COURSE DESCRIPTION

Methods for Testing the Biological Activity of Chemical Compounds

Academic year 2025-2026

1. Programme-related data

1.1. Higher Education Institution	Babeș-Bolyai University, Cluj-Napoca
1.2. Faculty	Chemistry and Chemical Engineering
1.3. Department	Doctoral School of Chemistry
1.4. Field	Chemistry
1.5. Level of study	Doctorate
1.6. Degree programme / Qualification	Doctorate / Doctor in Chemistry
1.7. Form of education	Full time

2. Course-related data

2.1. Course title	***Methods for Testing the Biological Activity of Chemical Compounds***			Course code	**SDC-19-13**
2.2. Course coordinator	Prof. Dr. Radu Lucian SILAGHI-DUMITRESCU				
2.3. Seminar coordinator	Prof. Dr. Radu Lucian SILAGHI-DUMITRESCU				
2.4. Year of study	**1**	2.5. Semester	**2**	2.6. Type of assessment	**Exam**
2.7. Course status	**Mandatory**	2.8. Course type	**Specialisation subject**		

3. Total estimated time (hours per semester of teaching activities)

3.1. Number of hours per week	**3**	of which: 3.2. course	**2**	3.3. seminar/ laboratory/ project	**1**
3.4. Total of hours in the curriculum	**36**	of which: 3.5. course	**24**	3.6. seminar/ laboratory	**12**

Time allocation for individual study (IS) and self-taught activities (ST)	**hours**
Learning from textbooks, course materials, bibliography, and notes (IS)	60
Additional research in the library, on subject-specific electronic platforms, and on-site	60
Preparing seminars/ laboratories/ projects, assignments, reports, portfolios, and essays	50
Tutoring (professional guidance)	20
Examinations	20
Other activities	4
3.7. Total hours of individual study (IS) and self-taught activities (ST)	**214**
3.8. Total hours per semester	**250**
3.9. Number of credits	**10**

4. Prerequisites (where applicable)

4.1. curriculum-related	Master's-level training in chemistry, biochemistry, pharmacy, or a related discipline, including undergraduate organic chemistry, biochemistry, and basic physiology/pharmacology.
4.2. skills-related	Familiarity with laboratory statistics (mean, SD, confidence intervals, dose-response fitting), basic cell-culture and microbiology concepts, and reading-level English.

5. Specific conditions (where applicable)

5.1. course-related	Students attend lectures having read the assigned material beforehand; mobile phones off or silent; active participation in the discussions on assay design and interpretation.
5.2. seminar/laboratory-related	Students attend the seminar having read in advance the week's assigned publicly-available primary journal article; active, evidence-based participation in the journal-club discussion of the case-study paper from the perspective of a synthetic chemist.

6.1. Competencies resulting from the completion of the degree programme

Professional competencies	
Competency code	**Competency**
PC1	Definition of notions, concepts, theories and advanced models in the field of Chemistry as well as their proper use within the professional community
PC4	Use of in-depth knowledge of chemistry to explain and interpret the tools and processes specific to the full pre-clinical research cascade — from in silico and physicochemical profiling through in vitro target engagement, ex vivo and in vivo pharmacology, safety pharmacology, and toxicology of chemical compounds
PC5	Identifying and applying advanced concepts, methods and theories to solve problems specific to the quantitative pharmacological, pharmacokinetic, toxicological and regulatory evaluation of chemical compounds during pre-clinical development
Transversal competencies	
Competency code	**Competency**
TC2	Execution of the requested tasks according to the specified requirements and within the imposed deadlines, in compliance with the norms of professional ethics and moral conduct, following a pre-established work plan
TC3	Solving the requested tasks in accordance with the general objectives established by integration within a working group

6.2. Learning outcomes relevant to the degree programme (as referred to in the curriculum)

Learning outcomes targeted by the subject		
Competency code	**Knowledge and comprehension**	**Specific academic skills**
PC1	Advanced and up-to-date knowledge in medicinal chemistry, biochemistry, pharmacology, pharmacokinetics and toxicology; principles of target validation, druglikeness, ADMET, target engagement, selectivity, efficacy, and safety liabilities; the full hit-to-candidate and IND-enabling pre-	Applies and synthesizes advanced concepts to formulate testable hypotheses on the biological activity of chemical compounds and to design an integrated pre-clinical programme; justifies the choice of in silico, biochemical, biophysical, cell-based, ex vivo and in vivo approaches within a Target Product Profile.

	clinical cascade; regulatory context (GLP, ICH, OECD, EMA/FDA).	
PC4	Advanced research methodologies: in silico screening (docking, pharmacophore, QSAR, ADMET); physicochemical and druglikeness profiling; biochemical and biophysical target engagement (ITC, SPR, MST, DSF, CETSA, NanoBRET); cell-based assays (viability, apoptosis, reporter, high-content, organoids, organ-on-chip); in vitro ADME (metabolic stability, CYP, transporters, permeability, IVIVE/PBPK); ex vivo tissue preparations (Magnus, Langendorff, Ussing, precision-cut slices); in vivo PK/PD and disease-model efficacy (pain, inflammation, CNS, oncology, infection, cardiovascular, metabolic); safety pharmacology ICH S7A/S7B core battery (CV, CNS, respiratory) including hERG and in vivo telemetry; general toxicology per OECD TGs (acute, repeat-dose, reproductive/developmental, carcinogenicity); genotoxicity battery (Ames, micronucleus, comet, chromosomal aberration); immunotoxicity; 3R principle and GLP.	Designs, plans and implements a pre-clinical development programme for a compound; applies quality, ethical and safety procedures (GLP, OECD TGs, ICH, biosafety, institutional animal-care rules and 3R) and documents stages and data with full traceability and audit-readiness.
PC5	Advanced strategies for the analysis, interpretation and integration of pre-clinical data (dose-response fitting, IC50/EC50/Ki, Hill slope, Z' factor, NCA and compartmental PK analysis, PK/PD modelling, exposure-response for efficacy and safety, TK integration with toxicology, benchmark-dose approaches, statistical design and power for animal studies); evaluation of methodological limitations, reproducibility, translational relevance, and regulatory acceptability.	Critically analyses complex pre-clinical datasets, estimates uncertainty and formulates conclusions regarding activity, selectivity, PK/PD, safety windows, and IND-readiness; proposes methodological improvements and directions for drug-discovery/innovation and for the integrated pre-clinical package.
TC2	Scientific terminology and communication in Romanian and English; the structure of scientific articles, regulatory documents, and study reports in medicinal chemistry / chemical biology / pharmacology / toxicology; good citation practices and correct reporting of pre-clinical data (ARRIVE 2.0, MIABE, GLP study reports, EPAR/Pharmacology Reviews).	Writes and presents scientific results in Romanian/English coherently; provides well-argued responses to comments and peer reviews; produces pre-clinical study reports in compliance with regulatory expectations.
TC3	Digital tools for research, citation, and data processing (GraphPad Prism / R / DoseResponse packages, Phoenix WinNonlin or equivalent for PK, PBPK platforms, PubChem, ChEMBL, BindingDB, docking and ADMET software, the OECD eChemPortal, reference managers); responsible use of digital resources.	Uses discipline-specific digital tools effectively; manages citations; uses digital resources responsibly in research and regulatory activities.

7. Subject-specific learning outcomes

Knowledge and comprehension
1. Applying appropriate quantitative pharmacology, pharmacokinetics and statistics (dose-response fitting, IC50/EC50/Ki, Hill slope, Z' factor, NCA PK, PK/PD modelling, power analysis for animal studies, ARRIVE 2.0 reporting) to the evaluation of biological activity across the pre-clinical cascade

2. Understanding and interpreting in silico, physicochemical, biochemical, biophysical, cell-based, ex vivo and in vitro-ADME assay readouts (docking/QSAR, solubility/logP/PAMPA, enzyme-inhibition kinetics, ITC/SPR, cytotoxicity, reporter assays, microsomal stability, CYP inhibition, isolated-organ preparations)
3. Critical analysis and correct use of in vivo methods: rodent and non-rodent pharmacology, PK sampling, disease-model efficacy studies (pain, inflammation, CNS, oncology, infection, cardiovascular, metabolic), alternative and complementary models (zebrafish, C. elegans, Drosophila, organ-on-chip, iPSC, humanized mice), safety pharmacology core battery (ICH S7A/B — hERG, CV telemetry, Irwin/FOB, plethysmography), general toxicology (OECD TGs), genotoxicity battery, reproductive/developmental toxicity, carcinogenicity, and immunotoxicity
4. Awareness of integrated case studies (successful and failed pre-clinical programmes) and of the regulatory framework that governs pre-clinical submissions — GLP, OECD Test Guidelines, ICH (S7A, S7B, M3(R2), S2(R1), S5, S9), the IND/CTA content, EPAR/FDA Pharmacology Reviews, NC3Rs guidance, and the ethical/legal basis of animal experimentation (EU Directive 2010/63/EU, institutional animal-care review)
Specific academic skills
1. Execution of the requested tasks according to specified requirements and within the imposed deadlines, in compliance with professional ethics and moral conduct, following a pre-established work plan
2. Concern for improving the results of the professional activity by active engagement in the assay-design and data-analysis workshops and by peer-review of classmates' analyses
3. Ability to prepare written reports and to publicly defend/support these reports

8. Contents

8.1. Course		
Course/ Seminar topic	**Teaching and learning methods**	**Remarks**
8.1.1. Introduction to pre-clinical drug discovery and development: target identification and validation; the hit-lead-candidate paradigm; attrition and failure modes; Target Product Profile (TPP); druglikeness (Lipinski, Veber, PAINS); the full pre-clinical cascade from in silico to IND/CTA; ethics, the 3R principle (Replacement, Reduction, Refinement) and the EU Directive 2010/63/EU; the regulatory landscape (GLP, ICH, OECD, EMA, FDA).	Presentation; Explanation; Conversation; Description; Debate	
8.1.2. Compound characterization — in silico and physicochemical: molecular docking (Glide, AutoDock, GOLD), pharmacophore modelling, QSAR, structure-based vs. ligand-based design; ADMET prediction (SwissADME, pkCSM, DEREK/Leadscope); measured physicochemical properties — kinetic and thermodynamic solubility, logP/logD, pKa, chemical stability, permeability (PAMPA, Caco-2); druglikeness filtering of screening libraries.	Presentation; Explanation; Conversation; Description; Debate	
8.1.3. Target-engagement assays — biochemical and biophysical: enzyme-inhibition kinetics (Michaelis-Menten, Cheng-Prusoff, reversibility and time-dependence, slow-tight and covalent inhibitors); calorimetric and biophysical methods — ITC (n, Ka, ΔH, -TΔS), SPR (kon, koff, KD), MicroScale Thermophoresis (MST), differential scanning fluorimetry / thermal shift (DSF), fluorescence polarization; cellular target engagement (CETSA, NanoBRET, BRET, PROTAC-style degradation readouts).	Presentation; Explanation; Conversation; Description; Debate	
8.1.4. In vitro cellular assays — viability, mechanism of action, and advanced models: viability and proliferation (MTT/MTS/XTT, SRB, Alamar Blue/resazurin, CellTiter-Glo); apoptosis (Annexin V, caspase, TUNEL), cell-cycle (PI +	Presentation; Explanation; Conversation; Description; Debate	

flow cytometry), autophagy, senescence, reporter-gene; high-content imaging; 3D spheroids and organoids, patient-derived cultures, organ-on-chip and microphysiological systems as translational in vitro platforms.		
8.1.5. In vitro disease-specific assays: antimicrobial (MIC/MBC microbroth dilution CLSI/EUCAST, time-kill, checkerboard synergy/FIC, biofilm MBEC); antiviral (CPE reduction, plaque reduction, reporter viruses); antiparasitic assays; antioxidant/oxidative-stress assays (DPPH, ABTS, FRAP, ORAC, intracellular DCFH-DA/MitoSOX) and their pharmacological limitations; HTS formats for receptors and kinases (GPCR cAMP/β-arrestin/Ca^{2+} flux, ADP-Glo and mobility-shift kinase); label-free assays (impedance, dynamic mass redistribution).	Presentation; Explanation; Conversation; Description; Debate	
8.1.6. In vitro ADME: metabolic stability in liver microsomes, hepatocytes and S9; CYP inhibition (IC50 and Ki) and induction (PXR/AhR reporter, primary hepatocytes); plasma protein binding (equilibrium dialysis, ultrafiltration); blood-brain-barrier surrogates (MDCK-MDR1); transporter assays (P-gp, BCRP, BSEP, OATP); intestinal permeability (Caco-2, MDCK); in vitro – in vivo extrapolation (IVIVE); introduction to physiologically based pharmacokinetic (PBPK) modelling.	Presentation; Explanation; Conversation; Description; Debate	
8.1.7. Ex vivo and isolated-organ bioassays: isolated-tissue preparations — Magnus bath for ileum/vas deferens, Langendorff isolated perfused heart, isolated aortic rings and mesenteric bed, Ussing chamber for epithelial transport; tissue slices — precision-cut liver and kidney slices, brain slices for electrophysiology; sandwich-cultured primary hepatocytes for canalicular transport; role of ex vivo assays as the bridge between cell-based and whole-animal pharmacology.	Presentation; Explanation; Conversation; Description; Debate	
8.1.8. In vivo pharmacokinetics and PK/PD: routes of administration (IV, PO, SC, IP, topical, inhalation, intrathecal) and their bioavailability; serial and sparse PK sampling in rodents; non-compartmental analysis (Cmax, Tmax, AUC, t1/2, F, CL, Vd) and compartmental PK; PK/PD modelling (direct and indirect effect models); target occupancy and exposure-response; dose-selection for efficacy studies and for first-in-human extrapolation; microsampling and cassette dosing.	Presentation; Explanation; Conversation; Description; Debate	
8.1.9. In vivo efficacy models across therapeutic areas: pain (von Frey and Hargreaves sensory thresholds, formalin test, CFA inflammatory model, CCI and SNL neuropathic-pain models); inflammation (carrageenan paw edema, collagen-induced arthritis, DSS colitis); CNS (forced-swim and tail-suspension for depression, open-field and elevated-plus-maze for anxiety, Morris water maze for cognition, MPTP and 6-OHDA for Parkinson's, amyloid-β and transgenic models for Alzheimer's); oncology (subcutaneous and orthotopic xenografts, syngeneic tumor models, GEMM and PDX, metastasis models); infection (bacterial, viral, parasitic in vivo challenges); cardiovascular (SHR hypertension, ischemia-reperfusion, heart-failure models); metabolic (DIO, STZ-diabetic, ob/ob and db/db, HFD NAFLD/NASH).	Presentation; Explanation; Conversation; Description; Debate	
8.1.10. Alternative and complementary animal models; the 3R principle in practice: zebrafish (Danio rerio) embryo and larval assays for developmental toxicity and phenotypic screening; Caenorhabditis elegans for lifespan, neurobiology and anthelmintic screens; Drosophila melanogaster for	Presentation; Explanation; Conversation; Description; Debate	

neurodegeneration and genetics; microphysiological systems (organ-on-chip); iPSC-derived cardiomyocytes, hepatocytes, and neurons (CiPA initiative for proactive cardiac safety); humanized mice; refinement measures (enrichment, humane endpoints, analgesia) and reduction (optimal n, factorial designs); ARRIVE 2.0 reporting guidelines and NC3Rs resources.		
8.1.11. Safety pharmacology and general toxicology per ICH and OECD: the ICH S7A/S7B safety pharmacology core battery — cardiovascular (hERG in vitro, conscious-dog or NHP telemetry, QT-interval evaluation, APD measurement), central nervous system (Irwin test, functional observational battery / FOB, locomotor activity), respiratory (whole-body plethysmography); general toxicology — acute (OECD TG 420/423/425), sub-acute 28-day (TG 407), sub-chronic 90-day (TG 408, 409), chronic (TG 452), with tissue histopathology, clinical chemistry, haematology, urinalysis and toxicokinetics (TK) integration.	Presentation; Explanation; Conversation; Description; Debate	
8.1.12. Genotoxicity, reproductive/developmental, carcinogenicity and immunotoxicity; integrated pre-clinical package and regulatory submission: genotoxicity battery per ICH S2(R1) — Ames (OECD TG 471), in vitro mammalian cell micronucleus (TG 487), in vitro chromosomal aberration (TG 473), in vivo micronucleus (TG 474), comet assay (TG 489); reproductive/developmental toxicity (TG 414 embryo-fetal, 416 two-generation, 421/422 screening); carcinogenicity (TG 451/453; 2-year rodent bioassay and transgenic alternatives); immunotoxicity (LLNA TG 429, sensitization, cytokine panels, TDAR); biomarker discovery and validation; the IND/CTA/NDA dossier (Module 4 Non-Clinical Study Reports), pharmacology and tox written summaries; reading an EPAR or FDA Pharmacology Review; integrated case studies — a successful pre-clinical programme (e.g. imatinib or osimertinib) and a failed one (fialuridine, TGN1412).	Presentation; Explanation; Conversation; Description; Debate	

Bibliography

1. Vogel, H. G. (Ed.) (2016). Drug Discovery and Evaluation: Pharmacological Assays, 4th ed. (3 volumes), Springer.

2. Hock, F. J. (Ed.) (2016). Drug Discovery and Evaluation: Safety and Pharmacokinetic Assays, 2nd ed., Springer.

3. Copeland, R. A. (2013). Evaluation of Enzyme Inhibitors in Drug Discovery: A Guide for Medicinal Chemists and Pharmacologists, 2nd ed. Wiley.

4. Sittampalam, G. S., et al. (Eds.). Assay Guidance Manual. NCATS / Eli Lilly Bookshelf (continuously updated, open-access).

5. Rang, H. P., Dale, M. M., Ritter, J. M., Flower, R. J., Henderson, G. (2019). Rang and Dale's Pharmacology, 9th ed. Elsevier.

6. Gabrielsson, J., Weiner, D. (2017). Pharmacokinetic and Pharmacodynamic Data Analysis: Concepts and Applications, 5th ed. Swedish Pharmaceutical Press.

7. Hughes, J. P., Rees, S., Kalindjian, S. B., Philpott, K. L. (2011). "Principles of early drug discovery." Br. J. Pharmacol. 162, 1239-1249.

8. Lipinski, C. A., Lombardo, F., Dominy, B. W., Feeney, P. J. (1997). "Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings." Adv. Drug Deliv. Rev. 23, 3-25.

9. Baell, J. B., Holloway, G. A. (2010). "New substructure filters for removal of pan assay interference compounds (PAINS)." J. Med. Chem. 53, 2719-2740.

10. Percie du Sert, N., Hurst, V., Ahluwalia, A., et al. (2020). "The ARRIVE guidelines 2.0: updated guidelines for reporting animal research." PLoS Biol. 18, e3000410.

11. OECD (2018–2023). OECD Test Guidelines for the Testing of Chemicals, Section 4: Health Effects (TG 401/420/423/425, 407/408/452, 414/416/421, 451/453, 471/473/474/487/489, 429). OECD Publishing.

12. ICH Harmonised Guidelines: S7A (Safety pharmacology for human pharmaceuticals, 2000); S7B (QT interval prolongation / hERG, 2005); M3(R2) (Non-clinical safety studies for clinical trials, 2009); S2(R1) (Genotoxicity, 2011); S5(R3) (Reproductive toxicity, 2020); S9 (Non-clinical evaluation for oncology, 2009).

13. EU Directive 2010/63/EU on the protection of animals used for scientific purposes; Commission Implementing Decision 2020/569.

14. Curtis, M. J., Alexander, S. P. H., Cirino, G., et al. (2022). "Experimental design and analysis and their reporting II: updated and simplified guidance for authors and peer reviewers." Br. J. Pharmacol. 179, 3605-3613.

15. Cook, D., Brown, D., Alexander, R., et al. (2014). "Lessons learned from the fate of AstraZeneca's drug pipeline: a five-dimensional framework." Nat. Rev. Drug Discov. 13, 419-431.

16. Scannell, J. W., Blanckley, A., Boldon, H., Warrington, B. (2012). "Diagnosing the decline in pharmaceutical R&D efficiency." Nat. Rev. Drug Discov. 11, 191-200.

17. Di, L., Kerns, E. H. (2015). Drug-Like Properties: Concepts, Structure Design and Methods, 2nd ed. Academic Press.

18. Pellegatti, M. (2012). "Preclinical in vivo ADME studies in drug development: a critical review." Expert Opin. Drug Metab. Toxicol. 8, 161-172.

8.2. Seminar/ laboratory

Course/ Seminar topic	Teaching and learning methods	Remarks
8.2.1. Journal-club seminar — the medicinal-chemistry campaign of an approved drug, read from a synthetic chemist's perspective. Case study: the published discovery of imatinib (Zimmermann et al., J. Med. Chem. 1996; Druker et al., Nat. Med. 1996) or of osimertinib (Cross et al., Cancer Discov. 2014). Discussion: how the Target Product Profile steered the SAR, and which assays triggered each new round of synthesis.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.2. Journal-club seminar — in silico and physicochemical profiling. Case study: a recent J. Med. Chem. or Eur. J. Med. Chem. paper that combines docking, ADMET prediction, and measured solubility/logP/permeability on a congener series. Discussion: where the predictions held up, where they failed, and which measurements a synthetic chemist must insist on before advancing an analog.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.3. Journal-club seminar — biochemical and biophysical binding. Case study: an ITC or SPR paper from a medicinal-chemistry team on an enzyme or protein-ligand system (e.g., HSP90, BRD4, a protease, or a kinase). Discussion: Kd vs. IC50, enthalpy–entropy compensation, and what the thermogram or sensorgram tells the synthetic chemist about substituent optimization.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.4. Journal-club seminar — cell-based viability and mechanism-of-action. Case study: a cytotoxicity / "selectivity index" paper on cancer vs. non-cancer cell lines, preferably authored by a synthetic-chemistry group. Discussion: spotting redox interference, PAINS, aggregation and solvent-control pitfalls; what the paper actually proves about the proposed mechanism.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.5. Journal-club seminar — high-throughput screening and hit-to-lead. Case study: a Nat. Chem. Biol. or ACS Chem. Biol. HTS paper on a target of interest. Discussion: Z' factor, hit-confirmation strategy, and what a synthetic chemist should learn about a chemotype before committing to an optimization programme.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	

8.2.6. Journal-club seminar — in vitro ADME. Case study: a Drug Metab. Dispos. or Bioorg. Med. Chem. Lett. paper that tracks microsomal stability, CYP inhibition and permeability across an SAR series. Discussion: identifying metabolic soft spots in the scaffold and which structural modifications removed them.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.7. Journal-club seminar — ex vivo and isolated-organ pharmacology. Case study: a classic Langendorff isolated-heart paper or an isolated-rat-aorta vasoreactivity paper. Discussion: what ex vivo data add between cell culture and whole-animal testing, and how they feed back to the synthetic chemist's next design.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.8. Journal-club seminar — in vivo pharmacokinetics. Case study: a rodent PK paper (J. Pharmacol. Exp. Ther., Xenobiotica or similar) on a lead compound. Discussion: reading Cmax, Tmax, AUC, F, CL, Vd; correlating scaffold modifications with PK and choosing the next structural move.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.9. Journal-club seminar — in vivo efficacy and animal models. Case study: Bennett & Xie, Pain 1988 (CCI neuropathic-pain model), or a DSS colitis / collagen-induced arthritis / MPTP Parkinson / xenograft oncology paper authored by a medicinal-chemistry group. Discussion: randomization, blinding, group size, ARRIVE 2.0 compliance; what counts as proof of concept before the next synthetic campaign.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.10. Journal-club seminar — alternative and complementary models. Case study: MacRae & Peterson, Nat. Rev. Drug Discov. 2015 on zebrafish, together with a published CiPA human-iPSC cardiomyocyte paper. Discussion: when these can replace mammalian studies for early triage of analogs by a medicinal-chemistry group, and what they cannot yet replace.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.11. Journal-club seminar — safety pharmacology and toxicology. Case study: Redfern et al., Cardiovasc. Res. 2003 (hERG safety-margin classification) together with a 28-day / repeat-dose toxicology summary from an openly-available EPAR. Discussion: translating hERG IC50 and NOAEL into a concrete therapeutic-margin target that the next analog must clear.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	
8.2.12. Journal-club seminar + final presentations — the integrated pre-clinical package. Case study: the non-clinical section of an EPAR (European Medicines Agency) or an FDA Multi-Discipline Review for a recently approved drug (e.g., osimertinib, sotorasib, finerenone). Each student presents a published pre-clinical programme of their choice, read through the eyes of a synthetic chemist, and defends it against peer questions and counter-arguments.	Journal-club critical reading of primary literature; Case-study discussion; Conversation	

Bibliography

1. Zhang, J.-H., Chung, T. D. Y., Oldenburg, K. R. (1999). "A simple statistical parameter for use in evaluation and validation of high throughput screening assays." J. Biomol. Screen. 4, 67-73 (the Z' factor).

2. Sebaugh, J. L. (2011). "Guidelines for accurate EC50/IC50 estimation." Pharm. Stat. 10, 128-134.

3. CLSI Standard M07: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically, 11th ed.

4. Redfern, W. S., Carlsson, L., Davis, A. S., et al. (2003). "Relationships between preclinical cardiac electrophysiology, clinical QT interval prolongation and torsade de pointes for a broad range of drugs." Cardiovasc. Res. 58, 32-45.

5. Thorne, N., Auld, D. S., Inglese, J. (2010). "Apparent activity in high-throughput screening: origins of compound-dependent assay interference." Curr. Opin. Chem. Biol. 14, 315-324.

6. Mortelmans, K., Zeiger, E. (2000). "The Ames Salmonella/microsome mutagenicity assay." Mutat. Res. 455, 29-60.

7. MacRae, C. A., Peterson, R. T. (2015). "Zebrafish as tools for drug discovery." Nat. Rev. Drug Discov. 14, 721-731.

8. Bennett, G. J., Xie, Y. K. (1988). "A peripheral mononeuropathy in rat that produces disorders of pain sensation like those seen in man." Pain 33, 87-107 (the CCI model).

9. Percie du Sert, N., Hurst, V., Ahluwalia, A., et al. (2020). "The ARRIVE guidelines 2.0: updated guidelines for reporting animal research." PLoS Biol. 18, e3000410.

10. Friesner, R. A., Banks, J. L., Murphy, R. B., et al. (2004). "Glide: a new approach for rapid, accurate docking and scoring." J. Med. Chem. 47, 1739-1749.

11. Obach, R. S. (1999). "Prediction of human clearance of twenty-nine drugs from hepatic microsomal intrinsic clearance data." Drug Metab. Dispos. 27, 1350-1359.

12. Suntharalingam, G., Perry, M. R., Ward, S., et al. (2006). "Cytokine storm in a phase 1 trial of the anti-CD28 monoclonal antibody TGN1412." N. Engl. J. Med. 355, 1018-1028 (classic pre-clinical-to-clinical translation failure).

13. Peters, J. U., Schnider, P., Mattei, P., Kansy, M. (2009). "Pharmacological promiscuity: dependence on compound properties and target specificity in a set of recent Roche compounds." ChemMedChem 4, 680-686.

14. Begley, C. G., Ellis, L. M. (2012). "Drug development: Raise standards for preclinical cancer research." Nature 483, 531-533.

15. Selected EPAR (European Public Assessment Reports) and FDA Multi-Discipline Review / Pharmacology Review documents for recently approved drugs (e.g., osimertinib, finerenone, sotorasib) — the non-clinical modules.

9. Evaluation

Type of activity	9.1 Evaluation criteria	9.2 Evaluation methods	9.3 Percentage in the final grade
9.4. Course	Correctness of answers — proper understanding and learning of notions and concepts discussed during lectures; correct use of learned concepts within new contexts. Correct solving of the problems as part of the examination subjects.	Written report with critical analysis of a chosen bioassay cascade	**50%**
9.5. Seminar/ laboratory	Correctness of answers — proper understanding and learning of notions and concepts discussed during seminars; correct use of learned concepts within new contexts. Quality of reports, and quality of the final oral defense.	Final oral colloquium with defense of critical-analysis essay	**50%**

9.6 Minimum standard for passing

Adequate knowledge of at least one case study per major assay family (in silico / docking; biochemical enzyme-inhibition; biophysical binding: ITC or SPR; cell-based viability and mechanism of action; antimicrobial; antioxidant; in vivo or alternative-model bioassay; safety pharmacology / genotoxicity); demonstrated ability to fit a dose-response curve correctly and to critically read and defend a primary paper reporting a bioactivity study.

10. SDG labels (Sustainable Development Goals)

(Select a single SDG label that best matches the subject; if none applies, select "No label applies". The Good Health and Well-being label has been selected for this course.)

☐ **1** No Poverty	☐ **2** Zero Hunger	☒ **3** Good Health and Well-being	☐ **4** Quality Education	☐ **5** Gender Equality	☐ **6** Clean Water and Sanitation	☐ **7** Affordable and Clean Energy	☐ **8** Decent Work and Economic Growth	☐ **9** Industry, Innovation and Infrastructure
☐ **10** Reduced Inequality	☐ **11** Sustainable Cities and Communities	☐ **12** Responsible Consumption and Production	☐ **13** Climate Action	☐ **14** Life Below Water	☐ **15** Life on Land	☐ **16** Peace, Justice and Strong Institutions	☐ **17** Partnerships for the Goals	☐ — No label applies

Date of entry: 21.04.2026	**Signature of course coordinator** …… *Prof. Dr. Radu Lucian SILAGHI-DUMITRESCU*	**Signature of seminar coordinator** …… *Prof. Dr. Radu Lucian SILAGHI-DUMITRESCU*
Date of approval in CDSC: ……	**Signature of the Director of the DSC** …… *Prof. dr. Niculina Daniela Hădade*	