

Introduction

Paediatric Inherited Metabolic Medicine (PIMM) is a well-recognized paediatric subspecialty. It encompasses prevention, recognition, diagnosis and management of all aspects of inherited metabolic disorders (IMD) that affect the body's normal biochemical processes. Many IMD patients have neurodevelopmental involvement and require life-long multidisciplinary family-centred care.

To equip a prospective metabolic paediatrician with attitude and skillsets for providing and driving high-standard professional PIMM services in Hong Kong, a PIMM subspecialty training programme is proposed as detailed in this document. The aim is to provide PIMM trainees an accredited curriculum, which provides a framework for training, articulating the standard required to work as a PIMM subspecialist, and encouraging the pursuit of excellence in all aspects of clinical and wider practice.

The proposed training programme comprises of minimum of 36 months' training with 4 core plus 1 elective modules, which covers the essential facets of fundamental knowledge and skills and forms the solid foundation for the lifelong PIMM career development.

Eligibility

- Specialists holding the qualification of FHKAM (Paediatrics) or its equivalent
 - Candidates who have completed 3 years basic training in general paediatrics and have passed the MRCPCH (UK) / HKCPaed Intermediate Examination are eligible to commence the PIMM subspecialty training during their higher training in General Paediatrics upon the approval by the PIMM Subspecialty Board. A maximum of 1 cumulated year's overlap is allowed during this period.
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PIMM curriculum

The purpose of the PIMM curriculum is to support the trainee paediatrician in developing the knowledge, skills and attitudes required to work safely and confidently as a PIMM subspecialist.

PIMM subspecialists provide care for children, young people and families who have inherited disorders that affect the body's normal biochemical processes and lead to organ dysfunction. They have detailed knowledge of normal human biochemistry and physiology and the impact of IMD. They are skilful to apply this knowledge in the diagnostic process (including identifying novel disorders) and patient- and family-centred management.

PIMM subspecialists work closely with laboratory scientists, metabolic dietitians, pharmacist specialists, nursing and allied health teams. They strive to improve the early recognition and diagnosis of metabolic diseases, including through newborn screening. They keep up to date with the rapid developments and innovations in therapeutics for IMD, and provide consistently high quality PIMM services.

By the end of the PIMM training, a PIMM trainee must demonstrate the achievement of the following learning outcomes, which are mapped to the domains of learning outcomes as listed in the 2023 Hong Kong College of Paediatricians (HKCP) Curriculum Statement.

Learning outcomes of PIMM curriculum

PIMM Learning Outcomes		HKCP curriculum statement domains
1	Applies up-to-date understanding of the full range of metabolic conditions to the holistic metabolic assessment and diagnosis to patients with suspected and confirmed IMD	1, 2, 3, 4, 5, 10
2	Prevents, recognises, assesses and manages the full range of acute paediatric inherited metabolic emergencies	2, 3, 4, 5, 6, 7
3	Supports patients and families with suspected or confirmed IMD presenting clinically or detected through the newborn screening	1, 2, 3, 4, 5
4	Counsels families the inheritance of IMD within a cultural context	1, 2, 3, 4, 5
5	Provides consistently high quality PIMM service across specialties, disciplines, sectors, in both community and hospital settings	1, 2, 3, 4, 5, 6, 7, 8, 9, 10
6	Contributes to multi-centre collaborations and research	2, 5, 6, 8, 10, 11

Specific diseases illustrations

A. Disorders of amino acid metabolism	
Demonstrates a sound knowledge and understanding of the following including:	
<ul style="list-style-type: none">- Argininaemia- Argininosuccinic Acidemia- Citrullinaemia Type I- Citrullinaemia Type II- Phenylketonuria- Homocystinuria- Maple Syrup Urine Disease- Tyrosinemia Type I- Ornithine Transcarbamylase Deficiency- Hyperornithinaemia- And others	
a.	Newborn screening technique, role and counselling for conditions that have newborn screening available
b.	Clinical presentation and long-term complications of the conditions
c.	Investigating the conditions such as <ul style="list-style-type: none">- Pyridoxine responsiveness test in homocystinuria- Sapropterin dihydrochloride responsiveness test in phenylketonuria
d.	Dietary treatment of the conditions, including monitoring and prevention of nutritional deficiencies
e.	Drug treatment in some conditions such as <ul style="list-style-type: none">- Sapropterin dihydrochloride for phenylketonuria- Nitisinone for Tyrosinaemia Type I- Betaine and pyridoxine for Homocystinuria- Carglumic acid, sodium benzoate, sodium/glycerol phenylbutyrate, citrulline and L-arginine in urea cycle disorders
f.	Indications for liver transplant in some conditions such as Tyrosinemia Type I, Maple Syrup Urine disease, Urea cycle disorders
g.	Management of acute illness including emergency protocols

B. Disorders of organic acid including vitamin and cofactor metabolism	
Demonstrates a sound knowledge and understanding of the following including	
<ul style="list-style-type: none">- Branched chain organic acidemias – Methylmalonic acidemia, Propionic acidemia, Isovaleric acidemia- Cobalamin metabolism defects- Glutaric Acidemia Type I- Multiple carboxylase deficiency- And others	

	<ul style="list-style-type: none"> - Fructosaemia - Fructose 1,6 bisphosphatase deficiency - And others
a.	Newborn screening technique, role and counselling for conditions that have newborn screening available
b.	Clinical presentation and long-term complications of the conditions
c.	Investigating the fasting tolerance of conditions such as <ul style="list-style-type: none"> - uncooked corn starch loading testing in glycogen storage disease - use of continuous glucose monitoring
d.	Dietary treatment of the conditions, including monitoring and prevention of nutritional deficiencies
e.	Drug treatment in some conditions such as <ul style="list-style-type: none"> - Empagliflozin and Granulocyte-colony stimulating factor in Glycogen Storage Disease type 1B
f.	Indications for organ transplantation in disorders of carbohydrate metabolism such as glycogen storage disease
g.	Management of acute illness including emergency protocols

E. Mitochondrial disorders

Demonstrates a sound knowledge and understanding of mitochondrial disorders

Examples of mitochondrial diseases include

- Mitochondrial encephalomyopathy, lactic acidosis and stroke like episodes (MELAS)
- Pearson syndrome, Kearns-Sayre syndrome
- Barth syndrome
- Leigh's disease
- And others

a.	Clinical presentation and long-term complications of the conditions
b.	Dietary treatment of the conditions, including monitoring and prevention of nutritional deficiencies
c.	Drug treatment in mitochondrial disease <ul style="list-style-type: none"> - Arginine and Taurine in MELAS - Ubiquinone, biotin, riboflavin and thiamine in mitochondrial disorders
d.	Management of acute illness including emergency protocols

F. Lysosomal storage disorders

Demonstrates a sound knowledge and understanding of lysosomal storage disorders

Examples of lysosomal storage disease

- Pompe Disease
- Mucopolysaccharidosis
- Acid Sphingomyelinase Deficiency
- Gaucher disease

	<ul style="list-style-type: none"> - Fabry Disease - And others
a.	Newborn screening technique, role and counselling for conditions that have newborn screening available
b.	Clinical presentation and long-term complications of the conditions
c.	Drug treatments for lysosomal storage disease <ul style="list-style-type: none"> - Enzyme replacement therapies - Substrate therapies
d.	Monitoring in those on enzyme replacement therapies according to agreed protocols for treatment monitoring and continuation.
e.	The role of stem cell transplantation in lysosomal storage disease
f.	The role of orthopedic surgeries in lysosomal storage diseases such as mucopolysaccharidosis
g.	The role of palliative care for lysosomal storage disease without any available treatment available

G. Other conditions	
Demonstrates a sound knowledge and understanding of the following including <ul style="list-style-type: none"> - Neurometabolic disorders, examples: 6-pyruvoyl-tetrahydropterin synthase deficiency, Disorders of purine metabolism such as Lesch-Nyhan syndrome, Cerebral folate deficiency and other neurotransmitter disorders - Congenital glycosylation disorders - Porphyrrias - Disorders of metal metabolism such as Menkes disease and Wilson's disease - And others 	
a.	Newborn screening technique, role and counselling for conditions which have newborn screening available
b.	Clinical presentation and long-term complications of the conditions
c.	Drug treatment in some conditions such as <ul style="list-style-type: none"> - Sapropterin dihydrochloride for 6-pyruvoyl-tetrahydropterin synthase deficiency - Zinc for Wilson's disease

PIMM training program at a glance

Module	Location in Hong Kong [^]	Duration
Core module 1@: Paediatric inherited metabolic medicine (clinical)	<ul style="list-style-type: none"> - PIMM full training centre - PIMM training unit/overseas[^] 	<p>Minimum 24 months (if being the only metabolic medicine team for training)</p> <p>Minimum of 3 months and up to 6 months plus a minimum of 18-21 months in a PIMM full training centre make up to a total of minimal 24 months</p>
Core module 2: Paediatric inherited metabolic medicine (laboratory)#	<ul style="list-style-type: none"> - Chemical pathology laboratories under Hospital Authority providing metabolic diagnostic services with training accreditation under The Hong Kong College of Pathologists - Newborn screening laboratory in Hong Kong Children's Hospital 	<p>3 months in either or both laboratories to make up to a total of 3 months</p>
Core module 3: Paediatric neurology with preference to neuro-metabolic medicine	<ul style="list-style-type: none"> - Accredited Paediatric Neurology training centre under The Hong Kong College of Paediatricians 	<p>3 months</p>
Core module 4: Clinical genetics & genomics#	<ul style="list-style-type: none"> - Accredited Paediatric Genetic and Genomics training centre under The Hong Kong College of Paediatricians 	<p>3 months</p>
Elective module: Clinical specialties closely related to paediatric inherited metabolic medicine	<p>PIMM board recognized centre providing the following:</p> <ul style="list-style-type: none"> - Paediatric subspecialty service closely related to PIMM such as Paediatric Endocrinology, Developmental Behavioural Paediatrics, Paediatric Neurology, Genetics and Genomics - Adult metabolic medicine unit@ - Overseas training institute[^] - Research laboratory on metabolic medicine (local: University of Hong Kong and Chinese University of Hong Kong; or overseas academic unit) 	<p>3 months</p>

Total minimum duration	36 months
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*An academic-oriented training with basic or clinical research component is highly encouraged.

^Overseas training in institutions with a recognized PIMM training programme is strongly recommended.

@Exposure to an adult metabolic medicine unit (inpatient and outpatient) e.g. Princess Margaret Hospital is highly encouraged.

#Specific learning objectives elaborated

Core module 2: Paediatric inherited metabolic medicine (laboratory)

Specific learning objectives

- Indications, selection, planning and interpretation of biochemical and genetic/genomic investigations, functional studies, histology and histochemistries, newborn screening, and peri-/post-mortem tests, including the understanding of analytical, physiological and nutritional factors that influence the results

Core module 4: Clinical Genetics and Genomics

Specific learning objectives

- a. Learning the skill in genetic counseling to explain in simple terms, adapted to cultural context:
 - The principles and impact of autosomal recessive, dominant, X-linked and mitochondrial DNA inheritance patterns
 - The utilization of pre-implantation / prenatal / postnatal / pre-symptomatic genetic diagnosis, taking cultural differences in attitudes in the consideration
- b. Be familiar with the currently available modalities of genetic/genomic analysis and principles of variant classification, to guide:
 - Appropriate modalities, samples, timing, and informed consents of the tests
 - Explanation of the results and the possible need of data reanalysis or additional testing in the future

PIMM training syllabus

PIMM training syllabus supports the completion of the PIMM curriculum. It provides a reference guide on how to acquire the minimum set of competencies in specific domains, demonstrate the acquisition progress, and achieve the learning outcomes during the course of PIMM training and career development.

At the completion of training, trainees should demonstrate competencies as PIMM subspecialist. They should have acquired detailed knowledge of normal biochemistry and physiology as well as the impact of such disorders (as listed on the International Classification of Inherited Metabolic Disorders) on the body, and are able to critically apply the knowledge, to strive for early recognition, diagnosis, and effective management of the affected babies, children and young people as well as their families, including through screening, multidisciplinary care, and research.

The following minimum set of competencies are mapped to the domains of training competence as listed in the 2023 Hong Kong College of Paediatricians (HKCP) Curriculum Statement.

Minimum set of competencies of a PIMM subspecialist

Minimal Competencies of a PIMM subspecialist		HKCP curriculum statement domains
1	Applies up-to-date understanding of the full range of metabolic conditions to the holistic metabolic assessment and diagnosis to patients with suspected or confirmed IMD	1, 2, 3, 4, 5, 10
	<p>A. Demonstrates sound understanding of the normal biochemistry and physiology:</p> <ul style="list-style-type: none">- Requirement, regulation and balance of fluid, electrolytes, acid/base and nutrients- Intermediary metabolism e.g. metabolic response to fasting, and metabolism of glucose, lactate, ammonia, amino acids, organic acids, fatty acids- Complex metabolite metabolism e.g. lipids, lipoproteins, cholesterol and other sterols, purines, pyrimidines, porphyrins, bilirubin- Vitamin, mineral/metal metabolism, including role of cofactors- Brain development and metabolism, including normal intellectual and psychological development, and role of blood brain barrier and neurotransmitters- Organelle functions and regulations, including mitochondria, endoplasmic reticulum, golgi, lysosome, peroxisome, ribosome- Enzyme biochemistry and tissue expression <p>B. Demonstrates sound understanding of the impact and corresponding diagnostics of IMD:</p> <ul style="list-style-type: none">- Genetic, biochemical, pathological, and clinical changes as a result of IMD- Consequence of specific nutritional excess or deficiencies- Indications, selection, planning and interpretation of biochemical and genetic/genomic	

	<p>investigations, functional studies, histology and histochemistries, newborn screening, and peri-/post-mortem tests, including the understanding of analytical, physiological and nutritional factors that influence the results</p> <p>C. Takes responsibility for appropriate investigations of the full range of IMD manifestations and holistic patient assessments in both acute and out-patient settings, and be aware of the possible non-IMD differential diagnoses:</p> <ul style="list-style-type: none"> - Neurological manifestations including developmental delay / regression, seizures, movement disorders, myopathy, encephalopathy etc - Liver manifestations including cholestasis, hepatomegaly, acute or chronic liver dysfunction - Other organ manifestations e.g. cardiorespiratory, muscle, kidney, eye, endocrine, bone, skin, dysmorphism etc - Abnormal growth and nutritional status <p>D. Undertakes bedside procedures including lumbar puncture, tissue biopsies, and dynamic tests</p> <p>E. Examples of conditions that the PIMM subspecialist needs to take responsibility in the management include:</p> <ul style="list-style-type: none"> - Disorders of amino acid metabolism - Disorders of organic acid including vitamin and cofactor metabolism - Disorders of fatty acid oxidation and ketone body metabolism - Disorders of carbohydrate metabolism - Mitochondrial disorders - Lysosomal storage disorders - And Others 	
2	<p>Prevents, recognizes, assesses and manages the full range of acute paediatric inherited metabolic emergencies</p> <p>A. Educates patients, families and schools on the risk factors and signs of impending metabolic decompensation, including advice and action plans for:</p> <ul style="list-style-type: none"> - Dietetic, exercise and fasting precautions - Anaesthetic and surgical considerations - Intercurrent illnesses - Impending metabolic decompensation <p>B. Prevents, recognises, assesses and manages the full range of acute metabolic emergencies including advice to clinicians from community and regional hospitals:</p> <ul style="list-style-type: none"> - Appropriate choice and timing of investigations and monitoring of patient conditions 	2, 3, 4, 5, 6, 7

	<ul style="list-style-type: none"> - Timely and practical use of emergency fluid/electrolyte/nutritional management, assisted ventilation and dialysis - Timely prescription and administration of a range of specialised drugs for IMD - Monitoring and management of IMD drug associated reactions and side effects <p>C. Examples of conditions that the PIMM specialist needs to take responsibility in the emergency management include acute decompensation in disorders of intermediary metabolism which may result in:</p> <ul style="list-style-type: none"> - Hyperammonaemia - Lactic acidosis - Hypoglycaemia - Metabolic acidosis including ketosis - Acute organ(s) dysfunction 	
3	<p>Supports patients and families with suspected or confirmed IMD presenting clinically or detected through the newborn screening</p> <p>A. Be skillful in counseling for a new diagnosis in simple terms:</p> <ul style="list-style-type: none"> - Classification, investigations, monitoring, as well as possible clinical presentations and long-term complications of the suspected or confirmed IMD - Role and indications of treatment modalities e.g. diet, drug, transplantation, palliation <p>B. Empowers families in the daily management, adapted to clinical settings and social context, including:</p> <ul style="list-style-type: none"> - Provides empathetic support to families especially during difficult circumstances - Appreciates patient and families' understanding and psychological stress towards the metabolic disease, and the influence of ethnic and culture difference on their attitudes - Understands patient and families' challenge in facing progressive disorders especially those where natural history is difficult to predict - Explores effective palliative care for degenerative diseases 	1, 2, 3, 4, 5
4	<p>Counsels families the inheritance of IMD within a cultural context</p> <p>A. Be skillful in genetic counseling in simple terms, adapted to cultural context:</p> <ul style="list-style-type: none"> - The principles and impact of autosomal recessive, dominant, X-linked and mitochondrial DNA inheritance patterns - The utilization of pre-implantation / prenatal / postnatal / pre-symptomatic genetic diagnosis, taking cultural differences in attitudes in the consideration <p>B. Be familiar with the currently available modalities of genetic/genomic analysis and principles of variant classification, to guide:</p> <ul style="list-style-type: none"> - Appropriate modalities, samples, timing, and informed consents of the tests 	1, 2, 3, 4, 5

	Explanation of the results and the possible need of data reanalysis or additional testing in the future	
5	Liaises effectively with clinicians and specialists (especially nurses, dietitians, pharmacists, laboratory scientists, allied health and social workers) in community, regional hospitals and specialist centres, to provide consistently quality service for patients with IMD.	1, 2, 3, 4, 5, 6, 7, 8, 9, 10
	<p>A. Takes responsibility for the long-term holistic management of families with IMD:</p> <ul style="list-style-type: none"> - Appropriately selects and prescribes supportive and specific treatment options including drug / diet / enzyme therapies, stem cell / organ transplantation and gene therapy - Understands the frameworks for the application and utilization of specialized medications (e.g. enzyme replacement therapy) - Understands the indications and interpretations of neuropsychometric assessments - Identifies the educational, social, psychological and palliative care needs early and initiates timely support <p>B. Contributes to effective running and development of the metabolic unit:</p> <ul style="list-style-type: none"> - Keeps the clinical team fully engaged with the rapid evolving development in diagnostics and therapeutics for PIMM and be a steadfast patient advocate - Develops clinical leadership, management and administrative skills e.g. business and budget planning, quality and safety, clinical audit, maintaining duty rotas and human resources - Be interested in the overall organization of departmental activities and management directions - Upholds a constructive attitude to the process of decision making and accepts shared responsibility for the use of resources - Responds effectively to clinical complaints <p>C. Contributes to effective and up-to-date local and regional multidisciplinary team (MDT) management:</p> <ul style="list-style-type: none"> - Communicates effectively with patients and families, colleagues and working partners, research staff and administrators, to understand the perspectives of stakeholders in patient care - Upholds a collaborative problem-solving attitude towards colleagues and families, recognising and coping with stress in self and others - Understands local management structure and perspectives of other stakeholders including policy makers - Contributes to the formulation, coordination, and execution of effective MDT care plans as both a core link and / or liaison person 	

6	Contributes to multi-centre collaborations and research	2, 5, 6, 8, 10, 11
<p>A. Be committed to continuing self-education and to teaching others</p> <ul style="list-style-type: none">- Be up-to-date with literature and online resources on IMD- Have a working knowledge on the design and execution of clinical studies and audit, including GCP (good clinical practice), critical appraisal, medical statistics, data organization and presentation, manuscript preparation, oral presentation- Contributes regularly to the organization of educational programmes and development of core teaching materials at both undergraduate and postgraduate levels- Teaches at various levels including undergraduate and postgraduate- Adheres to a positive empathetic approach to the supervision and motivation of junior medical staff and medical students <p>B. Be active and supportive in research</p> <ul style="list-style-type: none">- Be familiar with the current state of clinical trials and novel therapies for untreatable IMD, with a good understanding of the role of disease registries, natural history studies, and clinical trials in the IMD management and treatment development- Participates in MDT discussions about local and international collaborations at clinical and research levels, including study recruitment <p>C. Familiarization with rare disease registries</p>		

Competency Assessment

	Metabolic Mini Clinical Evaluation	Metabolic Case Based Discussion	Metabolic Directly Observed Procedures	Metabolic Multisource Feedback	Metabolic Exit Assessment
Applies up-to-date understanding of the full range of metabolic conditions to the holistic metabolic assessment and diagnosis to patients with suspected or confirmed IMD	●	●	●	●	●
Prevents, recognizes, assesses and manages the full range of acute paediatric inherited metabolic emergencies	●	●		●	●
Supports patients and families with suspected or confirmed IMD presenting clinically or detected through the newborn screening	●	●		●	●
Counsels families the inheritance of IMD within a cultural context	●	●		●	●
Liaises effectively with clinicians and specialists (especially nurses, dietitians, pharmacists, laboratory scientists, allied health and social workers) in community, regional hospitals and specialist centres, to provide consistently quality service for patients with IMD.	●	●		●	
Contributes to multi-centre collaborations and research	●			●	●

	Expected duration of assessment session	Minimum frequency	Recommended frequency
Metabolic Mini Clinical Evaluation	20 to 40 minutes	10 to 15 in three years	6 per year
Metabolic case-based discussion	30 minutes	6 in three years	Once every 6 months
Metabolic directly observed procedural skills	15 to 30 minutes	Until the trainee can perform the skill unsupervised	Nil
Metabolic Multisource Feedback	15-20 minutes	Once a year	Once a year

Standards for the accreditation of PIMM training centre in Module 1 (Clinical PIMM)

PIMM training centres shall be accredited based on the spectrum of inherited metabolic disorders being managed, availability of trainers, caseload, case complexity, support from related specialties and presence of advanced therapy including research.

A training centre should be a hospital unit with at least ONE trainer, and providing services and training in PIMM. If a hospital is only capable of providing some but not all of the aspects of training, that hospital may only be accredited for training for a proportion of the full training programme i.e. minimum of 3 and up to 6 months.

	PIMM full training centre	PIMM training unit
Duration of training		
	Minimum 24 months (if being the only metabolic medicine team for training)	Minimum of 3 months and up to 6 months plus a minimum of 18-21 months in a PIMM full training centre make up to a total of minimum 24 months
Trainer		
	>=2	1
Caseload		
Inpatient Beds	>=2	-
Consultation (inter- and/or intra-hospital)	>=100	>=20
Outpatient attendances	>=600	>=150
Complexity		
Highly complex	>=50%	5-10%
Complex	<50%	>=5%
Support from related specialties		
PNICU	Yes	Yes
Transplant e.g. bone marrow transplantation	Yes	-
Chemical pathology laboratory including newborn screening	Yes	-
Advanced therapy including research		
Gene therapy	Yes	-
Clinical trial	Yes	-

Benchmark references

1. SSIEM Syllabus for training in clinical paediatric metabolic medicine (Updated 30 Jun 2017)
https://www.ssiem.org/index.php?option=com_content&view=article&id=41&Itemid=176
2. RCPCH Progress+ Paediatric Inherited Metabolic Sub-specialty Syllabus (Approved by GMC on 1 Aug 2023)
<https://www.rcpch.ac.uk/sites/default/files/2023-07/progressplus-metabolic-medicine-syllabus-2023.pdf>
3. An international classification of inherited metabolic disorders (ICIMD). Carlos R Ferreira, Shamima Rahman, Markus Keller, Johannes Zschocke, ICIMD Advisory Group. J Inherit Metab Dis. 2021 Jan;44(1):164-177.doi: 10.1002/jimd.12348. <https://pubmed.ncbi.nlm.nih.gov/33340416/>

2021 ICIMD Categories of Inherited Metabolic Diseases

1. Disorders of amino acid metabolism
2. Disorders of peptide and amine metabolism
3. Disorders of carbohydrate metabolism
4. Disorders of fatty acid and ketone metabolism
5. Disorders of energy substrate metabolism
6. mtDNA-related disorders
7. Nuclear-encoded disorders of oxidative phosphorylation
8. Disorders of mitochondrial cofactor biosynthesis
9. Disorders of mitochondrial DNA maintenance and replication
10. Disorders of mitochondrial gene expression
11. Other disorders of mitochondrial function
12. Disorders of metabolite repair / proofreading
13. Miscellaneous disorders of intermediary metabolism
14. Disorders of lipid metabolism
15. Disorders of lipoprotein metabolism
16. Disorders of nucleobase, nucleotide and nucleic acid metabolism
17. Disorders of tetrapyrrole metabolism
18. Congenital disorders of glycosylation
19. Disorders of organelle biogenesis, dynamics and interactions
20. Disorders of complex molecule degradation
21. Disorders of vitamin and cofactor metabolism
22. Disorders of trace elements and metals
23. Neurotransmitter disorders
24. Endocrine metabolic disorders