

National Training Requirements

CROATIA

Specialty Clinical Pharmacology and Toxicology

Klinička farmakologija s toksikologijom

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Note: This is not a legally binding document. Any current official regulations must be obtained from the responsible National Medical Association or other organisation in charge of the training of medical specialists.

Table of Content

Name of Specialisation	3
Title acquired after Specialist's Exam.....	3
Duration of specialization	3
Specialization program.....	3
I. Introduction to specialization – 3 months.....	3
II. Clinical pharmacology – 13 months.....	3
III. Pharmacology – 6 months	3
IV. Clinical Toxicology – 3 months and 2 weeks	3
V. Clinical disciplines – 17 months.....	3
VI. Legislation – 1 month and 2 weeks	4
Holidays – 4 months	4
Postgraduate study "Clinical pharmacology and toxicology" – 3 months	4
Competencies acquired upon completion of specialization.....	4
1. General competencies	4
2. Specific competencies.....	6

Name of Specialisation

Clinical pharmacology and toxicology

Title acquired after Specialist's Exam

Specialist in clinical pharmacology and toxicology

Duration of specialization

48 months (4 years)

Specialization program

I. Introduction to specialization – 3 months

- Department or Division of Clinical pharmacology – 1 month
- Emergency / intensive units – 1 month
- Pharmacological Toxicology Laboratory – one month

(Laboratory for pharmacology and toxicology, laboratory for pharmacokinetics and pharmacogenetics)

II. Clinical pharmacology – 13 months

Department of Clinical Pharmacology:

- Department of Clinical Pharmacology – 4 months
- Centre for Medicines, stationary part, polyclinic section – 9 months

III. Pharmacology – 6 months

Department of Pharmacology, School of Medicine according to residency – 4 months

- Basics of pharmacogenomics – 2 weeks
- Basics of Pharmacoeconomics – 2 weeks
- Basics of biostatistics – 2 weeks
- Basics of pharmacoepidemiology – 2 weeks

IV. Clinical Toxicology – 3 months and 2 weeks

- Intensive care unit – 2 months
- Paediatric toxicology – 1 month
- Institute for Medical Research – 1 week
- Croatian National Institute of Toxicology – 1 week

V. Clinical disciplines – 17 months

- Paediatrics – 1 month
- Pulmonology – 1 month
- Infectious diseases – 2 months
- Cardiology – 2 months
- Neurology – 1 month

- Gastroenterology – 2 months
- Clinical immunology – 1 month and 2 weeks
- Haematology – 2 months
- Endocrinology and diabetology – 1 month
- Nephrology and renal replacement therapy – 1 month and 2 weeks
- Psychiatry – 1 month
- Oncology – 1 month

VI. Legislation – 1 month and 2 weeks

- The Agency for Medicinal Products and Medical Devices – 3 weeks
- Ministry of Health
 - Drug department – 1 week
 - Central Ethics Committee for clinical trials – 1 week
- Croatian National Insurance Company – 1 week

Holidays – 4 months

Postgraduate study "Clinical pharmacology and toxicology" – 3 months

Within the specialization in clinical pharmacology and toxicology, a resident must complete a postgraduate specialist study "Clinical pharmacology and toxicology."

During the residency, residents are obliged to attend courses of continuing professional development for physicians.

Competencies acquired upon completion of specialization

Level of competence adopted:

- 1: The resident in clinical pharmacology and toxicology has acquired knowledge in different topics at the basic level and needs assistance and supervision during work and clinical problem solving.
- 2: The resident in clinical pharmacology and toxicology has partially acquired knowledge in different topics areas and is able to work and solve problems with partial supervision.
- 3: The resident in clinical pharmacology and toxicology has fully acquired knowledge in different topic areas, has a knowledge from the relevant literature and is able to work independently and solve problems of the thematic areas.

The resident, chief mentor and tutor are responsible for acquisition of competencies.

1. General competencies

Upon completion of specialist training, the resident in clinical pharmacology and toxicology must have fully adopted the general competencies. Special attention must be given to the acquisition of general competencies relevant to a particular discipline of specialization.

Upon completion of residency in clinical pharmacology and toxicology, residents must:

- know and apply the principle of the medical profession (3);
- possess professionalism, humanity and ethics with an obligation to maintain the privacy and dignity of patients (3);
- know the skills of dealing with patients, colleagues and other professionals – communication skills (3);
- know the importance and apply the principles of good cooperation with other workers in the health sector (3);
- be able to understand and appropriately convey relevant information and explanations to the patient (oral and written), his family, colleagues and other experts for joint participation in planning and implementation of health care (3);
- be able to define, screen and properly document the relevant information about the patient, get informed consent and take into account the views of the patient and his family, the views of other colleagues and other experts (3);
- through continuous learning and self-evaluation be able to improve the competencies and attitudes necessary for improving the quality of professional work (3);
- adopt principles to manage their practice and career with the aim of professional development (3);
- have developed the skill of transferring knowledge to younger colleagues and other workers in the health sector (3);
- understand the importance of a scientific approach to the profession (3);
- participate in scientific research while respecting ethical principles of scientific research and clinical studies and participate in the preparation of papers for publication (3);
- be able to contribute to the creation, application and transfer of new medical knowledge and experience and participate in the implementation of the program of specialization and sub-specialization (3);
- know and apply the principles of evidence based medicine (3);
- know the importance and effective way of keeping detailed documentation and also apply it to their work in accordance with the regulation in force (3);
- be able to coordinate and prioritize teamwork and effectively participate in the work of a multidisciplinary team of health workers and associates (3);
- evaluate the need to involve other professionals in the process of providing health care (3);
- be aware of the importance of co-operation and actively cooperate with public health authorities and other bodies included in the health care system (3);
- know the organization of the healthcare system and be able for responsible participation in the management of the activities and needs of assessment, planning measures to improve and increase the efficiency and development of the system of quality health care (3);
- possess knowledge of regulations in the field of health, especially in the field of protection of the rights of patients (3);

- understand the meaning of their own responsibilities and data protection and the rights of patients (3);
- know the course, schedule and control of work processes and basics of management of resources, especially financial ones (3);
- understand and critically use available funds for health care, guided by the interests of their patients and community (3);
- be able to assess and appropriately respond to individual health needs and problems of patients (3);
- identify the health needs of the community and in accordance with them take appropriate measures aimed for the preservation and promotion of health and prevention of disease (3);
- promote health and healthy lifestyles of their patients, the community and the general population (3).

2. Specific competencies

This section lists the specific educational objectives, key competencies, skills, attitudes and patterns of behaviour that are expected to be acquired during specialization in clinical pharmacology and toxicology:

1. To carry out and interpret the results of early phase studies and drug action in humans (3):
 - to recognize and interpret the interaction of receptors of drugs and related principles, agonists, antagonists, the dose/effect, pharmacodynamics, pharmacokinetics, pharmacodynamics relations / pharmacokinetics, efficacy, potency of the drug;
 - understand and interpret the principles of the surrogate targets research, tolerance, side effects, show understanding of the limitations of preclinical research of biological products for human drug trials of early stages;
 - write a research protocol;
 - write an explanation to Central Ethics Committee for clinical trials;
 - be able to choose subjects to study and of obtain from them an informed consent;
 - conduct research in volunteers with regards to pharmacokinetics and pharmacodynamics;
 - be able to measure the research outcomes;
 - record data, analyse the data including the determination of the final dose in the Phase 3 studies;
 - identify, review and analyse the relevant literature as well as prepare an article for publication;
 - demonstrate communication skills in effective presentation of the article at a scientific conference;
 - properly advise, recognize the importance of the safety of prescribing drugs;
 - recognize the need for proper documentation of all procedures in research;
 - to be aware of the importance of oral and written presentation of their own results.
2. Use pharmacokinetic principles to optimize prescribing and drug effects (3):
 - explain the principles of choosing the route of drug administration, drug absorption, metabolism and excretion;

- interpretation of the results of drug concentrations in body fluids;
 - pharmacokinetics, pharmacokinetic modelling, mechanism of pharmacokinetic drug interactions;
 - pharmacogenetics, knowledge of individualization of therapy;
 - demonstrate knowledge of the main analytical methods and their limitations;
 - show knowledge of Good Laboratory Practice (GLP);
 - prepare and adequately adapt treatment regimens. Discuss with the patient an acceptable mode of treatment;
 - recognize the need for individualization of therapy
3. Use medicines rationally (3):
- demonstrate knowledge of mechanisms of action and principles of use of antihypertensives;
 - demonstrate knowledge of mechanisms of action and principles of use of antimicrobial drugs;
 - demonstrate knowledge of mechanisms of action and principles of use of oral antidiabetics and insulin;
 - demonstrate knowledge of mechanisms of action and principles of use of cytostatics;
 - demonstrate knowledge of mechanisms of action and principles of use of drugs affecting the central nervous system;
 - demonstrate knowledge of mechanisms of action and the principles of use of antiplatelet agents, fibrinolytics, and anticoagulant drugs;
 - demonstrate knowledge of mechanisms of action and principles of use of analgesics;
 - demonstrate knowledge about the sources of interindividual differences, including those caused by genetics, age, sex or differences caused by diseases of the liver or kidneys;
 - explain the role of national and European authorities responsible for the registration of drugs and medical devices;
 - knowledge of medicines obtained without a prescription (OTC);
 - knowledge how to communicate with patients, colleagues or within working groups and committees;
 - rationally select drugs and dosage according to the principles of individualization of therapy;
 - knowledge of the principles of isolation of patients and its proper application;
 - develop patterns and policies for prescription drugs;
 - develop guidelines and therapeutic forms, evaluate the guidelines on the use of drugs within the various working groups;
 - make clear submissions to the Agency for the registration of new drugs for the purpose of introducing a new drug to market ;
 - assess the expertise and opinions of various working groups;
 - assess indications for testing sensitivity and how to conduct the hypersensitivity test;

- advise pregnant women on the application of drugs, prepare clinical pharmacology opinion in pregnancy, search the literature about the application of drugs in pregnancy;
 - conduct continuous medical education about medicines and rational use of medicines, preparation of printed material, preparing presentations, search for rational, objective information about drugs;
 - solve problems of polypharmacy, recognize irrational administration of drugs, advise patients on medication, draw up opinions on medication, dose adjustment of drugs in accordance with concomitant diseases and therapy.
4. Critically evaluate the literature relevant to clinical use of drugs, including the field of basic pharmacology, toxicology and clinical studies of the Phase I, II, III and IV as well as meta-analyses. (3):
- knowledge of basic pharmacology and clinical medicine;
 - knowledge of methods and ways of reactions to ethically unacceptable advertising of medicines / medical devices;
 - critically analyse articles and writings on rational prescribing of medicines and drugs in early stages of clinical trials, analytical methods, potential sources of bias in the data, conflicts of interest, acceptability discussions, the validity of the conclusions;
 - use electronic databases (Medline, Embase, Toxbase, Cochrane, Micromedex);
 - respect ethical principles governing the "peer review";
 - evaluate expert opinions.
5. Plan clinical trials of all phases and contribute to their implementation and dissemination of results. Prospectively select appropriate statistical method for the planned experiments (including clinical trials) and conduct the analysis and interpret statistical data (3):
- describe sources of biological variation and explain the principles that are responsible for it;
 - describe common parametric and non-parametric tests including chi square test, t test, ANOVA, Bonferroni correction and Spearman regression, critically analyse the pros and cons of sequence analysis;
 - effectively consult with a statistician during the planning of complex experimental research, interpret p waves and confidence intervals including case studies with negative outcomes;
 - explain the concepts of absolute and relative risk.
6. Development of the research plan and its implementation:
- describe the different ways of designing clinical trials, demonstrate knowledge of the principles of controlled experiments, randomization, use of placebo and double-blind trials, describe the principles underlying ethics in research on humans including the duties, rights and benefits, demonstrate knowledge of the principles of Good Clinical Practice (GCP);
 - select the type of research consistent with the drug under investigation, write a report to the Ethics Committee, justified by objective research so that it is understandable by lay members of the Ethics Committee;

- be able to choose the research subject, assess possible subjects in the study according to the criteria of inclusion and exclusion, to obtain valid informed consent, organize visits to patients in research centres and clinical laboratories, perform or supervise clinical measurements, keep and maintain records according to the standards of GCP;
 - contribute in writing articles and publishing results (oral or poster presentations) in professional or scientific meetings;
 - adhere to the research protocol in which the external examiner has the right of final control, publishing or otherwise using data resulting from research, carefully record the details of research, recognize the importance of security of the respondents in the survey, maintain a professional relationship with sponsors and their employees.
7. Expect (and thus reduce), detect, report and analyse adverse drug reactions (3):
- demonstrate knowledge about the common (and serious) side effects of drugs administered in their indication, the mechanisms by which drugs cause side effects, most commonly clinic presentation side effects, proper clinical management of drug side effects, explain how the side effects of drugs are identified and reported, explain and classify adverse drug reactions;
 - treat severe and serious adverse drug reactions including anaphylaxis, use printed and electronic databases to identify uncommon side effects of medications;
 - critically analyse the results of phase IV study, properly report the side effects of drugs;
 - be aware that clinical condition may be due to side effects, be ready to expose doubts and share information regardless of the possible consequences, consult with colleagues on judgments about the risks/benefits, be critical in terms of marketing methods that obscure the market research on drugs.
8. Describe and identify factors influencing the consumption of drugs in different groups of patients (3):
- identify factors affecting the consumption of drugs including: social status, ethnicity, nationality (particularly within Europe), economic status, comorbidity, gender (especially in women, pregnancy, lactation), age; demonstrate knowledge of the factors affecting public perception of drugs and their use in the treatment of disease, including the effects of public media regarding the way to use drugs; describe the role of the pharmaceutical industry in the public perception of the use of drugs; explain the role of government in the process of licensing, describe determining the prices and cost-benefit (cost/benefit) and legal regulations on medicines; explain the role of local organizations (hospital committees for drugs) in defining the availability of drugs in the context of local health facilities;
 - apply knowledge of drugs in individual patients for the preparation of treatment guidelines, effectively communicate with the media and with the committees, establish conflict of interest and adhere to its principles;

- respect ethnic diversity, respect individual autonomy, contribute to public education about drugs and their use, respect the legislation for medicines, take part in the current reform of the system of health care in Croatia.
9. Ethics in clinical trials :
- identify ethical principles underlying human studies, explain ways of decision-making in cases of conflict with ethical principles;
 - explain the basis and structure of ethics committees, demonstrate knowledge of appropriate terminology concerning ethics committees, understand GCP and international guidelines for conducting ethically acceptable research in people, know the legal framework by which ethics committees in Croatia operate.
 - analyse application to Central Ethics Committee, pose appropriate questions to the applicants and members of ethical Commission, including specialists such as lawyers and statisticians, effectively communicate within the Ethics Committee;
 - respect the confidentiality of information, carefully read the submissions to the Ethics Committee and contribute to the discussion on committees' meetings, be able to adjust their positions in the light of the conclusions of the discussions conducted.
10. Advise in cases of overdose or poisoning, and take care of the patients who are relevant to the profession of clinical pharmacology and toxicology (e.g. paediatrics) (3):
- demonstrate knowledge of the mechanism of action of important toxins, including therapeutic drugs;
 - recognize clinical syndromes of intoxication;
 - demonstrate the ability of treating poisoned patients, personnel protection and other patients, know resuscitation methods, principles of monitoring, be familiar with specific antidotes (digoxin, iron, cyanide, cholinesterase inhibitors);
 - access information (including through the National Office for poisoning) and know access guidelines for treatment in cases of chemical attack, develop diagnostic skills relevant to the epidemiological context of a chemical attack, maintain qualifications in skills of resuscitation, possess skills in the management of overdoses with paracetamol, aspirin, opioids, benzodiazepines and tricyclic antidepressants, alcohol, drugs;
 - be familiar with the importance of preparedness for a possible chemical attack, self-defence, be capable to protect personnel and to avoid contamination, accept the necessary residual risk associated with caring for poisoned, observe patients with behavioural and psychiatric problems and, if necessary, consult with colleagues about the psychiatric support.
11. Infection control in hospitals :
- gain experience in solving the problem of infection control, including outbreaks of epidemics and their control;
 - become familiar with the functioning of the Committee for infection control at the local and regional level;
 - be familiar with the hospital wards, as well as parts of the general population who require special measures to control infection;

- cooperate with the nurse for control of hospital infections in the performance of their daily obligations, as well as in the education of all those involved in the control of infection;
- participate in a tour of clinical and other parts of the hospital in order to control infection.
- be familiar with the documents adopted at the state level or the level of the hospital relating to infection control;
- understand the principles of isolation of patients, and its proper application in infection control; be aware of specific working groups (e.g.: for MRSA control, disinfection, dialysis, etc.);
- monitor patients with a variety of systemic and local infections and advise on the application of reserve antibiotics and antifungals as a specific class of drugs;
- monitor and treat immunocompromised patients during and after chemotherapy, patients on immunosuppressive therapy;
- interpret the clinical condition and the need for the use of antimicrobial drugs in immunocompromised patients;
- identify the side effects of immunosuppressive therapy.

12. Antimicrobials use :

- empirical, targeted and prophylactic use of antimicrobial agents;
- methods of preventing the development of resistance; monitoring of antibiotic resistance;
- monitoring of patients with systemic and local infections.

13. Quality control :

- understand the concepts of quality control and security control of pharmaceutical products.

14. The process of registration of drugs (3):

- assess and evaluate the documentation on the medicinal product;
- assess and evaluate the package leaflet, the summary of the medicinal product;
- assess all the necessary documentation with the application for registration of a drug.

15. Management of healthcare facilities (3):

- important aspects of managing health care institutions including control of funding (pharmacoeconomics), personnel management and administrative jobs;
- be able to interpret the rationale behind pharmacoeconomic analysis;
- management of the institutional Committee for medicines, organizations of the Committee for drugs, preparation and conduct of meetings, administrative management, writing of certificates, letters and approvals, monitoring of the legal framework of the Committee for drugs.

The institution must meet the requirements of Article 4 or 5 of the Ordinance on specialist training for medical doctors. In addition to the above conditions, the set up:

- must include joint meetings with specialists in other fields (specialists in clinical microbiology, general internal medicine specialists and specialists of intensive medicine, specialists in anaesthesiology, resuscitation and intensive care);
- must quantitatively and qualitatively include at least 40 clinical pharmacology consulting examinations;
- must allow for cooperation with related disciplines in order to achieve adequate skills and a team approach to the patient;
- the institution must allow for specialized patient treatment (transplanted, haematology);
- the institution must be capable of appropriate diagnostics evaluation (Biochemistry, Toxicology Laboratory, Pharmacogenetics);
- there must be a Committee for medicines.
- there must be a library with professional and scientific clinical pharmacology literature.