EFLM Paper

Nuthar Jassam*, Jennifer Lake, Milena Dabrowska, Jose Queralto, Demetrios Rizos, Ralf Lichtinghagen, Hannsjörg Baum, Ferruccio Ceriotti, John O'Mullane, Evgenija Homšak, Charis Charilaou, Mats Ohlson, Ivana Rako, Dalius Vitkus, Gustav Kovac, Pauline Verschuure, Jaroslav Racek, Mariana Carmen Chifiriuc and Gilbert Wieringa

The European Federation of Clinical Chemistry and Laboratory Medicine syllabus for postgraduate education and training for Specialists in Laboratory Medicine: version 5 – 2018

https://doi.org/10.1515/cclm-2018-0344
Received April 4, 2018; accepted April 4, 2018; previously published online June 5, 2018

Abstract: Although laboratory medicine practise varies across the European Union's (EU) member states, the extent of overlap in scope is such that a common syllabus describing the education and training associated with high-quality, specialist practise can be identified. In turn, such a syllabus can help define the common set of skills, knowledge and competence in a Common Training Framework (CTF) for non-medical Specialists in Laboratory Medicine under EU Directive 2013/55/EU (The recognition of Professional Qualifications). In meeting the requirements of the directive's CTF patient safety is particularly enhanced when specialists seek to capitalise on opportunities for free professional migration across EU borders. In updating the fourth syllabus, the fifth expands on individual discipline requirements, new analytical techniques and use of statistics. An outline structure for a training programme is proposed together with expected responsibilities of trainees and trainers; reference is provided to a trainee's log book. In updating the syllabus, it continues to support national programmes and the aims of EU Directive 2013/55/EU in providing safeguards to professional mobility across European borders at a time when the demand for highly qualified professionals is increasing in the face of a disparity in their distribution across Europe. In support of achieving a CTF, the syllabus represents EFLM's position statement for the education and training that underpins the framework.

Keywords: education; EFLM syllabus; postgraduate training; specialist in laboratory medicine.

***Corresponding author: Nuthar Jassam,** Department of Clinical Biochemistry, Harrogate and District Foundation Trust, Harrogate, UK, E-mail: nuthar.jassam@hdft.nhs.uk
Jennifer Lake: Department of Clinical Biochemistry, Royal London Hospital, London, UK
Milena Dabrowska: Department of Haematological Diagnostics, Medical University of Bialystok, Bialystok, Poland
Jose Queralto: Clinical Biochemistry Department, Hospital de la Santa Creui Sant Pau, Barcelona, Spain
Demetrios Rizos: Aretaieio University Hospital, Athens, Greece
Ralf Lichtinghagen: Institute for Clinical Chemistry, Medical University Hannover, Hannover, Germany
Hannsjörg Baum: Institute for Laboratory Medicine, RegionaleKliniken Holding RKH GmbH, Ludwigsburg, Germany
Ferruccio Ceriotti: Clinical Laboratory Service, San Raffaele Hospital, Milan, Italy
John O'Mullane: Clinical Biochemistry Department, Cork University Hospital, Wilton Cork, Ireland
Evgenija Homšak: Department of Laboratory Diagnostics, University Medical Centre Maribor, Maribor, Slovenia
Charis Charilaou: Biomedical Lab, Nicosia, Cyprus
Mats Ohlson: Department of Clinical Chemistry, Sahlgrenska University Hospital, Gothenburg, Sweden
Ivana Rako: Department of Laboratory Diagnostics, University Hospital Centre Zagreb, Zagreb, Croatia
Dalius Vitkus: Department of Physiology, Biochemistry, Microbiology and Laboratory Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
Gustav Kovac: Institute of Laboratory Medicine, Slovak Medical School, Bratislava, Slovakia
Pauline Verschuure: Clinical Laboratory, St. Anna Hospital, Geldrop, The Netherlands
Jaroslav Racek: Department of Clinical Biochemistry and Haematology, University Hospital, Pilsen, Czech Republic
Mariana Carmen Chifiriuc: Department of Microbiology and Immunology, Faculty of Biology, Research Institute of the University of Bucharest, Bucharest, Romania; and University of Bucharest, Faculty of Biology, Bucharest, Romania
Gilbert Wieringa: Laboratory Medicine, Bolton NHS Foundation Trust, Bolton, UK

Introduction

A syllabus is a plan showing the subjects and/or books to be studied in a particular course, especially a course that leads to an examination [1]. When there is substantial similarity between syllabi, it opens the opportunity to harmonise common principles of education and training. The transposition of European Union (EU) Directive 2013/55/EC [2] (The Recognition of Professional Qualifications) into member states' national laws in January 2016 reflected that although there is demand for highly qualified individuals across the Union, there is also disparity in their distribution [3]. In creating a mechanism for mutual recognition of professional qualifications, the directive

- supports individuals seeking unhindered free professional movement across EU borders
- helps catalyse a more equitable distribution of human resource and services across the Union
- can obviate the need for member states to impose "compensation measures" (e.g. retraining, new qualifications, aptitude tests and adaptation periods) on each other's professionals, which may needlessly delay and deter migration.

Although the "sectoral" professions (e.g. doctors, nurses and midwives) already enjoy many aspects of free migration, there are over 600 professions across the Union for whom migration is restricted through lack of mutual recognition of qualifications. In recognising that safeguards need to be in place to ensure consumer and health protection in host/receiving states, the directive allows member states to decide on a common set of knowledge, skills and competences that are needed to pursue a given profession through introducing Common Training Frameworks (CTFs). Professionals who have gained their qualifications under a CTF will be able to have these recognised automatically without further compensation measures (for example, periods of adaptation or aptitude tests) being imposed.

In proposing a CTF for non-medical "Specialists in Laboratory Medicine", an underpinning building block is an up-to-date, representative syllabus that outlines the specialist skills, knowledge and competencies required for directing laboratory medicine services. In acknowledging that a CTF does not replace national programmes for education and training (unless a member state decides otherwise under national law), it is recognised that the overlap in scope of practise is sufficiently extensive to allow a common syllabus to be described as the European Federation of Clinical Chemistry and Laboratory Medicine's position statement for education and training. The fourth version of the syllabus [4] was built on the specialist's generic skills, knowledge and competencies, whereas the fifth version expands on individual discipline requirements in clinical chemistry/immunology, haematology, blood transfusion, microbiology/virology, genetics and in vitro fertilisation. For the first time also, the authors have provided guidance on the shape of a training programme and the resource allocation required by trainees, their supervisors and institutions.

Structure of the training programme

Objectives

Throughout training, the objective is to develop the knowledge, skills, competence, attitudes and behaviours consistent with specialist level clinical, scientific and professional practise. Clinically, the specialist assesses the appropriate clinical investigations for his/her local population; evaluates how those investigations relate to diagnosis, management and prognosis; and provides the expertise to ensure appropriate application. Scientifically, he/she is able to assess the scope of service need, plan and implement its delivery and ensure a safe and effective working environment. Professionally, the specialist is able to take personal responsibility for his/her actions, working autonomously to take the initiative in complex and unpredictable situations. Additionally, specialists assess, plan, conduct, report, diffuse and adopt their research, development and innovation output. Their clinical leadership training contributes to the evolution of health and healthcare services.

Training environments

The training should be a supervised, work-based placement undertaken in quality assured and accredited centres able to encourage experiential and independent learning. Training should be pursued in a multidisciplinary environment with colleagues across medical/scientific/pharmacy, nursing, allied health professions and non-clinical healthcare related professions. The trainee should be supported in attending relevant local, national and, if appropriate, international meetings and courses. Experience of working in more than one centre is important for achieving broader exposure to a variety of clinical and scientific environments.

The role of the training supervisor

The supervisor's objective is to support and mentor the trainee, promote opportunities for independent learning and reflective practise and encourage the pursuit of high-quality practise and standards. He/she should be an experienced professional (senior clinician) who is familiar with the speciality's education/training requirements, has demonstrable experience in teaching and training and can allocate sufficient time to support the training. He/she is responsible for agreeing a training plan, monitoring and assessing progress on a regular basis, ensuring regular internal and external appraisal and competency assessment.

The role of the trainee

Although some learning will be directed, seizing opportunities for self-directed learning and gaining work-based experience help shape the trainee's approach to future independent working. Examples include the following:

- Attendance and participation in multidisciplinary team meetings, ward rounds and clinics across primary and secondary care
- Contribution to team, management and leadership forums
- Liaison with the diagnostics industry in procurement, implementation and training in the use of new technology
- Communication with and experience of working alongside clinical and non-clinical healthcare professional colleagues on a 24-h, 7-day working basis
- Participation in test request guidance/results reporting and interpretation rotas
- Teaching
- Dissemination of research, development and innovation projects through publication and presentation

A log book based on the syllabus that captures the knowledge, skills and competence that should be acquired during the training period can provide a valuable reflection of experiences, strengths, weaknesses and learning needs. A log book for this version of the syllabus can be downloaded from the EFLM website.

Competency assessment

The supervisor should put in place a programme that

- provides evidence of satisfactory acquisition of the knowledge, skills and competence commensurate with a specialist
- provides evidence of the capability, professionalism and potential of the trainee
- enables the trainee to demonstrate readiness to progress
- generates feedback to inform progression and learning needs
- helps to identify a trainee who may be in difficulty and who may need additional support

Method of assessment

Example tools that can be used for academic, professional and workplace-based assessments include the following:

- Internal/external formal examination – components may include essays, short answer and/or multiple choice questions, laboratory-based practicals, oral examination, critical scenario appraisals and written dissertations.
- Direct observation – capturing the supervisor's and others' perception in internal and external environments of the trainee's understanding of the specialty, his/her skills acquisition, his/her personal and professional presentation and development.
- Multisource feedback – capturing others' perception of the trainee's knowledge, skills, competence, attitude, behaviour, learning need and potential.
- Case-based discussion – through capturing the trainee's perspective on a range of topics – clinical, scientific and professional – a picture builds of strengths, weaknesses, personal qualities, his/her understanding of roles and contributions.
- Use of log books/personal portfolios that record expectations of the education programme against achievements and progression milestones, and which may invite supervisor input.
- Evaluation of written output – examples include (peer reviewed) publications, audits, policy and procedure documents.
- Internal and external appraisal.

Achieving a common training framework

Although the syllabus represents an important milestone, a key inventory item in a CTF is a template that allows national governments to recognise each other's specialists' qualifications. Since 2002, the knowledge skills and

competence required to pursue practise at specialist level has been identified through a professional register [5, 6]; to be a registrant, individuals are required to meet updated Equivalence of Standards amongst medical, scientific and pharmacy-trained practitioners across the EU Community:

- Defines a Master of Science (MSc or equivalent) as an acceptable qualification after an initial 5 years of academic training, followed by an approved exit qualification after 4 years minimum (ideally 5 years) vocational training.
- Includes expectations for education and training to follow this syllabus, which also identifies the competencies required to assure patients that they receive safe and high-quality care.
- Requires specialists to be included in a professional register (if available) in their home country and to maintain their competence and knowledge base through participation in Continuous Professional Development (CPD) activities.

Based on the requirements of regulated countries, the framework should have a training content, including

- general chemistry of at least 35%
- general chemistry plus haematology of at least 65%
- flexibility as to the remaining 35%, including general chemistry, haematology, microbiology and genetics and IVF in a proportion consistent with the requirements in the country of destination, consisting of work experience, accredited courses, relevant exams of the national training programmes and traineeships.

Approach to the syllabus

The syllabus is divided into four main sections:

- Section A: the generic knowledge, skills and competencies that need to be acquired during training.
- Section B: the specialist knowledge within each discipline.
- Section C: the skills and competencies required to carry out research, development and audit.
- Section D: leadership skills and competencies.

By the end of training, the specialist should be able to foster a lifelong habit of CPD, taking personal responsibility, and working autonomously in complex and unpredictable situations.

A. Laboratory Medicine: generic knowledge, skills and competencies

A1: Basic knowledge requirements

1. Knowledge of the structure and function of the prokaryotic and eukaryotic cells, as well as of viruses
2. Understanding of the chemical, cellular and tissue level of organisation of the body
3. Understanding of normal anatomy, physiology and pathology of the body across the integumentary, skeletal, nervous, cardiovascular (including blood, blood vessels and lymphatic system), respiratory, endocrine, renal, gastrointestinal (including nutrition), urinary system and reproductive system
4. Knowledge of the process by which embryonic development occurs from conception to birth
5. Knowledge of the principles of inheritance, DNA and genetics including carrier status, genetic crosses/pedigree/punnet squares/cross diagrams
6. Knowledge of the cellular, tissue and system responses to disease, including cell death, inflammation, neoplasia, hypertrophy, hyperplasia and tissue responses to injury and repair
7. Describe the pathophysiology of disease development in common diseases across the body systems
8. In addition to the knowledge requirements of laboratory medicine disciplines described here, an understanding of the basic principles of histology, including microscopy and staining techniques
9. Understand the basic principles of pharmacology and toxicology, including pharmacokinetic, pharmacodynamic, pharmacogenomic, toxicokinetic, toxicodynamic, toxicogenomic and nutrigenomics
10. Understand the basic principles of epidemiology
11. Understanding personalisation of laboratory medicine based on “omics” advanced technologies (metabolomics, proteomics, transcriptomics and genomics)

Competencies

- Broad knowledge of all aspects of clinical laboratory sciences relevant to the discipline practised
- Broad knowledge of, and insight into, biochemical, haematological and immunological processes in human health and disease on a general and patient-specific level
- Appreciation of developments in science and technology and in the understanding of disease in order to ensure the appropriate use of laboratory investigations

A2: Indications for laboratory medicine procedures

Training objective: an understanding of the scope of application of laboratory medicine practise.

1. In the early detection of disease or disease susceptibility, screening and epidemiology
2. In organ- and disease-related diagnosis
3. In monitoring vital functions and predicting disease outcome
4. In treatment targeting, predicting and monitoring the response to therapy
5. Indications for subsequent specialised examinations
6. Indications for functional tests
7. Prognostic assessment

Competencies

- Appreciation of developments in science and technology and in the understanding of disease in order to ensure the appropriate use of laboratory investigations.

A3: Influence of collection and storage of specimens

Training objective: an understanding of preanalytical factors that may influence the reliability of test results.

1. Place and time of sample collection, preservation, influence of nutrition, drugs, posture, fasting state, etc.
2. Choice and correct use of anticoagulants and transport media, order of draw and tourniquet effects
3. Care of the specimens, patient identification, transport, storage, stability of analytes, influence of temperature and freezing/thawing

Competencies

- Recognition of preanalytical factors that influence the validity of the analytical process
- Ability to deliver the preanalytical requirements of a laboratory medicine service

A4: Analytical principles and techniques

Training objective: by the end of training, the specialist understands the principles of analytical techniques, their limitations and applications.

A4.1 Analytical principles and techniques

Training objectives: a broad understanding of the principles of analytical techniques used in laboratory medicine.

1. Separation techniques
   a. Chromatography – liquid, gas, thin layer, column, high pressure performance, affinity
   b. Electrophoresis – gel, capillary zone, isoelectric focussing
   c. Equilibrium dialysis
   d. Centrifugation – ultracentrifugation
   e. Liquid-liquid extraction and solid phase extraction
2. Standard analytical techniques
   a. Titrimetry
   b. Osmometry
3. Spectrometric methods
   a. Spectrophotometry – ultra violet, visible
   b. Atomic absorption
   c. Turbidimetry
   d. Nephelometry
   e. Fluorimetry
   f. Flame emission
   g. Reflectometry
   h. Mass spectrometry, tandem mass spectrometry
   i. Matrix assisted laser desorption/ionisation – time of flight (MALDI-ToF)
   j. Nuclear magnetic resonance
   k. Infrared
4. Electrochemical techniques
   a. Ion selective electrodes
   b. Biosensor impedance (cell counting)
5. Molecular genetic techniques
   a. Extraction, preparation and DNA/RNA separation techniques
   b. Polymerase chain reaction (PCR), reverse transcription PCR
   c. Quantitative PCR techniques (real-time PCR techniques, digital PCR techniques)
   d. Techniques for detecting single nucleotide polymorphisms (SNPs)
   e. Techniques for detecting more complex genetic variation, DNA sequencing methodologies
   f. Microsatellite and array technology
   g. Cytogenetic analysis
   h. Fluorescence *in situ* hybridization (FISH)
   i. Comparative genomic hybridisation
6. Immunological techniques
   a. Principles of antigen-antibody reactions, immunoassay design

   b. Competitive immunoassay
   c. Non-competitive immunoassay
   d. Homogeneous and heterogeneous assays
   e. Interferences
   f. Signal detection systems – radioisotopes, colorimetric/fluorimetric labels
   g. Immunoprecipitation – (immunofixation, immunoturbidometry, immune-nephelometry)
   h. Agglutination techniques
7. Enzymes
   a. Analytical techniques – reaction rate, end point analyses
   b. Enzymes as reagents
   c. Enzyme kinetics, inhibitors, allosteric behaviour
8. Microscopy
   a. Light brightfield, phase-contrast, polarising, interference contrast, darkfield, fluorescence microscopy
9. Flow cytometry
   a. Cell counting, cell markers detection and fluorochromes
   b. Subsystems; fluidics, optics and electronics
10. Haematological cell staining techniques and preparation of smears, slides or films.
11. Cross matching of blood for blood transfusion. Indirect antiglobulin test, direct antiglobulin test and Rhesus- and ABO-antagonism
12. Rheology
13. Culture and sensitivity; microbial culturing, selection of media, incubation conditions, organism identification techniques, antibiotic sensitivity testing
14. Microbial cell staining techniques – microbe, virus, parasite and fungus identification (including principal differential characteristics)
15. Diagnostic serology for infectious diseases

Competencies

- Knowledge of, and insight into, the use and limitations of technology and analytical techniques relevant to the field of specialisation.
- An appreciation of technological developments with innovative and creative approaches to their implementation.
- Specialist knowledge within chosen specialt(ies).

A5: Reference methodology

Training objective: an understanding of the principles of metrological traceability for standardisation of measurements.

1. Metrological levels of traceability depending on the existence of definitive and reference measurement procedures
2. Metrological levels of traceability depending on certified reference materials
3. Regulations of the European Parliament and of the Council on *in vitro* diagnostic medical devices (repealing Directive 98/79/EC) as the legal background for metrological traceability and standardisation of measurements in laboratory medicine
4. The international concept for metrological traceability of measurements in laboratory medicine according to a set of international standards

Competencies

- Ability to differentiate reasons for performance characteristics of definitive and reference measurements carried out in a routine diagnostic laboratory
- Ability to recognise the advantages of standardised measurements for the development of definitive reference intervals and decision limits.

A6: Evaluation and assessment

Training objective: to acquire the skills and competence to evaluate methods, new diagnostic tests and their application.

A6.1 Analytical evaluation of laboratory methods

1. Binding standards on EU and/or on the national level (e.g. “Regulation of the European parliament and of the council on *in vitro* diagnostic medical devices”)
2. Quality assurance: internal quality control and external quality assessment
3. Method performance: precision, accuracy, specificity and interference, laboratory statistics (e.g. ranges and limits) and carry over

A6.2 Clinical evaluation of laboratory methods

1. Biological variability. Genetic influences, environmental influences, population, age, sex, nutrition, season and time of day, influence of therapeutic agents.
2. Laboratory statistics (e.g. diagnostic validity) of analytical methods.

3. Diagnostic strategies and analytical goals in the use of clinical chemistry tests.

A6.3 Laboratory statistics

1. Basics
   a. Descriptive statistics (e.g. mean, median, quantiles, SD, CV, correlation measures)
   b. Inferential statistics (e.g. distributions, parameter estimation, confidence intervals)
   c. Design of experiments (e.g. power analysis, stratification, batch effects)
   d. Basic features of machine learning techniques
2. Biostatistics
   2.1. Hypothesis testing
      a. Comparison of two samples (e.g. t-, Wilcoxon-, F-test)
      b. Correlation testing (e.g. Pearson, Spearman, Fisher, chi-square)
      c. Goodness of fit (e.g. Kolmogorov-Smirnov, Shapiro-Wilk)
      d. Multiple testing (e.g. ANOVA, Kruskall-Wallis, Bonferroni)
   2.2. Comparison and visualisation of methods
      a. Robust linear regression (e.g. Deming, Passing-Bablok)
      b. Visualisation methods (e.g. Youden and Bland-Altman Plot)
   2.3. Ranges and limits
      a. Analytical ranges (e.g. limits of detection/quantification and linearity, critical difference)
      b. Reference intervals (direct and indirect methods) and laboratory data standardisation
      c. Other cutoff values (e.g. therapeutic ranges, risk ranges)
   2.4. Diagnostic validity
      a. Diagnostic sensitivity and specificity, predictive values
      b. AUROC analysis (including multiclass AUC)
      c. Odds ratio
   2.5. Diagnostic strategies
      a. Exploratory data analysis (e.g. box plots, PCA, clustering)
      b. Classification (e.g. logistic regression, decision trees)
3. Bioinformatics
   a. Omics technologies (genomics, transcriptomics, proteomics, metabolomics)
   b. Data bases (e.g. ENSEMBLE, RefSeq, ClinVar, dbSNP, PDB, MASCOT, MetaboAnalyst)
   c. Data formats and search algorithms (e.g. FASTA, BLAST)
   d. Sequence analysis (variant calling, scoring matrices)

Competencies

- Ability to determine the essential parameters required to evaluate a laboratory method
- Ability to conduct an evaluation using appropriate statistical tools, spreadsheets and databases
- Ability to determine the clinical significance of the outcome of a laboratory method evaluation
- Ability to obtain, explore and employ knowledge in the application of laboratory medicine tests
- Ability to take responsibility for the data and information produced, including knowledge of the influence of variation (biological as well as analytical) on interpretation of data
- Ability to understand the principles and results of multivariate data analyses
- Basic understanding of established bioinformatics algorithms and tools

A7: Case-related medical evaluation of laboratory tests

Training objective: To hold an evidence base evidence base for the choice of tests and interpretation of results.

1. Evaluation of individual results (identifying extreme values, recognition of significance of previous results, recognition of combinations of findings typical of diseases)
2. Use of reference values (influence of age, genetics, sex, lifestyle, interfering factors, effect of therapeutic agents, biological and analytical variation) and limits of decision
3. Longitudinal evaluation of critical differences during disease course, e.g. in long-term conditions, during therapeutic drug monitoring (TDM) and as a result of treatment regimen changes
4. Recommended testing strategies in response to clinical demand for intervention and guidance
5. Independent initiation and/or recommendation of further investigations, reflective testing
6. The laboratory report – provision of evaluation, guidance and interpretive comments

Competencies
- Provision of interpretive, advisory and intervention guidance in the application of laboratory tests, as appropriate
- Ability to communicate the value of laboratory investigations to service users

A8: Clinical training

Training objective: an appreciation of the contribution of laboratory medicine to better health and best care.

By the end of training, a specialist in laboratory medicine should be and evaluate high-quality clinical services that are targeted to meet the needs of individuals and groups of patients. Training requires exposure to clinical environments where laboratory medicine impacts on patient care. Examples include acute and critical care and application of point of care testing. Participation in ward rounds, provision of direct clinical care (as appropriate) as a member of the clinical team and other contact with the users of the laboratory is key to achieving clinical competency. Participating and leading seminars and case discussions also provide valuable experiences.

Competencies
- Ability to communicate effectively with colleagues in the planning and delivery of clinical services
- Understanding of his/her professional responsibility for the well being and personal safety of patients, colleagues and community and workplace environment
- Ability to provide direct clinical care, as appropriate
- Ability to advise appropriate laboratory tests for diagnosis of specific pathology and interpretation of obtained results
- Ability to prepare clinical reports interpreting the results of laboratory investigations

B. Laboratory Medicine disciplines: specialist knowledge [4, 7–10]

B1: Clinical chemistry/immunology

1. Serum fluid and protein and amino acid assessment: Understand the principles of protein measurement in body fluids. Know the principles of serum, urine, cerebrospinal fluid (CSF) and protein electrophoresis. Know the properties and function of the principle proteins such as albumin, protease inhibitors, transport proteins, caeruloplasmin, clotting factors and immunoglobulins. Understand the acute phase response and its effect on different biochemical measurements. Recognise key patterns of dysproteinemias and paraproteinemia, alpha-antitrypsin and immunoglobulin deficiencies.
2. Lipid assessment: understand the chemical structures, biosynthesis, classification, function and metabolism of lipids and lipoproteins. Understand the metabolic basis of inherited and acquired hyper- and hypo-lipoproteinemia. Understand and evaluate the biochemical basis for atheroma, coronary heart disease, associated risk factors and primary and secondary cardiovascular disease prevention. Know Fredrickson classification and treatment of hypercholesterolemia in adults and the classification of hyperlipidemia. Know the principles of analytic techniques for laboratory investigations of lipids.
3. Gastric, pancreatic and intestinal function: By the end of the training period, the trainee should understand the physiological and biochemistry of digestion. The endocrine function of the gut, the production and control of gastrointestinal hormones with examples of pathological conditions such as peptic ulcer disease, pancreatic tumours. Major pathological condition of the gut, e.g. pyloric obstruction, malabsorption, pancreatitis, anaemia due to bowel disease, intestinal failure, malignant tumours, including carcinoid syndrome and neuroendocrine tumours. Investigation of gut function, gut hormones, investigation of malabsorption and diarrhoea. The principles and practical problem of faecal analysis.
4. Glucose and evaluation of diabetes mellitus: Understand the metabolism of glucose and carbohydrates (insulin, C-peptide and other regulatory hormones). Be familiar with the classification of diabetes, the diagnostic criteria for diabetes, impaired glucose tolerance and impaired fasting glucose. Understand the principles of glycated haemoglobin and its role in diagnosis of diabetes. Understand the pathophysiology of type 1 and type 2 diabetes mellitus, secondary diabetes and gestational diabetes. Know the acute complications of diabetes such as diabetic ketoacidosis and hyperosmolar hyperglycaemic state, as well as chronic complications such as microvascular and macrovascular diseases. Understand the principles of treatment of diabetes and monitoring including glucose monitoring, the use of insulin and dietary control and other pharmacological agents. Develop knowledge in laboratory investigations of diabetes,

including blood glucose, oral glucose tolerance test, haemoglobin A_{1c} and urinary microalbumin. Be familiar with metabolic syndrome and understand the diagnosis and investigations of hypoglycaemia.

5. Mineral and bone metabolism: Understand the biochemistry and physiology of bone metabolism including calcium, phosphate, magnesium, parathyroid hormone and vitamin D. Know the causes, investigation, diagnosis and monitoring of conditions such as hyper and hypoparathyroidism, hyper- and hypocalcaemia, hyper- and hypophosphatemia, hyper- and hypomagnesemia. Be familiar with conditions such as osteoporosis, including steroid therapy, osteomalacia, renal osteodystrophy, Paget's diseases and chronic malabsorption. Know the hormones that regulate mineral metabolism (parathyroid hormone [PTH], calcitonin and vitamin D) as well as parathyroid hormone-related protein (PTHrP). Understand the methodologies for measurement of PTH assays, calcium (total, ionised and adjusted) and vitamin D.
6. Porphyrins: Understand the biochemistry and physiology of haemoglobin metabolism. The metabolic basis, diagnosis, investigation and monitoring of porphyrin conditions.
7. Neoplasia (tumour markers): Be familiar with the range of tumour markers undertaken by medical laboratories and their relationship to specific types of cancer, including prostate, lung, breast, ovarian, thyroid, pituitary, adrenal, liver, skin, testicular cancers and those of the gastrointestinal tract. Know the principles and limitations of laboratory methods of various tumour markers, the pathological process that lead to production of tumour markers and the criteria for an ideal tumour marker. Understand the value of tumour markers in diagnosis, screening, prognosis and monitoring.

   Neoplasia (liquid biopsy): be familiar with clonal heterogeneity and major genetic aberrations in human cancer. Know the most important molecular methods for the sensitive detection of mutant tumour genes in plasma.
8. Cardiac biomarkers and the assessment of cardiovascular system: Know the definition of myocardial infarction and understand the interaction of diagnostic modalities in its definition. Understand the current methods of calculating risk, their limitation and use of biochemical markers for risk stratification in acute coronary syndromes. Know the pathophysiology and evaluation of congestive heart failure. Understand the markers of congestive heart failure and their biological and technical limitations. Understand the utility of inflammatory markers in the evaluation of cardiac risk (e.g. homocysteine and high sensitivity C-reactive protein). Know the biochemical investigation and management of hypertension.
9. Endocrinology (Thyroid gland): Understand the structure, biosynthesis, secretion and metabolism of thyroid hormones. Know thyroid physiology and common causes of thyroid diseases including congenital hypothyroidism and screening programme, hypo- and hyperthyroidism, autoimmune disease, autoantibodies, tumours including adenoma and/carcinoma and medullary thyroid cancer. Know the laboratory tests for the investigation of thyroid disorders and be able to interpret these analytes in their clinical context with an appreciation for the euthyroid sick state. Be familiar with current analytical methodologies for thyroid testing and their limitations.

   Endocrinology (pituitary gland): Understand the feedback loops in endocrinology and how they are exploited in diagnostic testing. Understand the physiological action, biochemistry and regulation of anterior and posterior pituitary hormones. Understand the principles of various endocrine dynamic function tests. Understand the pathophysiology of disorders of the pituitary such as acromegaly, dwarfism, prolactinoma, diabetes insipidus, pan-hypopituitarism and isolated hormone deficiency. Understand the endocrine effects of cancer including ectopic hormones, multiples endocrine neoplasia and neuroendocrine tumours.

   Endocrinology (adrenal gland): Understand the physiological of adrenal cortex function and its disorders, including excess steroid production and deficiencies. Be familiar with the biochemistry, biosynthesis, chemical structure and metabolism of glucocorticoids and mineralocorticoids. Know how to assess adrenal reserve and how to investigate Cushing's syndrome, Conn's disease and congenital adrenal hyperplasia. Understand the pathophysiology of adrenal medulla, including catecholamine metabolism and metabolites, pheochromocytoma and neuroblastoma. Be familiar with the measurement of biochemical markers for the assessment of adrenal medulla. Understand the principles of suppression and stimulation testing of the adrenal gland. Understand regulation of the renin-angiotensin-aldosterone system. Understand the synthesis and metabolism of biogenic amines, including catecholamines and serotonin, as well laboratory tests for their evaluation.
10. Reproductive function and pregnancy: understand the endocrinology of the gonads, including

pituitary-gonadal axis, sexual dysfunction, precocious and delayed puberty, the ovarian cycle, metabolism of testosterone, ovarian failure and menopause and poly cystic ovarian syndrome. Be familiar with the biochemical assessment of hirsutism and virilisation. Understand the principles for hormone replacement therapy and oral contraceptives. Understand the physiology and clinical biochemistry of pregnancy and prenatal testing. Know the causes, investigations, monitoring and management of the complications of pregnancy such as hydatidiform mole and choriocarcinoma.

11. Paediatric biochemistry and in-born errors of metabolism: Understand the physiology and biochemistry of the neonatal development. The fluid balance of neonate and the biochemical disturbances associated with over hydration and dehydration. The causes, investigation, monitoring and management of conditions such as jaundice, hypoglycaemia, liver disease, hypomagnesemia, hyperammonemia, disturbances of calcium and phosphate homeostasis, disease of prematurity such as metabolic bone disease. Understand the differences and unique aspects of paediatric and neonatal chemistry, including reference intervals. The investigation of failure to thrive. Know the causes, investigation, diagnosis, monitoring and management of conditions such as hypoglycaemia, inherited and acquired calcium and phosphate disturbances, hyper-ammonaemia, lactic acidosis and renal disorders, including Fanconi's syndrome and tubular defect.
12. Know the key principles and criteria for establishing effective screening programmes. Understand the role of antenatal screening for disorders such as foetal anomalies (serum biomarker and foetal DNA analysis programmes); neonatal programmes such as those for phenylketonuria, congenital hypothyroidism; cancer screening programmes such as hose for prostate (risk management), breast and colorectal cancer.
13. Inherited metabolic disorders: Understand the pathophysiology and biochemistry, clinical presentation and management of inherited metabolic diseases. Understand the principles of enzyme blocks in metabolic pathways and consequential clinical and pathology signs in common inherited metabolic diseases. Know the methods for investigation, diagnosis and monitoring of cystic fibrosis, disorders of amino acids metabolism, glycogen storage disease, carbohydrate metabolism, cerebral lipidosis, fatty acid oxidation defects, disorder of metal metabolism, mitochondrial disorders, mucopolysaccharidoses, organic acid disorders, peroxisomal disorders, primary and secondary purine and pyrimidine disorders, transports defects and urea cycle disorders. Know the prenatal investigation of inherited metabolic diseases of the foetus. Understand the causes and investigation and monitoring of encephalopathy and hyperammonemia. Understand the analysis of amino acids, organic acids, carnitine, acyl carnitines, enzyme assays, mucopolysaccharidoses, tissue culture and DNA investigation.
14. Urogenital tract: By the end of training, the trainee should understand composition of urine, mechanism of stone formation, renal tubular function and defects and the features of renal tubular defect. Understand the diagnosis and assessment of prostatic disease and renal, bladder and prostate cancer.
15. Liver and biliary tract: Understand the function of the liver, mechanism of liver enzymes and the clinical utility of measuring hepatic enzymes. Understand bilirubin metabolism and formation, enterohepatic circulation, bile salt and the causes of jaundice. Understand the unique aspects of neonatal bilirubin and genetic defects that effect bilirubin metabolism. Know the disease of liver such as viral, autoimmune hepatitis, cirrhosis, alcohol/drug hepatotoxicity, non-alcoholic fatty liver disease, cholestasis, biliary obstruction and inherited disease such as hemochromatosis and Wilson's disease. Know the feature of hepatic failure and encephalopathy clinically and biochemically and the assessment of hepatic function.
16. Assessment of renal function: The trainee by end of the training period should know the renal physiology and how it can be assessed, including glomerular and tubular function; salt and water homeostasis, hydrogen ion homeostasis and renal production of hormones, e.g. renin, erythropoietin and vitamin D. Understand the physiology of renal function and distinguish between prerenal, intrinsic and postrenal disease, acute versus chronic renal failure and uremic syndrome. Know the laboratory analytical methods for the measurement of creatinine, urea nitrogen and proteinuria. Understand how renal function may be assessed, including measurement and estimation of glomerular filtration rate, markers of renal function, tubular function tests protein/creatinine ratio and drug interference in urine analysis.
17. Water and electrolytes: Understand the distribution of water and electrolytes, renal handling of electrolytes and key metabolites and the interpretation of urinary electrolyte measurements. Understand the definition of osmolality and calculation of osmotic

gap. Understand the common pitfalls and sources of error during estimation of the osmotic gap (e.g. hyperproteinaemia, hyperlipidaemia, hypermagnesaemia). Understand the differential diagnosis of an unexplained, increased osmotic gap, including alcohol or glycol ingestion, alcoholic or diabetic ketosis or ketoacidosis and osmotherapy (e.g. mannitol or glycerol administration), among others. Understand the principles of fluid balance, regulation of extracellular fluid, the role of antidiuretic hormone, renin-angiotensin-aldosterone and natriuretic peptides. Understand conditions in which water depletion and excess may occur and principles of intravenous fluid therapy.

18. Assessment of pulmonary function, blood gases and oxygen saturation, acid-base status and relevant electrolytes disorders: Understand the physiology of normal respiration, O_2, CO_2, transport and buffers. Understand the principles of the alveolar-arterial O_2 gradient and anion gap. Understand the causes and assessment of acid-base disturbances and understand the principles of H^+, pCO_2 and pO_2 measurements. Know the pathophysiology of ketoacidosis and lactic acidosis. Be able to describe the haemoglobin-oxygen dissociation curve and factors that affect the curve. Understand the principles of integrated blood gas, electrolyte and CO-oximetry systems.
19. Enzymes: Understand the mechanism of induction of enzymes, enzymes stability and the differences between first- and zero-order kinetics of drug metabolism and clearance. Understand structural basis and quantifications of isoenzymes. The enzyme assays such as amylase, lipase, alkaline phosphatase, aminotransferase, γ-glutamyl transferase, angiotensin converting enzymes, creatinine kinase and lactate dehydrogenase, cholinesterase and variants.
20. Trace element: Understand the biochemistry, physiology and metabolism of trace elements (iron, magnesium, zinc, copper, selenium, cobalt and fluoride). Know the biochemistry and clinical significance of metal-binding proteins. Know the clinical assessments of trace elements such as serum iron, iron-binding capacity, transferrin, transferrin saturation, serum ferritin, zinc, protoporphyrin and serum caeruloplasmin.
21. TDM, drug of abuse and toxicology: Understand the principles of pharmacokinetics: absorption, distribution, metabolism and excretion. Understand the differences between pharmacokinetics and toxicokinetics. To be able to explain in the context of TDM the impact that diseases of the GI tract, liver and kidney may have on the drug metabolism. Understand the differences between first- and zero-order kinetics of drug metabolism. Understand the principles of pharmacogenomics in the interpretation of drug levels. Be able to calculate steady-state, peak or trough drug levels throughout a dosing cycle. Understand the principles of toxicodynamics of major drugs and poisons. Understand the pathophysiological basis and be able to recognise the five major toxicological syndromes (cholinergic, anticholinergic, sympathomimetic, opiate and sedative-hypnotic). Understand laboratory evaluation and management of overdosed or poisoned patients. Understand the important differences between urine and blood for monitoring and detection of drugs. Understand the limitations of drug "screening" protocols. Understand the metabolic effect and toxicological profiles of specific agents. Be familiar with the major drugs of abuse and their clinical manifestations. Know the common methods for adulteration of urine and the techniques available in the laboratory to detect them. Understand the general measures used in the treatment of drug addiction including compliance testing for methadone and the testing compliance of commonly abused drugs such as ethanol, opiates, amphetamines, methylenedioxymethamphetamine (MDMA), benzodiazepines and cocaine. Understand the laboratory role in investigation of the unconscious patient in cases of suspected intoxication. Know the advantage and limitations of different analytical techniques for the analysis of both therapeutic and abused drugs and the common causes of false positives due to cross-reactivity. Understand the legal framework for screening for drugs, including preemployment screening, industrial health screening and drug of abuse screening. Understand the principles and legal implications of specimen collection, chain of custody, release of results and employer responsibilities related to drugs of abuse screening and forensic science. Understand the requirement associated with storage and security of drugs and how to investigate *postmortem* toxicology cases.
22. Vitamins: Know the definition and classification of vitamins, fat-soluble vitamins (A, D, E and K) and water-soluble vitamins (B1, B2, B6, B12 [cobalamin], C, niacin, nicotinamide, folic acid, biotin and pantothenic acid). Understand the clinical disorders associated with the deficiency as well as toxicity of vitamins.
23. Immune system: Understand the role of the immune system in defence against infection, in cancer and malignancy; functions of the humoral and cellular immune systems and their regulation; specific and

non-specific immune response, role of cytokines. Understand the application of tests for investigating the immune system; complement factors and hereditary and acquired disorders. Be familiar with primary and secondary causes of immunoglobulin deficiency, the role of cellular and humoral components in immune deficiency. Understand overproduction, monoclonal and polyclonal immunopathies. Understand the presentation, investigation and treatment of systemic autoimmune rheumatic disease and systemic vasculitides, including Rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, giant cell arteritis, haemolytic uraemic syndrome and glomerulonephritis. Understand the factor involved in development of atopic disease (allergy and hypersensitivity); production and role of IgE, mast cell degranulation; principles of investigation of allergy (including coeliac disease). Understand the principles of anaphylaxis and anaphylactoid reactions.

24. Body fluid analysis: Understand clinical indications for body fluid analysis and the principles and methodologies for analysis of fluids such as cerebrospinal, ascetic, pleural and synovial fluid. Understand how to distinguish between exudate and transudate fluids.
25. Nutrition: Understand the normal physiology of human nutrition. Know the causes, investigation, diagnosis and monitoring and management of protein-energy malnutrition, markers of nutritional status, effects and effects of vitamin deficiency or excess, trace element deficiency of excess. Be familiar with nutrition-related conditions such as refeeding syndrome, metabolic syndrome and obesity. Know the investigations, classifications, risk factors and complications of obesity. Understand the biochemistry of starvation. Understand the nutritional management of diseases such as inflammatory bowel disease, coeliac disease, short bowel syndrome, cancer, gall bladder disease, after major abdominal surgery, oesophagostomy and malabsorption.
26. Neuromuscular system: Understand the normal physiology of muscles. Understand the biochemistry of psychiatric disease and the biochemical disturbances associated with neuromuscular disorders. Know the causes, investigation, monitoring and management of neuromuscular disorders such as multiple sclerosis, muscular dystrophy, Parkinson's disease and muscle disease. Understand the pathophysiology, formation and composition of cerebrospinal fluid and its role in the investigation and diagnosis of neurological disorders such as meningitis and suspected subarachnoid haemorrhage.

B2: Haematology and blood transfusion (including blood cells, haemostasis, cellular immunology and transfusion serology

B2.1 Haematology

Understand the theoretical and clinical background of the following:

1. Haematopoiesis in health and disease
2. Morphology and kinetics of blood cells
3. Enzymology of blood cells
4. Haemoglobin synthesis and degradation; iron status
5. Pathophysiology and investigations of haemolysis
6. Classification, clinical indicators and laboratory markers of erythrocyte, granulocyte and lymphocyte disorders
7. Hereditary and acquired, non-oncological haematopoiesis abnormalities, including haemoglobinopathies and thalassemia
8. Symptoms, pathogenesis and laboratory investigation of anaemia (including erythrocytes membrane and enzyme abnormalities and status of iron, vitamin B12, folate, metabolite, etc.)
9. Symptoms, pathogenesis and laboratory investigation of haemato-oncological abnormalities (including leukaemias, myeloproliferative disorders, lymphomas, multiple myelomas, myelodysplastic syndrome, etc.)
10. Haematological, immunological, microscopic, cytogenetic and molecular methods used in the diagnostics of haematological disorders, along with interpretation of obtained results
11. The role and strategy of the laboratory diagnostics in haematological diseases diagnosing, differentiating, monitoring and evaluating the effects of treatment
12. Acquire the theoretical and practical knowledge related to diagnostic procedures in haematology:
    a. Complete blood count (CBC): WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, HDW, PLT, P-LCR, L-PLT, reticulocyte, CBC with differential; knowledge of haematological parameters
    b. Determination of erythrocyte sedimentation rate
    c. Preparation and staining of blood and bone marrow smears, along with microscopical evaluation
    d. Cytochemical staining including detection of MPO, FAG, PAS, Sudan black, acid phosphatase, esterase, iron
    e. Detection and measurement of variant and minor (HbA_2 and HbF) haemoglobins
    f. Detection of abnormal haemoglobin derivatives: spectrophotometric analysis

g. Haemoglobin electrophoresis on cellulose acetate, in agarose gel
h. Foetal haemoglobin testing (Kleihauer, flow cytometric HbF determination)
i. Molecular diagnostic approaches
j. Investigation of cellular characteristics and abnormalities by flow cytometry
k. Flow cytometry and leukocyte subgrouping
l. Flow cytometric immunophenotyping of hematopoietic malignancies

B2.2 Haemostasis

Understand the theory and principles of the following:

1. Haemostasis physiology, including the role of blood vessels, platelets, coagulation factors, fibrinolytic system and inhibitors of coagulation
2. Haemostatic risk factors for atherosclerosis and cardiovascular disease
3. Inherited and acquired coagulation abnormalities leading to bleeding and/or thrombotic disorders (including platelet and fibrinogen abnormality, vWD, haemophilia, DIC, TTP, HELLP, HIT, thrombophilia, etc.)
4. Haemostatic dysfunction related to various diseases and clinical stages
5. Clinical approach to investigation of haemostasis
6. Interpretation of test results relating to haemostasis and its components
7. Markers of coagulation activation
8. Monitoring of therapy in bleeding disorders
9. Anticoagulant treatment in clinical and outpatient conditions
10. Anticoagulant and antiplatelet therapy
11. Acquire the theoretical and practical knowledge for diagnostic procedures related to haemostasis:
    a. PT, APTT, TT, reptilase/ancrod time, concentration and/or activity of fibrinogen and other coagulation factors, correction tests, ELT, plasminogen, PAI, circulating anticoagulant, etc.
    b. Thrombin and plasmin activation: TAT, prothrombin fragments F1+2, D-dimer, PAP
    c. Platelet function (clot retraction, aggregation, PFA-100, thromboelastography, flow cytometry)
    d. Laboratory diagnostics of VWF abnormalities (e.g. vWAg, vWR:Cof, RIPA, multimers, ADAMTS13)
    e. Thrombophilia testing (including A-PCR, FV Leiden, FII, AT, PC, PS, APA, etc.)
    f. INR, APTT-R, anti-Xa

B2.3 Blood transfusion

1. Principles of patient identifications and pretransfusion testing:
    a. Blood group antigens and other antigen systems as considered in blood transfusion (including genetics).
    b. Selection criteria of donors for blood transfusion.
    c. Several types of transfusion reactions, foetal maternal bleeding.
    d. Medical applications, clinical relevance and indications for the administration of blood and blood components.
    e. Preparation and application of blood components.
    f. Organisation of blood banking.
    g. Platelet antibodies.
    h. Typing of leucocytes and tissue antigens.
    i. Recognition of cell markers using monoclonal antibodies; the application of plasmapheresis both in donors and in patients
2. Acquire the theoretical and practical knowledge related to diagnostic procedures in blood transfusion:
    a. Typing of irregular (auto) antibodies; determination of antibody titre
    b. Extended blood group typing
    c. Investigation of transfusion reactions
    d. Typing of B and T lymphocytes

B3: Microbiology (bacteriology, mycology, virology and parasitology)

B3.1 Clinical bacteriology

- Bacterial cells structures and associated functions
- Bacterial classification and phylogeny
- Bacterial physiology (metabolism, growth curve)
- Bacterial genetics: role of mobile genetic elements (plasmids, insertion sequences, integrons, transposons, etc.) in transfer of resistance and virulence genes, mechanisms of transfer (conjugation, transformation, transduction, etc.)
- Normal microbiota: definition, composition, roles
- Bacterial pathogenicity and virulence factors
- Microbial biofilms: definition, biofilm associated infections, resistance to antimicrobials
- Colonisation versus infection
- Commonly encountered bacteria and related infections (morphological, colony and cultural, biochemical, antigenic and pathogenic features)

- Aetiology, pathophysiology and presentation, including sources and routes of transmission of infectious diseases in the community and hospital-acquired infection (HAI)
- Emerging and changing patterns of bacterial infections

B3.2 Clinical virology

- Animal viruses classification
- Viral replication and modes of transmission
- Commonly encountered viruses and related human infections
- Emerging and changing patterns of viral infections
- Microbiology health and safety legislation and its application within the laboratory

B3.3 Sexually transmitted infections

- The aetiology, pathophysiology and clinical presentation of the more common sexually transmitted infections (STI)
- Congenital STI and associated risks
- Investigation and management of common infection problems in the intensive care unit (ICU)
- Infections specific to pregnancy (e.g. septic abortion, chorioamnionitis, endometritis)
- Infections that may compromise pregnancy (e.g. STI, fungal infection, parasitic disease)
- Pathophysiology of infectious disease in children (e.g. neonatal meningitis, group B sepsis, intraventricular shunt infections)
- Treatment of childhood infections, including the selective use of antimicrobials

B3.4 Mycology and clinical parasitology

- Fungal replication and modes of transmission
- Parasitic life cycles and modes of transmission
- Pathogenesis, epidemiology, clinical investigation and management of fungal and parasitic infection
- Commonly encountered fungal and parasitic infections
- Emerging fungal and parasitic diseases
- Principles and practise of treatment of fungal and parasitic infection
- Role of specialised microbiology laboratories in mycology and parasitology

B3.5 Principles of antimicrobial therapy

- Structure, classification and mechanism of action of commonly prescribed antimicrobial agents
- Antimicrobial resistance: definition, mechanisms, surveillance, assessment and risk to human health
- Natural vs. acquired resistance
- Natural resistance phenotypes of the most clinically relevant microorganisms
- Current guidelines relating to antimicrobial susceptibility testing and their use in clinical practise
- Methods for antimicrobial susceptibility testing – disc diffusion, agar diffusion, broth microdilution, E-test, etc.
- Emerging antimicrobial agents, e.g. revived and novel antimicrobials, bacteriophages, iRNA, vaccines, serotherapy, anti-pathogenic strategies (e.g. quorum sensing inhibitors), physical antimicrobial strategies based on physical agents (cold plasma, phtotodynamic therapy, etc.)
- Value of antimicrobial stewardship

B3.6 Epidemiology and health protection

- Communicable disease surveillance and reporting
- Role of laboratory services and techniques to support epidemiological investigation
- The principles of outbreak prevention, investigation and management
- Standards and guidelines in relation to occupational exposure to infectious agents
- Epidemiological consequences of hospital-acquired and community disease control with reference to tuberculosis, viral hepatitis, HIV and genitourinary disease
- Management of needlestick injuries in the clinical setting
- Decontamination, disinfection and sterilisation in the hospital, laboratory and primary care setting
- Principles of screening for certain organisms, e.g. MRSA, multiresistant Gram-negatives, including CPE, vancomycin-resistant enterococci
- Water safety within the healthcare setting, *Legionella*, *Pseudomonas*, *M. chimera*
- Investigation protocols and patient pathways relevant to hospital-acquired and community infection
- Environmental outbreaks, e.g. *Legionella*, *Norovirus*
- The role of health protection and surveillance agencies

B3.7 Public health worldwide: implications for clinical microbiology

- Pathogens involved in food- and water-borne infections
- Common causes of infection in returning travellers (e.g. malaria, viral haemorrhagic fever)
- Epidemiology, distribution and investigation of common tropical infections (e.g. malaria, tuberculosis, enteric fever, cholera, dysentery, schistosomiasis, onchocerciasis, trypanosomiasis, gastrointestinal GIT parasites, dengue, yellow fever)
- Epidemiology, distribution, investigation and management of pandemic influenza and other global infectious diseases. The role of the WHO, governments and health providers
- Bioterrorism and measures to reduce risk

B4: Genetics, genomics and cytogenetics

- Nucleic acid structure and function
- Chromosome structure, function and abnormalities (e.g. Down's syndrome, sex chromosome abnormalities, translocations)
- Nomenclature used to describe the human genome
- DNA replication, transcription and translation
- Meiosis, mitosis and Mendelian inheritance
- Patterns of inheritance (autosomal, X-linked, non-Mendelian)
- Use of genome analysis tools, the role of bioinformatics in the investigation and management of genetic and genomic disorders
- Common genetic and genomic disorders and their impact on patient and their families
- Scientific basis of inherited and sporadic cancers
- Principles and practise of genetic counselling

B5: *In vitro* fertilisation

1. A basic knowledge of sperm count, sperm vitality and mortality and sperm morphology
2. A basic knowledge of fresh and frozen sperm preparation
3. An understanding of the factors affecting oocyte quality
4. An understanding of the contribution of laboratory medicine investigations in assessment of fertility, assessment of opportunities for in vitro fertilisation and the monitoring of progression of pregnancy
5. Cryopreservation of gametes (sperm and oocyte) and embryos, and theoretical and practical aspect of slow cooling and verification

C. Research, development and audit

Training objective: by the end of the training, a specialist in laboratory medicine should be able to plan, conduct, supervise, clinically evaluate, interpret and report research, development and audit findings. Examples include original research, translation of research and adoption and diffusion of innovations into clinical practise. As laboratory medicine is continually and rapidly evolving involvement in research, development and audit is indispensable. Special attention must be paid to the following:

1. Development and improvement in technologies, techniques and methodologies, with special emphasis on new developments in areas such as molecular biology, proteomics, mass spectrometry
2. Procedures to test and evaluate the steps of a method and the components of an instrument
3. Initiation, conduct and evaluation of laboratory-based and clinical research and development based on best evidence of practise
4. Initiation, conduct and evaluation of clinical and laboratory audit to ensure quality, governance and patients' needs continue to be met
5. Generating outcomes of research and development, audit and service improvement programmes using recognised scientific and statistical techniques

Competencies

- Ability to conduct research, either basic or applied, in order to further knowledge in the field of laboratory medicine
- Ability to undertake literature/systematic reviews and design quantitative and qualitative programmes for research, development, audit and service improvement based on best evidence
- Ability to appraise the need and set priorities for research, development, audit and service improvement programmes
- Understanding of research governance, ethical and legal frameworks, funding streams, the influence of regulatory and healthcare-related organisations in local settings
- Ability to design and conduct the required experiments to ensure objectives are met

- The application of statistical and biostatistical procedures to evaluate quantitative and qualitative information and data
- Ability to appraise and translate outcomes to enhance activities, as appropriate
- Ability to communicate orally and in writing, including the production of clear, cogent reports and publications in international scientific journals

3. Risk management and procedures designed to minimise risks
4. Requirements for a quality management system – quality assurance, governance, monitoring of planned actions, audit, incident reporting
5. Managing internal quality control and external quality assessment performance
6. Data, information and knowledge management: use of medical informatics, data processing, spread sheets/databases, electronic/telecommunications

D. Leadership

Training objective: To operate as a clinical leader supporting and transforming health and health care services, depending on the working environment the specialist in laboratory medicine should be familiar with some or all aspects of the responsibilities listed below.

D1: Laboratory direction and leadership

1. Specifying service requirements
2. Setting strategy and establishing policy
3. Formulating laboratory plans
4. Assessing resource requirements – staff, space, equipment
5. Analysing costing (efficiency) and cost-benefits (effectiveness)

D2: Laboratory organisation

1. Design and utilisation of space and facilities
2. Selection of methodologies and equipment
3. Selection of information management and technology systems
4. Recruiting and managing a staff/skill mix appropriate for the service
5. Establishing preanalytical, analytical and postanalytical processes
6. Preparing protocols, procedures and guidelines
7. Preparing business and strategic plans and service level agreements
8. Budgetary responsibilities (contracting, performance management, financial controls)
9. Design of request and report forms

D3: Quality

1. The criteria and process of laboratory accreditation
2. Medical laboratory and point of care testing

D4: Education/training/continuous professional development

1. Demonstrate good communication, mentoring, supervising and assessing skills.
2. To be able plan and prepare teaching material using evidence based information and data.
3. Participate in range of teaching and assessment methods.
4. Build a good knowledge of the clinical context before teaching or training others.
5. Understand the range of different mentoring styles from perspective of the learner and the teacher.
6. Ensure skills, competencies and motivation of staff meet service requirements.
7. Ensure staff access education and training programmes appropriate for service needs.
8. Participate, as appropriate, in staff education, training and appraisal.
9. Ensure staff remain up to date by participation in CPD.
10. Ensure own training, education, appraisal and CPD needs are maintained.

D5: Laboratory health and safety

1. Handling of potentially infectious samples (e.g. HIV and hepatitis), handling of noxious chemicals and isotopes, mechanical and electrical safety, fire precautions, dealing with an accident, accident prevention and hygiene regulations, occupational diseases
2. Aware of all the legal rules and regulation of health care service that have to be met to ensure compliance with safe practise and maintaining attainment of accreditation status
3. Alert systems, incident reporting

D6: Legal, ethical and governance considerations

1. Laws, regulations, guidelines and recommendations on work in clinical laboratories: in particular, requirements for accreditation of services, education and training, health and safety, infection control, buildings, employment law, regulation and registration of staff.
2. Ethical aspects and conventions on production, interpretation, reporting and use of medical laboratory data.
3. Confidentiality, data protection and security.
4. Clinical and research governance expectations of government, health care-related organisations and employers for high-quality, evidence-based care.

Competencies

- Ability to safeguard and protect the public against misuse of medical laboratory investigations
- Knowledge of the principles of management leading to satisfactory direction, supervision and organisation of a laboratory department in a public or private hospital or in any other healthcare environment resulting in the provision of a competent service as laid down in a laboratory quality manual, based on good laboratory services as defined in EN-ISO document 15189 [11]
- Ability to determine the optimum distribution of resources across central laboratories, peripheral sites and near patient testing settings
- Ability to assess conflicting and various technical, financial and human considerations (e.g. care, quality, safety, cost and time scales) both in the short- and long-term, and to find the optimal solution in relation to patient care
- Ability to apply current techniques in human resource management
- Execution of judgement and leadership

D7: Professional practise and soft skills

Training objective: to demonstrate adequate knowledge and skills and appropriate attitudes to work largely autonomously and taking the initiative in complex situations and performing complex clinical and scientific by the end of 5 years training period.

The specialist in laboratory medicine develops sufficient skills to communicate fluently with patients, medical and other colleagues and develops skills to write meaningful reports. Finally, specialist in laboratory medicine should be able to critically appraise the literature and communicate outcome in writing or verbally with colleagues.

New specialists in laboratory medicine will

- have the breadth of knowledge and skills to take responsibility for safe clinical decisions
- have the self-awareness to acknowledge where the limits of their competence lie and when it is appropriate to refer to other senior colleagues for advice for advice
- critically apply their understanding of the role and importance of continuing professional development to ensure that professional knowledge and skills are being kept up to date
- act at all times in a manner that demonstrates probity in all aspects of professional practise and code of conduct
- display a professional commitment to ethical practise consistently operating within national and local ethical, legal and governance requirements

Acknowledgments: In preparing version 5, the authors acknowledge the historical contributions of the European Communities Confederation of Clinical Chemistry and Laboratory Medicine (EC4) to versions 1–4, which unified the expectations for education and training that identify the knowledge, skills and competence associated with specialist practice in laboratory medicine

Author contributions: NJ and GW drafted the manuscript. MD, JL, JQ and DR advised on the syllabus. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Guarantor: N. Jassam

Research funding: None declared.

Employment or leadership: None declared.

Honorarium: None declared.

Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

References

1. Cambridge English Dictionary & Thesaurus. Syllabus. Cambridge English Dictionary & Thesaurus [serial on the Internet]. Available from: http://dictionary.cambridge.org/dictionary/english/syllabus?q=Syllabus.
2. European Parliament and EU Council. Directive 2013/55/EU of the European Parliament and of the Council of 20 November 2013 amending Directive 2005/36/EC on the

recognition of professional qualifications and Regulation (EU) No 1024/2012 on administrative cooperation through the Internal Market Information System ('the IMI Regulation') 2013: Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2013:354:TOC.
3. European Commission Press release. Commissioner Michel Barnier welcomes the trilogue agreement on the modernisation of the Professional Qualifications Directive. Memo [serial on the Internet]. 2013: Available from: http://europa.eu/rapid/press-release_MEMO-13-552_en.htm.
4. Wieringa G, Zerah S, Jansen R, Simundic AM, Queralto J, Solnica B, et al. The EC4 European syllabus for post-graduate training in clinical chemistry and laboratory medicine: version 4 – 2012. Clin Chem Lab Med 2012;50:1317–28.
5. McMurray J, Zerah S, Hallworth M, Koeller U, Blaton V, Tzatchev K, et al. The European Register of Specialists in Clinical Chemistry and Laboratory Medicine: Code of Conduct, Version 2 – 2008. Clin Chem Lab Med 2009;47:372–5.
6. McMurray J, Zerah S, Hallworth M, Schuff-Werner P, Haushofer A, Szekeres T, et al. The European Register of Specialists in Clinical Chemistry and Laboratory Medicine: guide to the Register, version 3 – 2010. Clin Chem Lab Med 2010;48:999–1008.
7. NHS – Modernising Scientific Careers. HSST – Higher Specialist Scientist Training. Curricula for the Higher Specialist Scientist Training Programme NHS UK, 2016.
8. Simundic AM, Topic E, Cvoriscec D, Cepelak I. Clinical chemistry and laboratory medicine in Croatia: regulation of the profession. Biochem Med (Zagreb) 2011;21:15–21.
9. Smith BR, Wells A, Alexander CB, Bovill E, Campbell S, Dasgupta A, et al. Curriculum content and evaluation of resident competency in clinical pathology (laboratory medicine): a proposal. Am J Clin Pathol 2006;125(Suppl):S3–37.
10. The Royal College of Pathologists. Curriculum for specialty training in chemical pathology 2010; (G043): Available from: http://www.gmc-uk.org/Chemical_Pathology_Curriculum__AR.pdf_33506735.pdf.
11. ISO 15189:2012 Medical laboratories – Requirements for quality and competence. Available from: https://www.iso.org/standard/56115.html.