronic sequelae ● Iron Overload: monitoring, prevention, treatment ● Prognosis and follow-up ● Genetic counseling for affected persons and their families and family planning ● Psycho-social issues	3
4D **Hereditary Persistence of Fetal Hemoglobin (HPFH)**	● Pathophysiology ● Clinical Phenotype ● Genetic counseling for affected persons and their families and family planning	**2**

4D **Hereditary Persistence of Fetal Hemoglobin (HPFH)**	● Pathophysiology ● Clinical Phenotype Genetic counseling for affected persons and their families and family planning	**2**
4E **Methemoglobinemia**	● Pathophysiology and classification ● Etiology ● Clinical presentation ● Diagnosis ● Treatment ● Family counselling	**2**
4F **Other haemoglobinopathies**	● Pathophysiology ● Inheritance ● Clinical phenotype ● Evaluation and diagnosis ● Treatment Genetic counseling for affected persons and their families and family planning	**2**
4G **RBC membrane defects**	● Hereditary Spherocytosis ● Hereditary Elliptocytosis (HE) ● Hereditary Pyropoikilocytosis (HPP) ● Hereditary Stomatocytosis ● For each of the listed RBC membrane defects: ● Pathophysiology ● Clinical presentations ● Diagnostic testing ● Differential diagnosis ● Treatment options ● Prognosis Genetic counseling for affected persons and their families and family planning	**3**
4H **Enzyme Defects**	● Pyruvate Kinase Deficiency ● Glucose6-Phosphate Dehydrogenase Deficiency ● Other rare enzyme disorders ● For each of the listed enzyme defects: ● Pathophysiology ● Clinical presentations ● Diagnostic testing ● Differential diagnosis ● Treatment options ● Prognosis ● Genetic counseling for affected persons and their families and family planning	**2**
4I **Immune Haemolytic Anaemia**	● Classification: warm – cold agglutinins, paroxysmal cold hemoglobinuria ● Etiology ● Clinical presentation, diagnosis and therapy	**3**

4J **Congenital Dyserythropoietic Anaemias (CDA)**	● Classification: Type I-IV, CDA as part of a broader syndrome ● Clinical presentation ● Chronic sequelae ● Diagnosis ● Treatment ● Genetic counseling for affected persons and their families and family planning	**1**
4K **Blackfan-Diamond Anaemia** ***(also see bone marrow failure syndromes)***	● Genetic basis/inheritance/de novo, ribosomopathy ● Pathophysiology and genetic basis - ribosomopathy ● Clinical presentation ● Diagnostic testing – typical macrocytic, reticulocytopenic anaemia, bone marrow findings, ADA testing, genetic analysis ● Differential diagnosis – transient erythroblastopenia of childhood (TEC), congenital parvovirus infection, vitamin deficiencies, MDS, other BMF syndromes ● Clinical signs/symptoms ● Great range in clinical picture/severity (mild anaemia-transfusion dependence, genotype-phenotype) ● Possibility of trilineage involvement ● Physical anomalies – skeletal (triphalageal thimb), typical facies/upper body anomalies, G-U tract ● Increased risk for malignanacy – AML, ALL, lymphoma, breast cancer, colorectal carcinoma, osteogenic sarcoma ● Treatment options ● Steroids (recommended after 1st year, completion of vaccination schedule) ● Regular transfusion regimen – treatment of iron overload ● Stem cell transplantation, pre transplant iron overload need to be abated due exquisite sensitivity of DBA patients to this risk, post SCT late tumours risk ● Prognosis ● Genetic counseling for affected persons and their families and family planning ● Age related issues	**2**
4L **Transient Erythroblastopenia of Childhood**	● Pathophysiology ● Clinical manifestation ● Diagnostic testing ● Differential diagnosis ● Treatment options ● Prognosis	**3**
4M **Pure Red Cell Aplasia (aquired)**	● Pathophysiology – autoimmune, T-cell mediated ● Clinical manifestation ● Diagnosis/Differential diagnosis (rule out secondary causes) ● Treatment options – steroids, cyclosporin A	**1**

	● Prognosis ● Psycho-social issues	
4N **Pearson's Syndrome**	● Pathophysiology and genetic basis – Mitochondrial DNA disorders ● Clinical manifestation – neutropenia, pancreatic failure, delay/loss of developmental milestones ● Differential diagnosis ● Treatment options – supportive therapy ● Prognosis -poor ● Genetic counseling for affected persons and their families and family planning ● Psycho-social issues	**1**
4O **Nutritional Anemias**	● Iron Deficiency Anaemia ● Iron metabolism and pathophysiology ● Risk factors: diet, age, population ● Clinical presentation: microcytic anaemia ● Diagnosis: hemogram abnormalities, iron balance ● Prevention and treatment ● Iron-Refractory Iron Deficiency Anaemia ● Pathophysiology and epidemiology ● Clinical presentation: microcytic anaemia, peculiar iron pattern deficiency ● Diagnostic evaluation: iron balance, response to iron treatment, genetic testing ● Treatment: i.v. iron and supportive treatment ● Prognosis ● Genetic counseling ● Vitamin B12 and Folate Deficiency Anaemia o Pathophysiology o Etiology – Risk Factors o Clinical presentation: megaloblastic anaemia, neurological symptoms, neuropsychiatric symptoms ● Diagnosis: hemogram abnormalities, vitamin B12 and folate serum levels o Prevention and treatment	**3**
4P **NEONATAL ANAEMIAS**	● Normal CBC values by gestational and post-natal age ● Differential diagnosis of neonatal anaemia ● Reduced red cell production ● Parvovirus B19 ● Diamond Blackfan Anaemia ● Hemolysis ● Red cell enzymopathies ● Red cell membrane disorders ● Haemoglobinopathies presenting in the neonate ● Alloimmune (hemolytic disease of the newborn) ● Blood loss ● feto-maternal ● twin-twin	**3**

4Q ERYTHROCYTOSIS/ POLYCYTHEMIA	• Definition • Etiology: • Relative (i.e. volume depletion) • Secondary acquired (i.e. increased EPO production for cardiopulmonary disease or ectopic production, high androgens, etc.) • Juvenile/Familial erythrocytosis • Polycythemia Vera/myeloproliferative neoplasm, • Clinical presentation • Evaluation: hemogram, pulse oximetry, P50, serum EPO, serum chemistry, radiological evaluation, , enzyme deficiency, , genetic analysis - *HBB, HBA, BPGM, PKLR, VHL, EGLN1, EPAS1, EPO, EPOR, JAK1 or WGS/WES*) • Complications • Treatments and follow-up Genetic counseling for affected persons and their families and family planning	**2**

Section 5: Non-Malignant Haematology - Bone Marrow Failure Syndromes

Bone Marrow Failure Syndromes	Learning Points	Level
5A Congenital amegakaryocytic thrombocytopenia (CAMT)	• Pathogenesis/molecular basis(*c-mpl, TPO*) – megakaryocyte signaling • Differential diagnosis – NAIT (neonatal alloimmune thrombocytopenia), TAR, congenital infections • Diagnosis – plasma TPO level, mutation analysis, R/O NAIT, congenital infections, bone marrow analysis • Clinical manifestations – thrombocytopenia (neonatal), pancytopenia (by 2nd decade), MDS/AML • Treatment – TPO agonists, platelet transfusions, PC transfusions, GCSF, stem cell transplantation – NOT indicated if the causative mutation is in TPO! (produced in the liver) • MDS/AML screening, surveillance • Genetic counseling for affected persons and their families and family planning	**2**

**5B
CARD11**
	• Pathophysiology and genetic basis
	• Diagnostic testing –NGS panels vs WES, testing in non-hematopoietic tissue
	• Differential diagnosis – other bone marrow failure syndromes, MDS, ALPS, other causes of immune dysregulation
	• Systems involved, varied clinical presentations:
	  • Allergy and atopic disease
	  • Autoimmunity
	  • Immune dysregulation
	  • Susceptibility to infections
	  • Neutropenia
	  • Lymphoproliferative disease
	  • B cell defect and hypogammaglobulinemia
	• Bone marrow failure
	• Other
	• Cancer predisposition (Lymphoma)
	• Treatment options and indications:
	  • Stem cell transplantation
	  • Side effects and potential complications
	• Prognosis
	• Secondary malignancies surveillance program
	• Genetic counseling for affected persons and their families and family planning
	• Psycho-social issues
		1

5C DADA2 (adenosine deaminase deficiency)	• Pathophysiology, genotype-phenotype association • Diagnostic testing – enzymatic, molecular analysis • Differential diagnosis – other BMF, rheumatic diseases, autoinflammatory diseases • Clinical manifestations – hematologic, vasculitis (PAN, vascular accidents seen massive PE- erythema nodosum, livedo racemose, arthritis/algia, CNS), immune deficiency • Treatment options – TNF blockade, other immune suppression/modulation, regular transfusions, stem cell transplantation • Genetic counseling for affected persons and their families and family planning	**2**

5D
Diamond Blackfan Anaemia
 	
(also see Red Cell Disorders)
	• Genetic basis/inheritance/de novo, ribosomopathy
	• Pathophysiology and genetic basis - ribosomopathy
	• Clinical presentation
	• Diagnostic testing – typical macrocytic, reticulocytopenic anaemia, bone marrow findings, ADA testing, genetic analysis
	• Differential diagnosis – transient erythroblastopenia of childhood (TEC), congenital parvovirus infection, vitamin deficiencies, MDS, other BMF syndromes
	• Clinical signs/symptoms
	  ◦ Great range in clinical picture/severity (mild anaemia-transfusion dependence, genotype-phenotype)
	  ◦ Possibility of trilineage involvement
	  ◦ Physical anomalies – skeletal (triphalangeal thumb), typical facies/upper body anomalies, G-U tract
	  ◦ Increased risk for malignancy – AML, ALL, lymphoma, breast cancer, colorectal carcinoma, osteogenic sarcoma
	• Treatment options
	  ◦ Steroids (recommended after 1st year, completion of vaccination schedule)
	  ◦ Regular transfusion regimen – treatment of iron overload
	  ◦ Stem cell transplantation, pre transplant iron overload need to be abated due exquisite sensitivity of DBA patients to this risk, post SCT late tumours risk
	• Prognosis
	• Genetic counseling for affected persons and their families and family planning
	• Age related issues
		2

5E
Dyskeratosis Congenita
	• Pathophysiology and genetic basis
	• Diagnostic testing – telomere length flow-FISH vs ELISA, genetic analysis – panels vs WES, testing in non-hematopoieticc tissue
	• Differential diagnosis – short telomeres in SAA, MDS
	• Systems involved, varied clinical presentations, included age-related manifestations
	  ◦ Bone marrow failure, MDS, AML
	  ◦ Lung
	  ◦ Liver
	  ◦ GIT
	  ◦ Brain
	  ◦ Skin
	  ◦ Vascular fragility -bleeding
	  ◦ Other
	  ◦ Cancer predisposition
		2

	• Treatment options – indications, androgens – how they work, GSCF/TPO-RA (discuss possible clinical use, /EPO, • Stem cell transplantation - side effects, potential complications (including increased risk for late tumours as in all constitutional BMF) • Prognosis • Preventative cancer screening/surveillance regimen • Genetic counseling for affected persons and their families and family planning • Psycho-social issues	

5F
Fanconi anaemia
	• Pathophysiology and genetic basis
	• Diagnostic testing – chromosomal breakage (DEB and/or MMC test), evaluation of cellular cycle arrest in G2, Western Blot test for FANCD2 ubiquitination, genetic analysis – NGS panels vs WES, testing in non-hematopoietic tissue, somatic mosaicism
	• Differential diagnosis – telomeropathies, other bone marrow failure syndromes, MDS, other syndromes with VACTER-L anomalies
	• Systems involved, varied clinical presentations, included age-related manifestations
	  • Short stature and failure to thrive
	  • Genitourinary apparatus
	  • Bone
	  • Skin
	  • Bone marrow failure, MDS, AML
	  • Other
	  • Cancer predisposition
	• Treatment options and indications:
	  • Androgens and how they work,
	  • GCSF/EPO,
	  • Stem cell transplantation
	  • Gene therapy (available on selected experimental trials)
	  • Side effects and potential complications (i.e. Increased risk/earlier onset of post SCT tumours as in all constitutional BMFs)
	• Prognosis
	• Secondary malignancies surveillance program
	• Genetic counseling for affected persons and their families and family planning
	• Psycho-social issues
		3

5G **MECOM associated syndromes**	• Pathophysiology and genetic basis • Diagnostic testing –NGS panels vs WES, testing in non-hematopoietic tissue, dominant transmission, high percent *de novo* • Differential diagnosis – CAMT other bone marrow failure syndromes, MDS • Systems involved, varied clinical presentations, • Bone (especially radioulnar synostosis, RUS)	**1**

	• Bone marrow failure, amegakaryocytic thrombocytopenia • Congenital heart defects • Renal malformations • Deafness • Immunological impairment (B-cell deficiency and hypogammaglobulinemia) • Endocrine system • Other • Treatment options and indications: - • Stem cell transplantation • Side effects and potential complications • Prognosis • Genetic counseling for affected persons and their families and family planning • Psycho-social issues	
5H **OHDO syndrome**	• Pathophysiology and genetic basis • Diagnostic testing –genetic analysis –> gene-target deletion/duplication analysis or NGS/WES panels, testing in non-hematopoietic tissue • Differential diagnosis – other bone marrow failure syndromes, MDS • Systems involved, varied clinical presentations, included age-related manifestations • Craniofacial alteration • Short stature and failure to thrive • Development and behavior • Central nervous system • Musculoskeletal • Auditory and ophthalmological alterations • Genitourinary system • Cardiopulmonary system • Bone marrow failure • Other • Treatment options and indications: • GCSF/EPO • Supportive therapy • Stem cell transplantation • Side effects and potential complications • Prognosis • Genetic counseling for affected persons and their families and family planning • Psycho-social issues	**1**
5I **SAMD9/L mutation-syndrome**	• Pathophysiology – relationship to chromosome 7 aberrations (“self-correction”), marrow failure opposed to MDS/AML • Diagnostic testing – new player in the field of SAA/MDS analyses, need high clinical suspicion, include in all aplastic anaemia workup, • Clinical manifestations: cytopenias, Neurologic symptoms (e.g. ataxia)	**2**

	• Differential diagnosis – SAA vs MDS, other BMF syndromes, • AML/MDS work-up including cytogenetics, somatic analysis is essential • Treatment decision tree – watch-and-wait vs growth factors vs stem cell transplantation • Prognosis (still being discovered) • Genetic counseling for affected persons and their families and family planning • psycho-social issues – segregation studies are necessary, asymptomatic mutation "carriers"	

5J
Severe Congenital Neutropenia
	• Wide variety of genes involved, inheritance, pure neutropenia vs syndromic (SBDS is in a separate section), pathogenesis of the major sub-types (*ELANE, HAX1, SRP54*)
	• Diagnostic testing – autoantibody testing (positive does not rule-out!), typical bone marrow early maturation arrest (not in all cases), genetic analysis – panels, WES
	• Differential diagnosis – post-infectious, allo-immune, autoimmune, other BMF syndromes, MDS
	• Clinical picture
	  • Typical infections (early onset, gingivitis, skin, deep-seated), typical bacteria
	  • Cyclic vs chronic neutropenia
	  • Severity of neutropenia
	  • Syndromic cases (genes involved – e.g. G6PC3, SRP54, others)
	• Treatment options –
	  • GCSF preventatively vs per infection ** recommendation is for continuous GCSF treatment at the least effective dose, when to initiate GCSF therapy?
	  • proper antibiotic/antifungal therapy,
	  • need for expert infectious disease consults,
	  • Stem cell transplantation When to transplant?
	• MDS/AML surveillance – CBC vs marrow analysis, cytogenetic/chromosomal abnormalities, recognized somatic mutations (GCSF-R, RUNX1)
	• Prognosis – malignancy rates in various sub-types
	• Genetic counseling for affected persons and their families and family planning
	• Psycho-social issues – chronic treatment
		2

5K **Shwachman-Diamond Syndrome**	• Pathophysiology and genetic basis - ribosomopathy • Diagnostic testing□genetic analysis – NGS panels vs Sanger evaluation, testing in non-hematopoietic tissue, tests for pancreatic insufficiency (fecal elastase, low serum pancreatic trypsinogen (<3yrs) and low iso-amylase (>3yrs) • Differential diagnosis – telomeropathies, SCN, other bone marrow failure syndromes, MDS	**2**

	• Systems involved, varied clinical presentations, included age-related manifestations
	  • Short stature and failure to thrive
	  • Bone
	  • Exocrine pancreatic failure and malabsorption
	  • High susceptibility to infections
	  • Genitourinary apparatus
	  • Cardiovascular apparatus
	  • Endocrine system
	  • Skin
	  • Oral and dental alteration
	  • Bone marrow failure, MDS, AML
	  • Behavioral disorders and cognitive deficits
	  • Cancer predisposition
	  • Other
	• Treatment options and indications:
	  • GCSF
	  • Endocrine and malabsorption management
	  • Stem cell transplantation
	  • Side effects and potential complications (i.e Increased risk of post SCT tumours as in all constitutional BMFs)
	• Prognosis
	• Secondary malignancies surveillance program
	• Genetic counseling for affected persons and their families and family planning
	• Psycho-social issues	

5L Acquired Aplastic Anaemia	• Recognize and diagnose patients with acquired aplastic anaemia • Understand the potential causes (e.g. auto-immune, toxic) • Manage patients with acquired aplastic anaemia	**3**

Section 6: Non-Malignant Haematology - Isolated Neutropenia

Isolated Neutropenia	Learning Points	Level
6A Neutrophil normal ranges	• Awareness that neutrophil normal ranges vary between some populations/ethnicities	**1**
6B Neutrophil production defects	• See bone marrow failure section • See also PID section for discussion around neutrophil function defects • Neutropenia in prematurity -seen not uncommonly in preterm infants; often of multifactorial cause	**2**

6C **Transient viral neutropenia**	• Transient neutropenia-common following viral infection in children; generally self-resolving	**3**
6D **Drug induced neutropenia**	• Importance of knowledge of medication history • Drugs known to cause neutropenia, including but not limited to carbamazepine, colchicine, some antibiotics	**3**
6E **Immune mediated neutropenia**	• Alloimmune neutropenia -transplacental antibodies to human neutrophil antigens due to mismatch between maternal and paternal antigens. • Autoimmune neutropenia as a post viral phenomenon in children -Diagnosis – anti-neutrophil antibodies -Natural history – the majority resolve but can take many months -Clinical management – most children do not need any regular medication and need advice and education around management of fever. Prophylactic antibiotics and/or GCSF rarely required.	**3**
6F **Chronic immune neutropenia due to immune dysregulation**	• Non remitting neutropenia with and without antibodies against neutrophils • Delayed diagnosis • Sometimes anticipatory sign of immune dysregulation • Underlying variants of immune-dysregulation	**2**

Section 7: Non-Malignant Haematology - Primary Immunodeficiencies (PID)

Primary Immunodeficiencies	Learning Points	Level

7A
PID Classification
	Knowledge of main PID categories:
	• **Immunodeficiencies affecting both cellular and humoral immunity**
	  ◦ T-B+ Severe Combined Immune Deficiency (SCID)
	  ◦ T-B- SCID
	  ◦ Combined Immunodeficiency (CID), generally less profound than SCID
	• **Combined immunodeficiencies with associated or syndromic features**
	  ◦ Immunodeficiency with congenital thrombocytopenia
	  ◦ DNA repair defects
	  ◦ Thymic defects with additional congenital anomalies
	  ◦ Immuno-osseous Dysplasia
	  ◦ Hyper IgE Syndromes (HIES)
	  ◦ Defects of vitamin B12 and folate metabolism
		1

	• Anhidrotic Ectodermodysplasia with immunodeficiency (EDA-ID) • Calcium channel defects • Others • **Predominantly antibody deficiencies** • Severe reduction in ALL serum immunoglobulins (Igs) isotypes with profoundly decreased or absent B cells, Agammaglobulinemia • Severe reduction in at least 2 serum Igs isotypes, with normal or low number of B cells, Common Variable Immune deficiency (CVID) phenotype • Severe reduction in serum IgG and IgA, with normal/elevated IgM and normal number of B cells, Hyper IgM • Isotype, light chain, or functional deficiencies with generally normal numbers of B cells • **Diseases of immune dysregulation** • Familial Hemophagocytic Lymphohistiocytosis (FHL syndromes) • FHL with Hypopigmentation • Regulatory T-cell defects • Autoimmunity with or without lymphoproliferation • Immune dysregulation with Colitis • Autoimmune Lymphoproliferative Syndrome (ALPS) • Susceptibility to EBV and lymphoproliferative conditions • **Congenital defects of phagocyte number and function** • Congenital neutropenias • Defects of Motility • Defects of Respiratory Burst • Other non-lymphoid defects (incl. GATA2 deficiency) • **Defects in intrinsic and innate immunity** • Mendelian Susceptibility to mycobacterial disease (MSMD) • Epidermodysplasia verruciformis (HPV) • Predisposition to Severe Viral infections • Herpes Simplex Encephalitis (HSE) • Predisposition to INVASIVE Fungal disease • Predisposition to Mucocutaneous Candidiasis • TLR Signaling Pathway deficiency with Bacterial susceptibility • Other Inborn Errors of Immunity related to non-hematopoietic tissues • Other Inborn Errors of Immunity related to leukocytes	

	• **Autoinflammatory disorders**
	  • Type 1 Interferonopathies
	  • Defects affecting the Inflammasome
	  • Non-Inflammasome related conditions
	• **Complement deficiencies**
	• **Bone marrow failure**
	• **Phenocopies of inborn errors of immunity**
	  • associated with somatic mutations
	  • associated with autoantibodies	

7B
PID - Diagnosis
	• Recognize PID patterns and main Warning Signs of PID in paediatric patients.
	• Take an accurate personal and family history
	• If PID is suspected or runs in the family, delay live-attenuated vaccinations and do not postpone immunological investigations.
	• Investigate clinical history, including maternal pregnancy and neonatal history, growth and development, vaccine history, ongoing/previous treatments, concomitant/previous disease, family history, social history
	• Investigate features of infections (age at onset, length/ frequency/severity of infectious episodes, sites of infections, recurrence at particular sites, microbiological etiology, treatment and response to it)
	• Perform a focused complete clinical examination to assess for nutritional status, dysmorphic features, alterations in skin and annexes/oral cavity/ENT/lungs/heart/lymphoid tissue/joints/nervous system, clubbing, hepatosplenomegaly
	• Set up a clinical presentation-guided diagnostic process, including general screening tests and immunological investigations.
	• Use age-matched reference values to avoid misinterpretation of immunological test results.
	• First step investigations:
	  • CBC with leucocyte differential
	  • Immunoglobulin isotype levels (Ig GAME)
	• Second step immunological investigations:
	  • Lymphocyte subsets analysis
	  • Specific antibody response to vaccine antigens
	  • IgG subclasses analysis
	  • Lymphocyte function testing (with mitogen and Ag stimulation)
	• In case of hypogammaglobulinemia, exclude causes of secondary forms.
	• In case of CD4+ T-cell lymphopenia, exclude HIV infection
		2

	• Indication to more specific tests according to suspected type of PID (based on clinical presentation):
	  • Neutrophil oxidation burst
	  • Complement screening
	  • Phagocyte studies
	  • Enzymatic activity (e.g. ADA, PNP)
	  • NK cytotoxicity studies
	  • Cytokine/Cytokine receptor studies, anti-cytokine antibodies
	• Genetic counseling for affected persons and their families and family planning
	• Family/genetic studies (single gene analysis, NGS panels of selected genes, WES/WGS, trioanalysis – functional tests for validation needed in selected cases)
	• Newborn screening for PID available in some countries	

7C **PID - SCID**	• Knowledge that SCID is a medical emergency! • Maternal engraftment should be excluded in case of apparently normal T-cell count in high clinical suspicion • Knowledge that “Leaky” SCID or Omenn Syndrome (OS) can be caused by hypomorphic mutations in genes known to cause classical SCID	**1**
7D **PID - Non - SCID**	• T-cell defects are at risk for infections from opportunistic pathogens □ PJP prophylaxis is needed • Timely recognition of antibody deficiency prevents future organ damage.	**2**
7E **PID - CVID**	• Knowledge that morbidity is not limited to infections, but also to non-infectious complications: splenomegaly, chronic gastrointestinal disease, chronic pulmonary disease, bronchiectasis, autoimmune cytopenias, granulomas, tumours. • Monitoring and early treatment of associated diseases	**2**
7F **PID - Treatment**	• Antimicrobial prophylaxes (bacterial, fungal viral, PJP) • Aggressive and timely treatment of infections • Immunoglobulin replacement (sc/iv) • Immune suppressants • Biologic agents in selected diseases (es. Abatacept in LRBA deficiency) • Allogeneic HSCT • Autologous Gene therapy	**2**
7G **PID - Other**	• Prognosis and follow-up (including autoimmune manifestations and tumours) • Genetic counseling for affected persons and their families and family planning • Psycho-social issues	**1**

Section 8: Non-Malignant Haematology - Platelet Disorders, Thrombosis and Hemostasis

Platelet Disorders, Thrombosis and Hemostasis	Learning Points	Level
8A Bleeding disorders – General	• Relevant and accurate personal and family bleeding history • Focused clinical examination to assess for abnormal bleeding symptoms and signs • Comprehensive differential diagnosis, including acquisition of relevant laboratory tests • Management plan for patients with abnormal bleeding, including familial genetic counseling, management in case of bleeding, trauma or surgery and multidisciplinary guiding • coagulation pathways including control mechanisms and fibrinolysis	**3**
8B Hemophilia A and B	• Clinical manifestations of hemophilia • Diagnosis of hemophilia A and B by interpretation of laboratory tests, diagnosis of patients with inhibitors to FVIII and FIX • Genetics of hemophilia patients and carriers, the impact of genetics upon future risk (e.g.: inhibitor formation) • Hemophilia treatment in case of bleeds, trauma or surgery (desmopressin, factor replacement, bypass agents, antifibrinolytics) • Hemophilia prophylaxis - replacement therapy (primary and secondary prophylaxis, use of coagulation concentrates) and non-replacement therapy (NRT, e.g. Emicizumab) • Joint pathology and long term outcomes in hemophilia • Hemophilia treatment in the presence of inhibitors including treatment of bleeds, immune tolerance induction therapy and treatment with prophylaxis, including NRT (e.g. emicizumab). • Current status and studies of gene therapy in hemophilia. • Genetic counseling for affected persons and their families and family planning	**3**
8C Von Willebrand Disease (VWD)	• Understanding the incidence, inheritance, classification (including molecular and genetic aspects), clinical manifestations, natural history and clinical complications of patients with VWD • Diagnosis and classification of VWD subtypes (Type 1, 2A, 2B, 2M, 2N and 3) by interpretation of laboratory tests including coagulation factors levels and activity, platelet aggregation studies and	**3**

	interpretation of VW multimers' studies and molecular diagnostics. ● Treatment of bleeds and surgery in patients with VWD, including use of desmopressin acetate, FVIII/VWF concentrates, antifibrinolytics and supportive care (e.g.: oral contraceptives for women).	
8D Rare Bleeding disorders	● Pathophysiological mechanisms, incidence, clinical manifestations and treatment of quantitative and qualitative disorders of factor II, V, VII, X, XI, XIII, fibrinogen, and other isolated and combined rare bleeding disorders and relate this to clinical management of patients with these disorders ● Predisposition syndromes, genetic methodologies incl. interpretation of the results, genetic counseling ● Management of patients with rare bleeding disorders during prophylaxis or interventions (eg: acute bleeding, surgery)	**2**
8E Platelet Disorders	● Diagnostic pathway for patients with thrombocytopenia and platelet function defects ● Diagnosis and management of patients with immune thrombocytopenia (ITP), indications for treatment and treatment options, including steroids, immunoglobulins, Anti D, anti-CD20, thrombopoietin mimetics and splenectomy. ● Diagnosis and management of patients with drug-induced platelet disorders ● Diagnosis of patients with hereditary disorders of platelet function, including Bernard Soulier syndrome and Glanzmann thrombasthenia. Interpretation of results of light transmission aggregometry and flow cytometry analysis of these disorders. ● Genetics of hereditary platelet disorders ● Management of patients with hereditary disorders of platelet function. Treatment plans of bleeding episodes, surgical interventions etc., taking into consideration the status of anti- platelet antibodies ● Diagnosis and management of patients with congenital and acquired thrombotic thrombocytopenic purpura (TTP) as well as other microangiopathic disorders ● Diagnosis and management of patients with heparin-induced thrombocytopenia (HIT)	**3**
8F Hemostasis in the newborn	● Relating knowledge of developmental hemostasis to the interpretation of laboratory coagulation tests (coagulation factors activity, natural coagulation inhibitors and global hemostatic assays) for clinical management of neonates and children	**2**

	• Diagnosis and management of hemorrhagic disease of the newborn, including vitamin K deficiency • Diagnosis and management of thrombocytopenia in neonates including applying and interpreting tests for diagnosis of fetal and neonatal alloimmune thrombocytopenia	
8G Bleeding diathesis without diagnosis	• Differential diagnosis in case no coagulation disorder is found, with laboratory testing and when and to whom to refer (i.e. non-accidental injuries (child abuse, auto-mutilation), hormonal causes of menorrhagia, hereditary hemorrhagic telangiectasia, connective tissue disease like Ehlers Danlos).	**1**
8H Thrombotic disorders	• Epidemiology and molecular basis of thrombotic disorders in children affected by these conditions • Relevant personal and family history • Understanding the normal hemostatic parameters in neonates, children and adolescents, particularly in relation to inhibitors of coagulation and the fibrinolytic system • Diagnosis of hypercoagulable states (inherited and acquired) by interpreting laboratory tests, and the use of age adjusted normal ranges during childhood • Indications for thrombophilia testing • Recognizing the presentation of homozygous protein C and S deficiency and treatment plan • Interpretation of the clinical relevance of heritable thrombophilia to venous and arterial thrombosis in paediatric patients and provide family counseling in case of thrombophilia and/or positive family history for thrombosis • Diagnosis and management of thrombosis during childhood (including treatment options, treatment duration, supportive care and follow-up)	**3**
8I Clinical aspects of venous thromboembolism	• Understanding the types and locations of thrombosis observed in neonates, children and adolescents • Risk factors for thrombosis in neonates, children and adolescents • Diagnosis of patients with suspected VTE by request of appropriate imaging examination (US-Doppler, CTA, CTV, MRV) • Treatment of patients with acute VTE • Risk of recurrence in patients with VTE and risk-based treatment plans • Recognition and management of patients with post-thrombotic syndrome	**3**

8J **Clinical aspects of arterial thromboembolism**	• Types and locations of arterial thrombosis observed in neonates, children and adolescents • Risk factors for arterial thrombosis in neonates, children and adolescents • Diagnosis of patients with suspected arterial thrombosis by proper imaging studies (CT, CTA, MRI/ MRA) • Treatment of patients with acute arterial thrombosis (including indications for thrombolysis / thrombectomy) • Relating the principles of the epidemiology of arterial thrombosis to clinical care of children affected by these disorders • Age-related therapy considerations relevant to perinatal stroke, perinatal arterial thrombosis and arterial thrombosis in children/ adolescents • Evaluation and management of patients with arterial thrombosis, including cerebrovascular risk factors and anatomic malformations (eg: Moya – Moya syndrome, Kawasaki disease)	**3**
8K **Antithrombotic therapy**	• Indications and methods of anticoagulation, thrombolysis, thrombectomy in neonates, children and adolescents • Indications and methods of prophylactic anticoagulation in children and adolescents (primary and secondary) • Applying the understanding of the mechanisms of action and therapeutic indications of anticoagulant agents in patients' management • Management of children receiving anticoagulants, including advice on duration and intensity and interactions with other medications • Interpretation of tests for anticoagulant control (e.g. INR, aPTT, anti-Xa levels, thrombin clotting time, specific trough/ levels) • Management of anticoagulation and antiplatelet therapy in association with invasive procedures • Management of patients with anticoagulant associated bleeding • Management of patients on antiplatelet agents • Management of patients on fibrinolytic drugs, including streptokinase, urokinase, t-PA	**2**

Section 9: Hematopoietic Stem Cell Transplantation and Gene Therapy (HSC-GT)

HSCT and HSC-GT	Learning Points	Level
9A Indications to allogeneic HSCT	• Hematologic malignancies (Leukemias, Lymphomas, Myelodysplastic syndromes) • Inherited Bone Marrow Failure Syndromes • Hemoglobinopathies (Thalassemia, Sickle Cell Disease) • Inborn Errors of Immunity (including Primary HLH and autoinflammatory diseases) • Inborn errors of metabolism (MLD; X-ALD; MPSIH; MPSIIIA; others) • Infantile Malignant Osteopetrosis • Secondary HLH • Autoimmune Diseases (selected cases)	**3**
9B Indications to autologous HSCT	• Malignancies requiring high-doses chemotherapy • Autoimmune Diseases (selected cases)	**3**
9C Indications to HSC-GT	• Inborn errors of immunity (ADA-SCID; SCID-X1, WAS, X-CGD and p47 CGD; LAD, RAG1-SCID; Artemis-SCID) • Hemoglobinopathies (ß-Thalassemia; Sickle Cell Disease) • Inherited Bone Marrow Failure Syndromes: Fanconi Anaemia • Inborn Errors of Metabolism (MLD; C-ALD, MPSIH, MPSIIIA, Fabry disease) • Clinical trials vs standard of care	**2**
9D Indications for CAR T cells	• CAR cell therapy for acute lymphoblastic leukemias • Emerging indications for lymphomas and other haematological malignancies • Emerging indications for solid and brain tumours	**3**
9E Other cellular therapies	• DLI • Virus-specific T cells • NK cells • Cytokine-induced killer (CIK) cell • Mesenchymal stromal cells • Dendritic cells • CARs: T, NK and CIK	**1**
9F Mobilization, collection and manipulation of HSC	• Identification of target dose • Bone marrow harvesting, Leukapheresis and cord blood procurement • Graft manipulation	**1**

9G Criteria for selection of intensity for the preparative regimens	• Myeloablative conditioning (MAC), Reduced Toxicity conditioning (RTC), Reduced Intensity Conditioning (RIC) • Chemotherapy, irradiation, serotherapy and biological agents	**1**
9H Identification and selection of stem cell donor	• Donor type (autologous, HLA-identical family donor, unrelated donor, haploidentical family donor) • HSC source (BM-derived HSC, mobilized peripheral HSC, cord blood) • HLA and other non-HLA compatibility assessment	**1**
9I Acute and chronic graft-versus-host disease (GvHD)	• Pathogenesis • Clinical presentation and grading • Therapy	**2**
9J Other (early) complications	• Infectious complications • Bleeding and thrombotic complications • Graft failure • Early complications of endothelial origin • Chemo & radiotherapy-related acute toxicities • Cytokine Release Syndrome • Autoimmune cytopenias • Thymic exhaustion	**2**
9K Late complications	• Late complications from chemo/radiotherapy, biologicals and immunosuppressive agents • Secondary cancer, Post-Transplant Lymphoproliferative Disease (PTLD) • Insertional mutagenesis (only HSC-GT) • Growth and development issues	**2**
9L Post-transplant monitoring	• CVC management • Infection control and isolation procedures • Prevention and management of GvHD, graft rejection, relapse of malignancy • Psychological support, schooling and education program during HSCT • Monitoring and management of the principal advanced cellular therapies toxicities • Monitoring of immune reconstitution and chimerism • Monitoring of chimerism	**1**
9M Paediatric fertility preservation program	• Specific fertility preservation strategy and gametes cryopreservation • Protection of gonadal function during chemotherapy	**2**

Section 10: Special Aspects of Paediatric Transfusion Management

Transfusion Management	Learning Points	Level
10A **Neonatal and Paediatric compatibility testing**	• Maternal antibody testing for neonates • Importance of maternal transfusion history and baby's transfusion history (including transfusions given in utero) • Compatibility requirements for neonates and infants	**2**
10B **Component specifications**	• Fetal/Neonatal/Infant specification components (donor specifications, antibody testing, CMV testing, age of red cell components) -use of neonatal split red cell packs for top up transfusion (minimizing donor exposure) -component specifications for small and large volume transfusions in neonates (including neonatal exchange) -knowledge of specification and volumes available (country-specific in terms of exact unit specifications) • Components for cardiac surgery -age of product (theoretical risks of hyperkalemia)	**1**
10C **Neonatal and paediatric transfusion thresholds and indications**	• Red cells -transfusion thresholds in neonate and children - formula to calculate volume required (in mL) • Platelets -transfusion thresholds in neonates and children -volume for transfusion • Plasma/cryoprecipitate -inductions for transfusion -volumes required • Granulocyte transfusions -indication – refractory infections in severe neutropenia	**3**
10D **Special requirements relevant to neonatal and paediatric practice**	• Knowledge of appropriate use of : -CMV negative components -Irradiated components -Rh phenotype matched (sickle, thalassemia and other chronically transfused patients) -age of red cell components	**3**

10E **Special transfusion situations in neonates and children**	• Intrauterine transfusions -product specifications and special requirements • Fetal/Neonatal alloimmune thrombocytopenia -laboratory investigation of FNAIT -transfusion and clinical management of NAIT (for example HPA1a5b negative platelets*) • Neonatal exchange transfusion -management of hemolytic disease of the newborn -provision of red cells • Exchange transfusion in red cell disorders (in older children) -red cell requirements -complications of exchange transfusion • Massive hemorrhage in infants and children -Evidence for and use of tranexamic acid -Blood product management -Management of coagulopathy	**3**
10F **Transfusion complications/reactions and hemovigilance**	• As per adult practice but to include more paediatric complications of transfusion such as TANEC (transfusion associated necrotizing enterocolitis), issues with patient identification and • inappropriate volumes transfused.	**2**
10G **Paediatric aspects of PBM (Patient blood management)**	• As per adult practice but also: -Minimizing blood sampling/sample volume -Use of near patient testing -Delayed cord clamping -Appropriate management of iron deficiency/hematinic deficiency • -If appropriate use of cell salvage	**2**

C. Governance

The paediatric oncologist is the coordinating pillar of the oncological team. Thus, continuous medical education is highly recommended. The first step is to allow access to information and practical skills, secondly to allow trainees to practice under supervision so that, thirdly, they can become self-sufficient in their practice.

Of note, it is also important to consider that not all European countries have a combined training pathway of haematology and oncology. In such situations, each country should be allowed to keep their separate training programmes and subspecialize in either haematology (malignant and non-malignant) or oncology (solid tumours). Recommendations for the requirements in knowledge will be presented together in this document but should be adapted to each country's training pathway circumstance.

3. CONTINUOUS MEDICAL EDUCATION

Training opportunities should be available for postgraduate professionals, namely trainees. Continuous professional development for both young and experienced paediatric oncologists and the junior faculty must be mandatory. Proper funding opportunities for these activities should also be encouraged by institutions, national societies, and European authorities, to strengthen the multistakeholder network in paediatric oncology.

Training courses, workshops, and fellowship programmes should be organised at national and international levels, so as to allow access to expert opinion and experience in order to achieve basic and clinical knowledge. Continuous professional development needs to be done by participating in national and international conferences and meetings. Furthermore, institutions or local/European societies should encourage participation in training courses held by experts in the field. Courses are based on novelties regarding diagnosis, treatment, prognosis and clinical research, but can also be based on experience (e.g., case reports). Funding mobility is a common hurdle and must be encouraged by institutions, local societies, and European authorities. Appropriate resources and time for attendance at training and education meetings must be built into the programme for all staff members. Parents' associations may also help with funding, when healthcare institutions do not allocate funds.

Educational training opportunities in paediatric haematology/oncology

Access to updated information must be available through the local institution for published articles,

through access to novel treatment protocols and the organisation of educational programmes. Educational programmes can be performed at national level (e.g., lectures on national topics, courses to develop practical skills) or at European level (e.g., online interactive webinars, onsite courses).

Clinical fellowship programmes should be offered at national and international level in order to ensure a higher level of training, to give access to a larger range of diseases, and access to work with experienced professionals. Fellowship programmes must give access to the area of interest of the trainee and be individualised. Cross-cultural training programmes must also be an option as there are many differences in approaching patients and families.

SIOPE is committed to continuing valuable collaborative initiatives already established with the European School of Oncology (ESO; e.g., masterclass, e-learning, fellowship programme), the European Society of Medical Oncology (ESMO), ERN PaedCan (European standard clinical practice recommendations, webinars), and other partners to seek similar opportunities.

EHA also supports several educational programmes and activities to promote the development of trainees in this field of expertise.

TRAINING REQUIREMENTS FOR TRAINERS

1. PROCESS FOR RECOGNITION AS TRAINER

A. Requested qualification and experience

The training staff at a Centre should include at least two trainers in order to provide close personal monitoring of the trainee during his/her training. The number of trainees should not exceed the number of trainers in the Centre. Each trainee should have a dedicated Lead Educational supervisor or trainer for the duration of their training. The Lead Educational supervisor or trainer must have been practicing Paediatric Haematology/Oncology for at least 5 years and have specialist accreditation in those countries where the subspecialty is recognized. There should be additional Clinical supervisors/trainers who should provide training across all aspects of the specialty and be research active.

B. Core competencies for trainers

A Trainer is a person who holds acknowledged expertise in one or several aspects of Paediatric Haematology/Oncology. This person's contribution may be restricted to these areas of expertise. Both educational supervisors and trainers must have practiced Paediatric Haematology/Oncology for a **minimum of 2 years after completion of specialist training**.

Trainers should:

- Work out a training programme for the trainee in accordance with the trainee's own qualities and the available facilities of the institution.
- Regular review will be required to allow for flexibility and for early identification of problems/deficiencies. The trainer should work with the Trainee to create a Personal Development Plan. Trainers are expected to provide appraisal and assessment of progress. Appraisal consists of determining what is needed and what evidence is required to show that this has been achieved. Assessment evaluates progress against objectives.
- Trainee assessment should be provided in terms of:
    - Training and career ambitions
    - Training experience related to syllabus
    - Achievements related to personal development plan

Reviews of progress should take place at yearly intervals to appraise the individual. An annual

assessment should be undertaken, ideally at a national level, to review competencies achieved and to allow progress within the teaching programme. Assessments should be detailed and contain statements of theoretical and practical experience accumulated by the trainee. It is expected that the trainee will also provide an account of the training received and problems encountered (*curriculum vitae*). Reports will be submitted to the Trainer.

2. QUALITY MANAGEMENT FOR TRAINERS

The Training Program Director is responsible for ensuring and maintaining the quality of the paediatric haematology/oncology training program. The educational work of trainers and Training Programme Directors should be appraised not less than on annual basis within their Institution as local circumstances determines.

Trainers, supervisors, and teachers should be officially recognized within their training institution. The skills, responsibilities, and duties required for each position should be clearly specified. Transparent procedures should be in place for the appointment of each role, specifying the competencies required for each position.

Since the core competencies of trainers include experience in the medical field and regular updating of their educational skills, each institution should ensure that trainers are provided with regular training opportunities and sufficient time and resources to effectively support their educational role. Continuing education should be encouraged through regular updates to the training curriculum in accordance with the latest medical advances and educational methodologies, and through training opportunities provided by national and international paediatric haematology and oncology societies.

The quality of training should be evaluated regularly. Trainers, supervisors, and teachers should receive regular and constructive feedback on their performance to ensure progressive professional development. This quality assessment should include input from trainees through methods such as interviews and requests for feedback, as well as monitoring of trainees' progress under the trainer's supervision.

TRAINING REQUIREMENTS FOR TRAINING INSTITUTIONS

1. PROCESS FOR RECOGNITION AS TRAINING CENTRE

Training institutions for Paediatric haematology/oncology should comprise expertise in both malignant and non-malignant areas, or via a collaboration with other national or international units. The quality of care provided by the institutions is dictated by the minimum recommended staffing level depending on the annual average activity and represented as a multidisciplinary team. These multidisciplinary teams should consist of paediatric hematologists/oncologists, nurses, psychologists, allied health professionals, paediatric surgeons and neurosurgeons, paediatric intensivists and anesthesiologists, and additional paediatric subspecialties depending on the patients' needs. This includes 24/7 on-call doctors as well as trainee doctors, dedicated to a ward. Therefore, a training institution should be able to provide the following standards:

- Paediatric hematologists/oncologists - in charge of documenting diagnosis, classification, stage of disease, stratification, and recruitment into clinical trials. They are expected to enter the child into an appropriate national or international clinical trial and if not available to establish an individual treatment scheme based on maximal scientific proof and expertise. The physician in charge is also responsible to lead the communication between patients, parents, and caregivers.
- Nursing staff - adequate and specifically trained nurses are necessary to cover the workload. Depending on the local structure, this may include a link nurse, providing the link between the treating unit, parents, and the local paediatrician or general practitioner.
- Psychological service and child life specialists - fundamental professionals that should be introduced as soon as possible following diagnosis.
- Allied health professionals including physiotherapy, occupational therapy, speech and language therapy, dieticians, and pharmacist should be available
- Social workers, ward teachers, and activity/play therapy including music and arts should be available to help patients and their families find their way to cope with the situation in the best possible manner.
- Medical secretaries and data managers are necessary to help physicians in daily consultations as well as for clinical trials.
- Physical and Rehabilitation Medicine physicians are necessary for short- and long-term recovery. Patients need to be monitored for potential late effects of cancer treatments, provide surveillance for disease recurrence, and offer comprehensive support to survivors to help

them lead healthy and fulfilling lives after the end of treatment.

- A paediatric oncology centre must have a functioning supportive care team at its disposal directed at quality of life and palliative care.
- Institutional multidisciplinary scientific/tumour board
- Adequate number of new diagnoses per year
- Standard Operating Procedures
- Scientific activity at a National and International level
- Training activity
- Medical technical equipment at clinical and laboratory level to support the basics of diagnostics

2. QUALITY MANAGEMENT WITHIN TRAINING INSTITUTIONS

A. Accreditation

For each EU Member country, a list of centres, units, training directors, tutors and teachers should be compiled and updated on an annual basis. Each centre is characterised by the available modules or areas of teaching activity, tutors and teachers available and the size of the clinical practice as defined by the needs of the trainee.

B. Clinical Governance

Effective clinical governance within paediatric haematology/oncology training programs rests upon collaborative oversight by the Training Programme Director (TPD) and the involved institutions. The TPD assumes primary responsibility for the program's governance, ensuring that it aligns with established standards and objectives. Concurrently, the hosting institutions are accountable for providing an environment conducive to high-quality training delivery.

Each trainer bears direct responsibility to the TPD for imparting comprehensive training within their respective areas of specialization. This accountability necessitates a structured approach to workforce management within training institutions, accommodating the specific demands of specialty training. Central to this approach is the effective management of workload, where priority is consistently given to fostering a supportive environment for training activities.

C. Manpower planning

In the realm of paediatric oncology/hematology training, effective manpower planning is fundamental to the success and sustainability of specialised educational programs. It is recommended that training institutions appoint a dedicated coordinator tasked with orchestrating the composition, implementation, and supervision of the specialty training program. This coordinator plays a pivotal role in ensuring that the program meets defined educational goals and adheres to regulatory standards.

Clear delineation of roles between trainers and trainees is crucial to the smooth operation of the training program. It is imperative that both parties understand their respective responsibilities and expectations. To facilitate optimal learning outcomes, scheduled sessions specifically allocated for interactive specialty training sessions should be established. The frequency and duration of these sessions should be tailored to local infrastructural capabilities and resource availability, ensuring consistency and depth in training delivery.

Manpower planning within paediatric haematology/oncology training programs falls under the jurisdiction of individual member states, each tasked with assessing and responding to the specific regional and national needs for skilled specialists in the field. This adaptive approach ensures that the allocation of resources and the deployment of personnel align closely with evolving healthcare demands and educational priorities.

D. Regular report

Regular reports should be submitted annually. Assessments should be detailed and contain statements of theoretical and practical experience accumulated by the trainers and trainees. Reports will be submitted to the TPD or national body.

E. Transparency of training programmes

According to national and regional guidelines, UEMS highly recommends that training institutions create clear training programmes and make them accessible to the public. These will be publicly available on the websites of SIOP-E and EHA, respectively. Training centres are expected to detail the training they offer, including specifics about the clinical services provided and the trainers involved. This information should cover the structure of the training programmes, the clinical or laboratory experiences available to trainees, and the support and interaction with the trainer and TPD. Additionally, there should be a designated person for prospective trainees to contact for more information about the programme.

F. Structure for coordination of training

A TPD is required to oversee and organize the official education program. The TPD will be supported by trainers who contribute their expertise to the program. In some centers, an Educational Supervisor may assist the TPD in coordinating the training program for trainees, ensuring the smooth delivery of educational activities.

APPENDIX

- Training objectives for UEMS specialists pertaining to the care of adolescents and young adults Version September 2022 (https://www.eapaediatrics.eu/wp-content/uploads/2022/12/Adolescent-Medicine-Health_training-objectivesSeptember-2022.pdf)