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INSTITUTE FOR MEDICAL RESEARCH AND OCCUPATIONAL HEALTH

Annual report



ZAGREB, 2023

14. ORGANISATION OF THE INSTITUTE

Date and place of establishment: 27 Dec 1947 in Zagreb.

Founder: Prof Andrija Štampar, president of the Yugoslav Academy of Sciences and Arts.

Status: public research institute under the Ministry of Science and Education of the Republic of Croatia.

Fields of research: toxicology, radiation and chemical weapon protection, environmental radioactive contamination, air quality, determination of drug abuse, occupational medicine, distribution of metals and inorganic and organic pollution in the environment, and the exposure of human beings to environmental contaminants, as well as various psychogenic factors.

Types of registered fields: scientific, professional, teaching, and publishing.

The mission of the Institute is to become:

- a research institute of excellence in central and south-eastern Europe that shifts the boundaries of discovery regarding anthropogenic impacts on health and the environment,
- the standard for academic distinction and quality.

The vision of the Institute:

- insist on high standards of scientific excellence,
- create new values in science,
- ensure the transfer of knowledge to the wider community,
- contribute to the economy through research results,
- educate future experts in the fields of fundamental and applied sciences.

STRUCTURE OF IMROH'S EMPLOYEES (31	DEC 2022)	Number of employees	%
Distribution according to funding	State budget	138	86
	IMROH	10	6
	Croatian Science Foundation	13	8
Distribution according to sex	Women	119	74
bisting to sex	Men	42	26
Employees with academic titles	PhD	74	46
Employees with teaching titles	Assist Prof (3); Assoc Prof (5); Prof (3)	11	7
Employees with specialist titles	Epidemiology (1);	3	2
	Occupational Medicine and Sports (2)		
WORK POSITIONS	Devenent Colontific Advisor	15	0
	Scientifie Advisor	15	9
Employees on scientific work positions	Scientific Accoriate	10	0 12
Employees on scientific work positions		19	12
	Total	59	36
	Postdoctoral researcher	11	7
Employees on associate work positions	PhD student, Assistant	14	9
	Total	25	16
	Professional Advisor	2	1
Employees on professional work	Senior Professional Associate	3	2
positions	Professional Associate	14	9
	Total	19	12
Employees on technical work positions		25	16
Employees in Shared Services		32	20
TOTAL NUMBER OF EMPLOYEES:		161	100



The organisational scheme of IMROH

MANAGEMENT OF THE INSTITUTE	
MANAGEMENT COUNCIL	
CHAIR Prof Stipan Jonjić, MD, PhD, Faculty of Med	dicine, University of Rijeka
DEPUTY CHAIR Prof Nada Čikeš, MD, PhD, School of Medic	ine, University of Zagreb
MEMBERS Božo Pavičin, Croatian Chamber of Econom Nevenka Kopjar, PhD (Representative of IM Branka Roić, BEc (Representative of IMROF	iy IROH's research staff) 1's employees)
DIRECTOR	DEPUTY DIRECTOR
Prof Ana Lucić Vrdoljak, PhD	Assist Prof Irena Brčić Karačonji, PhD, ERT

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SCIENTIFIC COUNCIL	QUALITY MANAGER
CHAIR	
Assoc Prof Branko Petrinec, PhD	Ranka Godec, PhD
DEPUTY CHAIR	DEPUTY MANAGER
Davorka Breljak, PhD	Tomislav Meštrović

ETHICS COMMITTEE

CHAIR

Prim Jelena Macan, MD, PhD

MEMBERS

Prof Selma Cvijetić Avdagić, MD, PhD Assoc Prof Adrijana Bjelajac, PhD Martina Piasek, MD, PhD Prof Tomislav Mašek, DVM, PhD, Faculty of Veterinary Medicine, University of Zagreb

SECRETARY

Jagoda Mandić

14.1. The work of the Ethics Committee

The Ethics Committee received a total of 15 claims during 2022 and all were discussed according to the criteria of Code of Ethic of the Institute for Medical Research and Occupational Health. Applicants were given written opinions which were officially filed, except in three claims in which a supplementation of documentation was requested and new documentation was not submitted until the end of 2022. During the meetings held in person and consultations via e-mail, ethical principles were considered in:

- a doctoral thesis proposal with a co-mentor from IMROH (1)
- project proposals submitted by IMROH's researchers to HORIZON 2020 (2) and HORIZON Europe (1)
- an international call with cooperation from another research institution (1)
- research project proposals submitted to the Croatian Science Foundation calls by IMROH's researchers
 (2), and in cooperation with other research institutions (2)
- proposals for internal projects with leaders from IMROH (1) or as cooperations with other research institutions (2)
- research proposals from other institutions (3).

15. RESEARCH UNITS

UNIT	CODE	HEAD	CONTACTS
Analytical Toxicology and Mineral Metabolism	604	Jasna Jurasović, PhD	Tel. (01) 4682 530 e-mail: jurasovic@imi.hr
Biochemistry and Organic Analytical Chemistry	609	Snježana Herceg Romanić, PhD	Tel. (01) 4682 553 e-mail: sherceg@imi.hr
Environmental Hygiene	610	Assoc Prof Gordana Pehnec, PhD	Tel. (01) 4682 580 e-mail: gpehnec@imi.hr
Molecular Toxicology	606	Davorka Breljak, PhD	Tel. (01) 4682 622 e-mail: dbreljak@imi.hr
Mutagenesis	616	Nevenka Kopjar, PhD	Tel. (01) 4682 630 e-mail: nkopjar@imi.hr
Occupational Health and Environmental Medicine	615	Prim Jelena Macan, MD, PhD	Tel. (01) 4682 600 e-mail: jmacan@imi.hr
Radiation Dosimetry and Radiobiology	608	Ivica Prlić, PhD	Tel. (01) 4682 570 e-mail: iprlic@imi.hr
Radiation Protection	602	Assoc Prof Branko Petrinec, PhD	Tel. (01) 4682 658 e-mail: petrinec@imi.hr
Toxicology	603	Assist Prof Irena Brčić Karačonji, PhD, ERT	Tel. (01) 4682 532 e-mail: ibrcic@imi.hr
Independent Researcher	387	Aleksandra Fučić, PhD	Tel. (01) 4682 522 e-mail: afucic@imi.hr
Independent Researcher	389	Ante Miličević, PhD	Tel. (01) 4682 524 e-mail: antem@imi.hr
Independent Researcher	373	Jasmina Sabolović, PhD	Tel. (01) 4682 526 e-mail: jsabolov@imi.hr



HEAD

Jasna Jurasović, PhD, permanent scientific advisor

RESEARCHERS

Zorana Kljaković-Gašpić, PhD, permanent scientific advisor since 7 Feb 2022 Alica Pizent, PhD, permanent scientific advisor Maja Lazarus, PhD, scientific advisor Assoc Prof Ivana Vinković Vrček, PhD, scientific advisor Nataša Brajenović, PhD, senior scientific associate Tatjana Orct, PhD, senior scientific associate since 11 Apr 2022 Ankica Sekovanić, PhD, scientific associate since 11 Apr 2022 Maja Beus, PhD, postdoctoral researcher Buket Bakan, PhD, postdoctoral researcher since 31 Oct 2022 Ivona Capjak, PhD, postdoctoral researcher (8h/week) Antonija Sulimanec Grgec, PhD, postdoctoral researcher Tanja Živković Semren, PhD, postdoctoral researcher until 30 Nov 2022 Rinea Barbir, MSc, PhD student-assistant until 30 Jun 2022 Lucija Božičević, MSc, PhD student-assistant Nikolina Kalčec, MSc, PhD student-assistant Barbara Pem, MSc, PhD student-assistant until 22 Mar 2022 Nikolina Peranić, MSc, PhD student-assistant Borna Karnaš, MSc, professional associate in research since 1 Aug 2022

TECHNICAL STAFF

Mladen Komesar, senior technician Vesna Triva, senior technician Snježana Mataušić, technician Krešimir Nekić, technician

PARTICIPATING RETIRED RESEARCHER

Martina Piasek, MD, PhD, permanent scientific advisor

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

Long-term research activities

Study of toxic and essential elements: health effects in the general population and assessment of environmental exposure

We compared the concentrations of As, Cd, Cr, Hg, Ni, and Pb in the blood of subjects with prostate cancer and control subjects from Croatia and Serbia. The contribution of environmental exposure to these metal(loid)s on oxidative stress parameters and prostate specific antigen (PSA) was assessed (71, 220).

Results of the elemental and lipid composition of the muscle tissue in the four most commonly consumed marine fish species from the Adriatic Sea based on the data collected by a food frequency questionnaire (FFQ) in postpartum women (n = 100) from coastal Croatia were published. We assessed the potential risk of

fish consumption for women during the child-bearing period through exposure to the highly toxic element Hg (as total Hg representing mainly methyl Hg in fish) and total As (based on the inorganic As fraction) as well as the benefits gained through the intake of the essential ultra-trace element Se and eicosapentaenoic (EPA) and docosahexaenoic (DHA) long-chain omega-3 polyunsaturated fatty acids abundant in fish (120).

We continued to study the multi-element composition of staple foods, such as white and integral rice (310) and meat of the Adriatic hake (228) as well as non-commercial plants, such as Rowan berries, which could be useful for industrial food fortification (202).

We continued our research in environmental monitoring and assessment of exposure of organisms and people to metals in the environment. We investigated the distribution of metal(loid)s in the aquatic environment (water, sediment, six fish species) of the upper and middle reaches of the Raša River with the aim of assessing the environmental quality of the sensitive karst water system under the long-term anthropogenic influence of the Raša coal mines. The results of these researches were summarised in an original scientific paper that was accepted for publication (110). Also, the long-standing cooperation with the Biochemistry and Organic Analytical Chemistry Unit in the analysis of inorganic and organic pollutants in marine organisms was extended to freshwater systems. Within this collaboration, we investigated for the first time the biological availability of a suite of metal(loid)s and persistent organic pollutants in an eastern Adriatic karstic river using the European eel as a biological indicator of contamination. The results of this research were partly presented at an international scientific meeting (283) and resulted in an integral original scientific paper accepted for publication (109).

In cooperation with the Ruđer Bošković Institute, as part of the research project of the Croatian Science Foundation (BIOTOXMET, IP-2020-02-8502), we presented results on the quality of water (300, 311, 317) and the sediment (300, 317) and the effects of exposure to metals on biological markers metallothioneins in brown trout (317) from the upper part of the Krka River watercourse, polluted by inadequately purified wastewaters.

Long-term collaboration with the Faculty of Veterinary Medicine University of Zagreb continued. Results of the possible effect of biological factors and metal(loid)s on reproductive hormones in brown bear hair from Croatia and Poland were presented on an international conference (247). Bones of Dinara-Pindos and Carpathian brown bears were used to investigate the temporal distribution of anthropogenic pollutants (Sr-90, stabile metal(loid)s) in the last 50 years (116). Levels of metal(loid)s with neurotoxic potential were quantified in the brains of Croatian large carnivores and their potential for interrupting essential element homeostasis was investigated (112).

We evaluated the influence of the natural gas treatment plant Molve on the surrounding terrestrial ecosystem. We tracked multiple stabile metal(loid)s and radionuclides in the soil and their transfer to indicator organisms (moss, earthworms, livestock and wildlife animals) (47).

We were invited by the Ministry of Economy and Sustainable Development to collaborate by providing our research data in the preparation of the State of the Environment Report of the Republic of Croatia for the period 2017. – 2020.

In-house scientific projects (Chapter 16.1.A.3.)

1. Assessment of the effects of MT2A +838 G/C and MT2A –209 A/G gene polymorphisms on the levels of toxic and essential elements at childbirth

We completed research on the associations of metallothionein *MT2A* gene polymorphisms and element levels in the biological samples of mother-infant pairs (maternal blood, cord blood and placenta) collected during the research project METALORIGINS, HrZZ (n = 156) and archive samples from the previous studies in the Unit (n = 268). We determined the genotype frequency of *MT2A* +838G/C and started final analysis on the potential effects of metallothionein *MT2A* gene polymorphisms on the toxic and essential element levels in healthy postpartum women as well as prepared a manuscript on the obtained results.

2. Bioactive potential, metal and nicotine content in edible Boletus mushrooms regarding the toxic metal burden of soil

We completed the collection of edible *Boletus* mushrooms and nearby soil from Croatia aiming for an investigation of human exposure to potentially toxic chemicals transferred from soil to mushrooms. Quantification of radionuclides (¹³⁷Cs and ⁴⁰K) and stable metals (Cd, Pb, Hg) was carried out as planned, while measurements of nicotine and bioactive potential in mushrooms is ongoing.

Other research activities and collaborations

In collaboration with colleagues from universities from the Republic of Kosovo, we assessed the effects of V and Cr on biomarkers of carbohydrate and lipid metabolism (glucose, cholesterol and triglycerides) in the workers occupationally exposed to coal fly ash (98).

In a collaborative study, we analyzed essential (Se, Cu, Zn, Fe, Ca, Na, Mg and K) and toxic elements (Pb, Cd, Hg, As, Al and Ni) in subjects supplemented with a certified clinoptilolite zeolite (PMA-zeolite) within three clinical trials with different supplementation regimens. We performed a comprehensive and controlled monitoring of the relevant mineral and contaminants levels in human subjects supplemented with a certified clinoptilolite material within three clinical trials with different supplementation regimens. The PMA-zeolite did not increase levels of metal contaminants in the blood. All of the measured metal levels were within the reference range in the short- and medium-term applications. Lower concentrations were observed for Cu in patients with osteoporosis, which normalized again in the long-term supplementation trial, whereas Na and Ca levels diminished below the reference values in patients with osteoporosis. Checking the balance of the minerals Cu, Ca, and Na after 1 year of supplementation might be prescribed for PMA-supplemented patients with osteoporosis (46).

Following the Croatian Science Foundation project AGEMETAR (IP-2013-11-1481) finalized in 2019, where we participated with the analysis of metals and antioxidant enzymes, results in experimental animals study were published on the relationship between aging and oxidative stress with melatonin and resveratrol as antioxidants and anti-aging compounds (8).

We continued research on the subchronic toxicity of low doses of α -cypermethrin by assessing primary DNA damage and determining the activity of the antioxidant enzyme glutathione peroxidase in the blood, brain, liver, and kidneys of male Wistar rats after 28 days of oral exposure (41).

We published research results of the toxic effects of the ochratoxin A and citrinin interaction with and without resveratrol on their accumulation in the liver and kidney of Wistar rats (80).

We studied the toxic effects of synthetic opioids (252), codeine and morphine (306) and ketamine (270, 313) on the human neuroblastoma cell line SH-SY5Y and ketamine on the HepG2 cell line (286).

Results of the TEMPHYS project funded by the Croatian Science Foundation showed high temperature (simulation of global warming) changes in the nutritive value of broccoli seedlings. The plant's ability to adapt to temperature variations was reflected on the phytochemicals, micro- and macroelements, antioxidant capacity, and *in vitro* cytotoxic potential of broccoli extracts tested on five different cell lines (106).

Invasive alien plant Himalayan balsam (*Impatiens glandulifera* Royle) honey from the Međimurje area was characterized. In addition to melissopalynological, sensoric, and physicochemical analyses, elements, phenolic content, carbohydrates and antioxidant capacity were also measured (73).

Salivary cortisol concentrations were determined by ELISA method in a group of students (n = 43) recruited from the University of Zagreb. Results of the association between daily cortisol levels as an indicator of stress, body composition, and heart rate variability parameters in young people were published (10).

RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Assessment of daily exposure to metals and maternal individual susceptibility as factors of developmental origins of health and disease (METALORIGINS, HrZZ-IP)
- 2. Exposure to Pyrethroid and Organophosphate Insecticides in Children Risk Assessment for Adverse Effects on Neuropsychological Development and Hormonal Status (PyrOPECh, HrZZ-IP)

- 3. Role of blood-brain barrier, innate immunity, and tau protein oligomerization in the pathogenesis of Alzheimer's disease (ALZ-BBB-STOPINNATETAU, HrZZ-IP)
- 4. Integrated evaluation of aquatic organism responses to metal exposure: gene expression, bioavailability, toxicity and biomarker responses (BIOTOXMET, HrZZ-IP)
- 5. Indirect effect of global warming on mammals physiological parameters via high temperature-stressed plant diet (TEMPHYS, HrZZ-IP)

International research projects (Chapter 16.2.)

- 1. Partnership for the Assessment of Risks from Chemicals (PARC, Horizon Europe)
- 2. Science-based risk governance of nano-technology (RiskGONE, Horizon 2020)
- 3. Pharmaceutical Open Innovation Test Bed for Enabling Nano-pharmaceutical Innovative Products (Phoenix, Horizon 2020)
- 4. Development of functional beverage in sustainable packaging (JamINNO+, EFRR)
- 5. Safe-by-Design Approach for Development of Nano-Enabled-Delivery Systems to Target the Brain (SENDER, HrZZ-PZS)
- 6. Cancer nanomedicine from the bench to the bedside (Nano2Clinic, COST)
- 7. Endocrine disrupting mechanism of typical environmental pollutants (EmergeTox, Bilateral CRO-CN)
- 8. Modified bacterial cellulose as artificial biomimetic membrane for biological blood-brain barrier (Bilateral CRO-SI)

PROFESSIONAL SERVICES

The Unit provides expert trace element analysis in clinical or environmental samples to assess occupational or environmental exposure, deficiencies, and nutrient intake. The laboratory provides a specialist assay for about 20 individual elements in whole blood, urine, plasma/serum, liver/biopsies, and other biological matrices, using the atomic absorption spectrometry (AAS) or state-of-the-art inductively coupled plasma-mass spectrometry (ICP-MS) methods.

A total of 305 analyses of specific indicators of exposure and effect to toxic metals and essential trace element status in the humans were performed. Most of the laboratory tests were provided at the requests of companies and specialists in occupational medicine practices: a total of 145 analyses of Pb exposure markers [concentrations of Pb and erythrocyte protoporphyrin (EP) and activity of δ -aminolevulinic acid dehydratase (ALAD) in blood] and 80 analyses of metals (Al, As, Cd, Co, Cr, Cu, Hg, Ni, Sb) in the urine of workers. For diagnostic purposes, the concentration of Cu in a liver tissue biopsy samples (n = 9) were analysed. Additionally, analyses of Al, As, Cd, Co, Cr, Cu, Hg, I, Mn, Pb, Se, and Zn in urine, blood, serum, and hair (n = 71) were carried out upon the request of other institutions and individuals.

In addition to analyses in biological samples, we also analysed the content of Pb in lead-based coatings used for the protection of metal structures from two hydroelectric power plants in Guinea (n = 3). The measurements were performed at the request of the renovation contractor (Končar – Engineering Ltd., June 2022) in order to protect the health of the workers who performed the renovation (removal of old paint and corrosion by sandblasting, and repainting of the cleaned structure) and may have been exposed to lead by inhalation.

ORGANISER	TEST	AREA	DATE
Frimley Health, NHS Foundation Trust, Guildford, Surrey, United Kingdom	UK NEQAS for Trace Elements	Analysis of elements in blood (As, Cd, Co, Cr, Hg, Mg, Mn, Pb, Se, Tl, Zn) and urine (As, Cd, Cr, Cu, Fe, Hg, Ni, Pb, Se)	4/2022–12/2022 (two samples of each medium (blood, urine) per month)

Participation in intercomparison programmes

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

J. Jurasović

Member of the Organizing Committee of the 1st Symposim in Analytical Atomic Spectrometry (1. SAAS22), Zagreb; member of the Presidency of the Croatian Society of Toxicology.

Z. Kljaković-Gašpić

Guest editor of the journal *Toxics*: *Special Issue on Biomonitoring of Elements in Wildlife Animals. M. Lazarus*

Guest editor of the *Special Issue on Biomonitoring of Elements in Wildlife Animals, Toxics*; secretary of the Croatian Laboratory Animal Science Association (CroLASA).

A. Pizent

Guest editor of the Special Issue on Oxidative Stress Induced by Environmental and Lifestyle Stressors: Impact on Reproductive Health and Development II, Antioxidants.

I. Vinković Vrček

Member of the Thematic Innovation Council for Health and Quality of Life of the Ministry of Economy of the Republic of Croatia; member of the Working Group for Regulation in the Field of Novel Food, Ministry of Health of the Republic of Croatia; representative of the Republic of Croatia for the Network on Risk Assessment of Nanotechnologies in Food and Feed of the European Food Safety Agency (EFSA).

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

The scientific-teaching title of Associate Professor was gained by *I. Vinković Vrček* at the Faculty of Medicine, University of Rijeka.



HEAD

Snježana Herceg Romanić, PhD, permanent scientific advisor

RESEARCHERS

Assoc Prof Zrinka Kovarik, PhD, permanent scientific advisor Goran Šinko, PhD, permanent scientific advisor since 1 Jun 2022 Anita Bosak, PhD, senior scientific associate Sanja Fingler Nuskern, PhD, senior scientific associate Maja Katalinić, PhD, senior scientific associate Darija Klinčić, PhD, senior scientific associate Gordana Mendaš Starčević, PhD, senior scientific associate Assist Prof Sanja Stipičević, PhD, senior scientific associate Marija Dvoršćak, PhD, scientific associate Nikolina Maček Hrvat, PhD, scientific associate Josip Madunić, PhD, scientific associate since 1 Jun 2022 Nikola Maraković, PhD, scientific associate Antonio Zandona, PhD, postdoctoral researcher Tamara Zorbaz, PhD, postdoctoral researcher Marija Bartolić, MSc, PhD student-assistant Tena Čadež, MSc, PhD student-assistant Karla Jagić, MSc, PhD student-assistant Dora Kolić, MSc, PhD student-assistant Ana-Marija Lulić, MSc, PhD student-assistant Ana Matošević, MSc, PhD student-assistant

TECHNICAL STAFF

Nikolina Medved, technician (substitute: Petra Bajt, MSc, until 20 Jun 2022) Maja Meštrović, technician

PARTICIPATING RETIRED RESEARCHER

Prof Vlasta Drevenkar, PhD, permanent scientific advisor

SCIENTIFIC RESEARCH

ACTIVITIES AND COLLABORATIONS WITH INSTITUTIONAL FINANCING

Scientific collaborations

In collaboration with Dr Višnja Stepanić (IRB) and Vesna Pehar (MORH), we tested selected commercially available herbicides as inhibitors of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Given that herbicides can cause different types of toxicity from reproductive toxicity, hepatotoxicity to neurotoxicity, cytotoxicity was tested on several selected cell lines. This research will form part of the results of V. Pehar's dissertation (217, 246).

Our internal research included a detailed pharmacokinetic and pharmacodynamic characterization of aldoxime RS194B, which due to its dipolar properties passes through the blood-brain barrier and can thus be a reactivator of acetylcholinesterase (AChE) in the brain, inhibited by exposure to nerve agents (206). In collaboration with the Croatian Institute for Brain Research, research on oxime neuroprotective activity,

i.e. preventing the development of neuroinflammation caused by exposure of mice to sarin, began (245). This collaboration included research related to the plasma membrane (214, 221, 222, 249, 308, 320, 323). Oxime solubility in different natural solvents was tested in cooperation with the Faculty of Food and Biotechnology and it was shown that the solvent affects the kinetics of AChE (64).

A review paper on carbamates recently included in Schedule 1 of the Chemical Weapons Convention was written in collaboration with the Organization for the Prohibition of Chemical Weapons, OPCW (63).

A simple QSAR model was developed to evaluate the inhibitory potential of AChE ligands. The QSAR model is based on three simple molecular descriptors: topological connectivity index, number of 10-membered rings and number of OH groups. The model showed a high correlation in predicting the AChE inhibition constant (= 0.937) (55). A QSAR model for evaluating the inhibitory potential of BChE-related ligands was developed using inhibition constants for 289 chemically diverse compounds. The model with three descriptors also showed a high correlation in predicting the inhibition constant of BChE (r = 0.827). The model included the topological connectivity index, the water-octanol partition coefficient and the descriptor fragments with an oxygen atom in the center (56).

The inhibitory potential and selectivity towards certain cholinesterases and the possibility of crossing the blood-brain barrier for 46 fluorinated Cinchona derivatives were determined. Using machine learning, multivariate linear regression models of AChE and BChE inhibition were developed, which enabled finding new potential structural bases for the synthesis of inhibitors active in the central chewing system (76, 307).

As part of the last in-house scientific project "Persistent organic pollutants – Environmental impact assessment and stability of human genetic material" (June 2018 – December 2021, leader S. Herceg Romanić) in cooperation with the Singidunum University, Belgrade, Serbia in the master's thesis of candidate Igor Dučić, the principles of statistical classification and clustering methods and their application to the relationship between OCP and fatty acids in marine fish samples are described, namely principal component analysis – PCA (Principal Component Analysis), self-organizing maps – SOM (Self Organizing Maps) and WARD clustering method. The benefit-risk ratio for fish consumers was assessed based on the results of the analysis of essential fatty acids and persistent organochlorine compounds (57).

Sampling continued within the framework of the MONET project continued, active since 2009 under the auspices of the RECETOX, the Regional Center for Environmental Chemistry and Toxicology, Masaryk University, Brno, Czech Republic).

Salivary cortisol and cortisone concentrations of subjects occupationally exposed to noise (27 samples) and of control group (56 samples) were determined. The research was carried out in cooperation with the School of Public Health "Andrija Štampar" of the Faculty of Medicine, University of Zagreb. The research is part of the doctoral thesis of Roko Žaja, MD, entitled "The role of cortisone concentration and features of auditory evoked potentials of the brainstem in risk assessment of of early professional noise hearing damage".

In-house scientific projects (Chapter 16.1.A.3.)

1. Analysis of organic pollutants in biological systems and the environment

In air quality research using artificial intelligence methods XGBoost, SHAP, Fuzzy clustering, the key factors shaping the distribution of B[a]P were investigated (86). The same artificial intelligence methods were applied in the evaluation of indoor and outdoor air quality (146). Atmospheric deposition investigation continued within the cooperation with the Environmental HygieneUnit, sampling of atmospheric deposition, soils and analysis. Data on polycyclic aromatic hydrocarbons (PAH), polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) in atmospheric bulk deposition samples in the colder period of the year were evaluated (135). In cooperation with scientific institutions in Serbia, specifically, with the Institute of Physics Belgrade and Faculty of Chemistry, University of Belgrade, pollutants in mosses and pine needles collected in Serbia and Croatia were examined for the purposes of passive biomonitoring of air quality (145).

Investigations of simulation gastrointestinal resorption of persistent organic compounds, macro and micro elements and bioavailable fractions of elements from breast milk was continued.

Cooperation with the Public Institution AQUATIKA – Karlovac Freshwater Aquarium regarding pollution of sediment, chub from the Danube basin and from the Adriatic basin rivers was continued. The research was

extended to the frequently consumed fish of the Kupa River: carp *Cyprinus carpio*, pike *Esox lucius*, perch *Sander lucioperca*, catfish *Silurus glanis* and grass carp *Ctenopharyngodon idella*.

2. Bioactive potential, metal and nicotine content in edible boletes regarding the toxic metal burden of soil

In order to consider the results of toxic metal loading in the soil and their transfer to fungi, the total and organic carbon content in 55 soil samples from Croatia was analysed (localities: Crni Lug, Malinska, Bilogora, Glina, Kalnik, Klenovnik).

3. Establishment of three-dimensional cell culture model as a platform for toxicity evaluation of xenobiotics

The goal of this research project is to establish a 3D model of HepG2 and A549 cell lines as a system for toxicity assessment and to implement it as a new method in *in vitro* research as part of the professional and scientific activities of the IMROH. The project was approved for funding at the 262nd Scientific Council on April 6, 2022. The project will start in January 2023.

PROJECTS FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Development of Bioactive Molecules for Neurodegenerative Diseases Treatment (BioMol4ND, HrZZ-IP)
- 2. Analysis of Butyrylcholinesterase Interactions with Novel Inhibitors and Reactivators (AnalyseBChE, HrZZ-IP)
- 3. Molecular Mechanisms Underlying the Toxicity of Antidotes and Potential Drugs (CellToxTargets, HrZZ-UIP)
- 4. Development, validation and application of analytical methods for PBDE determination (DeValApp, HrZZ-UIP)
- 5. Polybrominated diphenyl ethers in the dust of public spaces do they pose a risk to human health? (HAZU Foundation)
- 6. Establishment of a cellular model of the blood-brain barrier for in vitro assessment of the passage of potential drugs into the brain (HAZU Foundation)
- 7. Oximes as potential inhibitors glucose transfer in prostate cancer cells (HAZU Foundation)
- 8. Synthesis and biological evaluation of carbamates as potential cholinesterase inhibitors in the treatment of Alzheimer's disease (HAZU Foundation)

International research projects (Chapter 16.2.A.)

- 1. In vivo efficacy of novel uncharged bis-oximes in OP poisoning treatment (NIH, USA)
- 2. Genome Editing to Treat Humans Diseases (GenE-Humdi, COST)
- 3. P2X receptors as a therapeutic opportunity (PRESTO, COST)
- 4. Effects of selected pesticides on neuronal acetylcholinesterase expression (Bilateral CRO-CN)
- 5. Persistent organochlorine compounds in human milk and their potential effect on the level of primary DNA damage in human cells (Bilateral CRO-RS)
- 6. Effect of oxime analogues on skeletal muscle cell viability (Bilateral CRO-SI)
- 7. Identifying interactions of renal and hepatic organic cation transporters (OCTs) with oximes, antidotes in treatment of organophosphate poisoning (Bilateral CRO-DE)

Educational and science popularization projects (Chapter 16.2.B.)

- 1. Meet toxicity live safely (MeeTox, Erasmus+)
- 2. About science through sport (STEMsport, ESF)
- 3. Rivers of knowledge (ESF)

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

A. Bosak

Treasurer and member of the Executive Board of the Croatian Society of Natural Sciences until July 7; member of the Supervisory board since July 7, 2022; guest editor of the Special issue of *Pharmaceuticals*; member of expert commissions for accepting and evaluating the topic of doctoral theses, Faculty of Science, University of Zagreb.

S. Fingler Nuskern

Member of the TO 147 Water Quality at the Croatian Standards Institute; member of the Working Group for monitoring EU Action Plan "Towards Zero Air, Water and Soil Pollution".

S. Herceg Romanić

Member of the Working Group for monitoring and meeting the requirements of the Third National Plan for the Implementation of the Stockholm Convention on Persistent Organic Pollutants; member of the provisional Workgroup for passing a scientific opinion on the exposure of Croatia's adult population to dioxins and dioxin-like polychlorinated biphenyls (DL-PCBs) from various food types. *M. Katalinić*

Member of the Courte of Honour of the Croatian Society of Biochemistry and Molecular Biology (HDBMB); member of the Public Relations Committee of the HDBMB; member of the Collaboration and Development Committee of HDBMB; member of the Organising Board of the international Congress HDBMB22 "From Science to Knowledge", Brela, Croatia; member of the Organising Committee of the "The 22nd FEBS Young Scientists' Forum (YSF 2023)", Tours, Francuska.

Z. Kovarik

President of the Croatian Society of Natural Sciences until July 7, 2022; member of the Supervisory board since July 7, 2022; member of the Executive Board of the Croatian Chemical Society; member of the Supervisory Board of HDBMB and member of several commissions; member of the Working group "TWG on the Analysis of Biotoxins" of the Scientific Advisory Board of the Organization for the Prohibition of Chemical Weapons (SAB OPCW); member of the Board for Chemistry, Agency for Science and Higher Education; panelist and evaluator of the Croatian Science Foundation; member of the NATO working group "Translating Medical Chemical Defense Research into Operational Medical Capabilities against Chemical Warfare Threat Agents"; member of two expert boards: International Advisory Board on Cholinesterases and International Advisory Board on Cholinergic Mechanisms; organizer of the 17th International Symposium on Cholinergic Mechanisms, ISCM2022, Dubrovnik, Croatia; member of the Scientific Committee CBRNE Research & Innovation Conference, Lille, France; member of the International Organizing Committee of the 4th International Meeting on Cholinesterases & 8th International Conference on Paraoxonases, Bologna, Italy; member of the Scientific Committee of the HDBMB22 Congress "From Science to Knowledge", Brela, Croatia; section editor of Periodicum biologorum; member of expert commissions for accepting and evaluating the topic of doctoral theses, Faculty of Science, University of Zagreb; member of expert commissions for selection to a scientific position, Ruder Bošković Institute, Zagreb.

N. Macek Hrvat

Member of the Organizing Committee of the 17th International Symposium on Cholinergic Mechanisms, ISCM2022, Dubrovnik, Croatia.

J. Madunić

Member of the Public Relations Committee of the Croatian Society of Biochemistry and Molecular Biology (HDBMB); member of the Management Committee of COST actions CA 21113 and CA 21130.

G. Mendaš Starčević

Member of the Committee for Risk Assessment (RAC) at the European Chemicals Agency (ECHA); member of the configuration "Food, Bioeconomy, Natural Resources, Agriculture and Environment" of the Horizon Europe Programme Committee; member of the Working Group for monitoring and meeting the requirements of the Third National Plan for the Implementation of the Stockholm Convention on Persistent Organic Pollutants; member of the provisional Workgroup for passing a Scientific opinion on the exposure of Croatia's adult population to dioxins and dioxin-like polychlorinated biphenyls (DL-PCBs) from various food types; guest editor of the Special issue on *Environmental Monitoring and Analysis of Persistent Organic Pollutants, Toxics.*

M. Meštrović

Delegate representing the non-scientific staff at the Independent Trade Union of Science and Higher Education for the branch IMROH.

S. Stipičević

Member of the Commission for drafting the Rulebook on additional conditions for pesticides intended for professional users for professional use and for non-professional users and the Commission for Pesticides, Ministry of Agriculture of the Republic of Croatia; IMROH coordinator for the Information System of Science of the Republic of Croatia (CroRIS); IMROH coordinator for the implementation of professional practice, Career Center of the Faculty of Science, University of Zagreb.

A. Zandona

Member of the HDBMB Young Scientists' Forum.

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

Scientific degree of scientific advisor was gained by A. Bosak.

Scientific degree of senior scientific associate was gained by *N. Maček Hrvat*. PhD degree was gained by *T. Čadež* at the Faculty of Science, University of Zagreb. PhD degree was gained by *K. Jagić* at the Faculty of Science, University of Zagreb.



HEAD

Ivica Prlić, PhD, professional advisor in science

RESEARCHERS

Ivan Pavičić, PhD, scientific advisor since 1 Aug 2022 Ana Marija Marjanović Čermak, PhD, scientific associate Krunoslav Ilić, PhD, postdoctoral researcher since 15 Dec 2022 Luka Pavelić, PhD, postdoctoral researcher since 1 Jun 2022 Ana Buinac, MSc, senior professional advisor in science (3h/week) Tomislav Meštrović, MSc, senior professional associate in science Jerko Šiško, MSc, senior professional associate in science Branimir Zauner, PhD, professional associate in science Martina Dragičević, MSc, professional associate in science since 1 Aug 2022 Mihovil Jurdana, professional associate in science

TECHNICAL STAFF

Selvije Sefić, BSc, senior technician Silvija Kobešćak, BSc, technician

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

In-house scientific projects (Chapter 16.1.A.3.)

1. Thermometry, thermography and sensory evaluation of electromagnetic radiation in medicine (TTSem2)

We conducted research using experimental methods of IR thermography in the clinical departments of KBC Zagreb. We tried to continuously monitor the thermographic characteristics of female breasts with invasive ductal carcinoma. The continuation of the investigation of the thermographic characteristics of the healing of clavicle and humerus fractures in children (in cooperation with the KBC Zagreb and the Clinic for Children's Diseases, Zagreb) in pandemic working conditions is underway. The preliminary results obtained during 2019 were processed for the purpose of publication. It is planned to continue clinical research on the topic of temperature symmetry mapping of skin regions in children and adults of both sexes. Measurements would be carried out during outpatient examinations in the polyclinic of the Clinic for Surgery of KBC Zagreb. The goal of this research is to standardise physiological deviations in a healthy population and determine standard deviations for individual anatomical regions. Until now, similar measurements have already been made, but without a study of differences by age. After creating the optimal number of thermometer sensors, the plan is to carry out the measurements in patients of the KBC Zagreb Surgery Clinic who are undergoing a standard fracture treatment procedure. A protocol is being prepared for the patient's consent to participate in the implementation of the project.

2. Thermometry, thermography and sensory evaluation of electromagnetic radiation in medicine (TTSem3)

New scientific research topics were formed on the TTSem3 project (W1 – W6): W1 Thermometry of healing of forearm bone fractures in children.

W2 Thermometric monitoring of skin reinnervation after breast reconstruction with a free flap and implants. On the above topic, in cooperation with the Faculty of Medicine, Clinic for Plastic Surgery, documentation was prepared for the HrZZ research project application (IP-2022-10) entitled "Recovery of breast sensation following implant-based breast reconstruction (ReSens)" under the leadership of Prof Krešimir Bulić, MD, from the Faculty of Medicine, University of Zagreb.

Other work packages continue with their activities that were disabled during the pandemic.

W3 Development of a human analgesic test model using the axo-axonal reflex and IR camera.

W4 Daily variations of frontal temperature in children.

W5 Frontal temperatures in obese children.

W6 Cooperation in the development of dosimetric methods and measurements during surgical procedures in the Clinic for Surgery and the Clinic for Interventional Neurology of KBC Zagreb, where X-ray radiation is used as standard for diagnosis and implementation of surgical procedures.

3. Development of UV radiation sensors (SUVIndex)

Field measurements were carried out using developed prototypes of UV sensors developed at IMROH in cooperation with external partners. The collection of data that could indicate certain UV behaviors at the time of pandemic restrictions is underway.

Other research activities

The evaluation of the results of the intercomparison of the thermoluminescent dosimeters received in the spring and autumn of 2022 and the assessment of the necessary corrections to the method of determining the personal dose equivalent of Hp (10) and Hp(3) from photon radiation sources are in progress.

National Program for Screening and Early Detection of Lung Cancer 2020–2024

Due to the pandemic operating conditions of the clinics, the implementation of the entire program of the Ministry of Health of the Republic of Croatia was largely postponed to the fall of 2022. In the part of the program related to the quality control of low-dose CT devices, the employees of the Unit under the leadership of I. Prlić, coordinator of the Commission of the Ministry of Health of the Republic of Croatia for Implementation quality control of low-dose CT devices during the implementation of the National Program. The program officially started in October at the Jordanovac Lung Disease Clinic, KBC Zagreb. More about the project: https://zdravlje.gov.hr.

RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Significance of interaction of metal nanoparticles with sulphur biomolecules for nano-bio interface (NanoFaceS, HrZZ-IP)
- 2. Application of Nanobiotechnology for Nutritional Supplementation with Selenium (NutriNTENSe, HrZZ-IP)

International research projects (Chapter 16.2.A.)

- 1. European Partnership for Radiation Protection Research (PIANOFORTE, Euroatom)
- 2. Science-based risk governance of nano-technology (RiskGONE, H2020)
- 3. Safe-by-Design Approach for Development of Nano-Enabled-Delivery Systems to Target the Brain (SENDER, HrZZ-PZS)
- 4. Single layer gamma-ray polarimeter for medical imaging applications and fundamental physics research (SiLGaP, HrZZ-PZS)
- 5. Enhancing Regulatory and Metrological Infrastructures Needed to Ensure Radiation Safety in Naturally Occurring Radioactive Materials Industry (IAEA)
- 6. Improving Environmental Monitoring and Assessment for Radiation Protection in the Region (IAEA)
- 7. Modified bacterial cellulose as artificial biomimetic membrane for biological blood-brain barrier (Bilateral CRO-SI)

PROFESSIONAL SERVICES

The same protocols for IMROH employees in the field of radiation protection were implemented as in the previous year. The implementation of field work, especially those carried out by the Unit's associates as part of the Authorized Expert Technical Service for Radiological Safety (IMROH STS), was partially difficult during part of the year for users in the Republic of Croatia. Prescribed epidemiological measures to alleviate pandemic living and working conditions, especially in health care institutions (clinical hospitals) in the Republic of Croatia, significantly prolonged the performance of certain quality control tasks and the implementation of QA/QC procedures with sources of ionizing radiation carried out by the Unit's employees. Despite this, all contractual obligations of IMROH STS were successfully fulfilled. Employees who process personal dosimeters additionally collected and processed dosimeters that professionals used in hospitals, the so-called COVID, departments. For the health safety of its employees, the Unit has introduced special protocols for the protection of employees and the disinfection and chemical treatment of dosimeter carriers.

Activities of the Authorized Expert Technical Service for Ionizing Radiation (IMROH STS)

Tasks for the INA Group, related to: i) the development of a protocol for the implementation of business activities during oil and gas exploration on the territory of the Republic of Croatia, which include the manipulation of natural radioactive materials (NORM), especially residues, ii) the preparation of an activity plan in the event of an extraordinary event, which contains radiological risks and iii) determination of the need for specialist professional training and the implementation of safety measures related to ionizing radiation and the appearance of residues at the production locations of the INA Group, additional jobs were contracted for the preparation of several studies, four of which were specialized reports during 2022 for the needs of activities carried out by STSI d. o. o., a member of the INA Group, and field surveys and monitoring of radiological works were carried out at the gas production sites of Molva and Gola.

The result of the business cooperation with the INA Group will also be visible in the additional projectresearch activities of the Radiation Protection Unit, whose collaborators are developing an environmental model for residue monitoring in the gas and oil production industry in the Republic of Croatia using samples from the research production fields of the INA Group, with a special research focus on the impact of residues on the biota of the locations where these facilities are located. During 2022, the foundations were prepared for the continuation of the project professional-technical, innovation and research cooperation between INA and IMROH.

Professional experimental work at the location of STSI d. o. o. in Strušac resulted in the development of an internal institute research project, the experimental development part of which was carried out during 2022 under the strictest pandemic restrictive measures in the field and in cooperation with external collaborators ALARA instruments d. o. o. and Haj-Kom d. o. o. The aforementioned activities are a link to the sustainability of the IPPSO project, IMI_Ericsson Nikola Tesla d. d. (www.ippso.imi.hr), financed from the structural funds of the EU program.

An experimental measuring system with the working name ALARA UAV (Unmanned Aerial Vehicle) was developed and is still being further developed. Documentation is being prepared for the application of that pilot project for international co-financing and experimental technological development in full experimental form (research/technological development of measuring instrumentation) and congress announcements have been sent as the first step of publishing complete works.

Professional risk assessment studies

As many as 25 risk assessment studies were carried out for performing activities with sources of ionizing radiation in dental medicine, research and industry with different contractors. Several studies are in the further process of creation.

Professional reports of personal dosimetry and employee categorization

On the basis of the contract on personal dosimetric monitoring and testing of sources of ionizing radiation, during 2022, in compliance with the prescribed epidemiological measures, the Unit carried out personal dosimetric monitoring, radiological monitoring of the workplace and testing of sources of ionizing radiation

for 181 contracted users from various fields of activity. In 2022, about 2500 categorizations of exposed workers were made for contractual users of personal dosimetric monitoring.

The Unit is working on the preparation of the IMROH e-dosimetry protocol, which will enable the transition to online delivery of dosimetry reports to users of the Authorized Technical Service of IMROH and thereby further modernize business and the relationship with users – customers of services by including personal dosimetry of IMROH in the Republic of Croatia system e-Citizens. This expert project is in the initial implementation phase and is being worked on by the expert associates of the Unit. Project e-dosimetry IMROH continued in 2022 with the testing of all relevant IT components and certificates for the protection of users' personal data.

Expert reports on quality control of sources of ionizing radiation

With the continuation of the strictest observance of epidemiological measures in the field and respect for the mobility of people and goods between the counties of the Republic of Croatia, more than 600 field tests – quality control and measurements as part of the radiological monitoring of the workplace were made for about 570 electrical devices that produce ionizing radiation (X-ray devices and linear accelerators) and close to 50 radioactive sources/isotopes used in medicine, industry, and scientific institutions. More than 1250 expert reports and more than 1300 expert opinions were prepared on the basis of the tests performed.

The Unit is working on the further modernization of the IMROH e-radiation sources protocol, which will enable the transition to online delivery of reports on the implementation of QA/QC measurements to users of the IMROH STS service and thereby further modernize business and the relationship with users-customers of services by including the sending of electronically signed reports. This expert project of the Unit is also in the test implementation phase during the next year. The plan is to test all relevant IT components and certificates for the protection of users' personal data, methods of accepting/storing and sending documentation and reporting to the regulatory body of the Ministry of Interior of the Republic of Croatia.

During 2022, more than 26,000 dosimetric measurements were performed, based on which more than 3000 dosimetric reports were prepared for contractual users of personal dosimetric monitoring.



Number of tested dosimeters by month: blue are dosimeters whose results are reported to the national dose-register of exposed workers; red are dosimeters whose results are reported to users

Participation in international laboratory intercomparisons

ORGANISER	TEST	AREA
Institut Jožef Stefan, Ljubljana, Slovenia	PRIMER 2021 Primerjalne meritve hitrosti doze in spektrometrije gama	Measurement of the ambient dose equivalent rate H*(10)/t

List of accredited methods (4)

TEST METHOD	TYPE OF TEST, RANGE
ME-608-001 (In-house method)	Personal dosimetry of the photon radiation using TL dosimeters in the range 85 μSv–100 mSv and energy range 33 keV–1.3 MeV
ME-608-002 (In-house method)	Determination of ambient dose equivalent rate; H*(10)/t, H*(10)/t range 100 nSv/h–100 mSv/h and energy range 36 keV–1.3 MeV
ME-608-003 (vlastita metoda)	Ring dosimetry of ionizing radiation using thermoluminescent dosimeters in the range 170 μ Sv-500 mSv and range of radiation energies 33 keV-1.3 MeV
ME-608-004 (vlastita metoda)	Environmental dosimetry of photon radiation using thermoluminescent dosimeters in the range 180 μ Sv-100 mSv and range of radiation energies 33 keV-1.3 MeV

The Unit's quality manager: J. Šiško.

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

T. Meštrović

Radiation protection expert for the areas of personal dosimetric monitoring – assessment of external radiation, personal dosimetric monitoring – assessment of internal radiation, activities in medicine, dentistry and veterinary medicine with sources of ionizing radiation, activities in industry and science with radioactive and ionizing radiation sources.

L. Pavelić

Associate member of the European Radiation Dosimetry Group (EURADOS) Working Group WG3-S2; member of the of the Executive Board of the Croatian Nuclear Society.

I. Pavičić

Member of the Working Group for the development of the Croatian Position in the field of protection against electromagnetic fields.

I. Prlić – nominations

Member of the Reference Group of the Croatian Ministry of Health for cooperation with the EU EURATOM; member of the Scientific Expert Group ART 31 EURATOM, EC 2020–2025; member of the Scientific Expert Group ART 37 EURATOM, EC 2020–2025; member of IRPA (International Radiation Protection Association – Task Group on Radioactive Source Security, national nomination 2019-2024.

I. Prlić – responsibilities

Expert-advisor of the Group for drafting the Position of the Republic of Croatia in the field of protection against non-ionizing radiation, Working Group for 5G technological solutions; member of the Commission of the Ministry of Health of the Republic of Croatia for the implementation of the Health Strategy of the Republic of Croatia – National Program for Screening and Detection of Lung Cancer 2020–2024; member of the Working Group of the State Institute for Standardization and the Ministry of Health of the Republic of Croatia for work on legal metrology in the field of medical equipment; member of the Board of Directors of the Croatian Society for Biomedical Engineering and Medical Physics; member of the Education and Training Committee of the European Federation of Organizations for Medical Physics (EFOMP); member of the International Atomic Energy Agency (IAEA); member of the EC Environmental Radition-Effect Working Group: International Perspectives – part of the project for Croatia; member of the Commission of the Ministry of Health for review and evaluation of studies in the field of non-ionizing radiation sources; member and expert of the European ALARA Network for Naturally Occurring Radioactive Materials (EAN NORM); international

expert for the International Road Transport Union and the International Labor Organization; member of the Board of Directors of MELODI (Multidisciplinary European Low Dose Initiative); member of the Steering Committee of the international project CONCERT (H2020); member of the Steering Committee of ALLIANCE (The European Radioecology Alliance), Croatian member of the working group, Task Group on Radioactive Source Security, ICRP (International Committee for Radiation Protection).

J. Šiško

Associate member of the European Radiation Dosimetry Group (EURADOS) Working Group WG3-S2; radiation protection expert.

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

A PhD degree was gained by K. Ilić at the Faculty of Pharmacy and Biochemistry, University of Zagreb.



HEAD

Assoc Prof Gordana Pehnec, PhD, scientific advisor

RESEARCHERS

Ivan Bešlić, PhD, scientific advisor Ranka Godec, PhD, senior scientific associate since 1 Aug 2022 Silva Žužul, PhD, senior scientific associate since 25 May 2022 Silvije Davila, PhD, scientific associate Ivana Jakovljević, PhD, scientific associate since 11 Apr 2022 Jasmina Rinkovec, PhD, scientific associate Iva Šimić, MSc, PhD student-assistant Suzana Sopčić, PhD, professional associate in science Valentina Gluščić, MSc, professional associate in science Nikolina Račić, MSc, professional associate in science Zdravka Sever Štrukil, MSc, professional associate in science

TECHNICAL STAFF

Ana Filipec, statistician, senior technician until 15 Jun 2022 Samuel Ljevar, senior technician Gordana Pršlja, senior technician since 3 Oct 2022 Magdalena Vincetić, MSc, senior technician Marija Antolak, technician until 25 Dec 2022 Matea Kuzel, technician until 1 Sep 2022 Karmenka Leš Gruborović, technician Ivan Marić, technician since 10 Nov 2022 Martin Mihaljević, technician Tereza Puzjak, technician (1–25 Dec 2022) Martina Šilović Hujić, MSc, technician

PARTICIPATING RETIRED RESEARCHERS

Krešimir Šega, PhD, permanent scientific advisor Vladimira Vađić, PhD, permanent scientific advisor Mirjana Čačković, PhD, senior scientific associate

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

Long-term research activities

Measurements of polycyclic aromatic hydrocarbons (PAH) in airborne particulate matter were carried out at several locations of different characteristics. The study of spatial and seasonal variations and the assessment of the dominant pollution sources continued (121, 133, 189). Two methods for the preparation of particulate matter samples were compared: the accelerated solvent extraction method (ASE) and the ultrasonic extraction method (UZV). Both methods were found to be suitable for the preparation of PAH samples, but ASE had a slightly better efficiency compared to UZV (127). The carcinogenic activity of PAHs in the air was evaluated in an area with minimal influence of human activities (area of the Plitvice Lakes National

Park) (224). During the previous period, PAH concentrations were also determined in other environmental samples (14, 15, 135, 168). A method was developed for determination of PAH concentrations in household dust samples (15, 33, 195). For the preparation of soil samples, the matrix solid phase dispersion method (MSPD) was optimized. Different mixtures of solvents and sorbents were tested as a part of a master thesis (168). The PAH content was determined in soil samples collected in the Labin area, where various activities related to the exploitation, transport, storage and use of coal were present in the past (34).

Measurements of elemental (EC) and organic (OC) carbon in PM_{2.5} fraction of particulate matter continued at the measuring stations of the state network for air quality monitoring of different characteristics (urban background, urban traffic and rural measuring stations). A comparison was carried out with other fractions of particulate matter (PM₁₀ and PM₁) (48, 192, 193, 281).

Carbohydrate analysis in the PM₁₀, PM_{2.5}, and PM₁ fractions of particulate matter continued at measuring stations of different character (urban background, urban traffic, rural measuring station). The results reveal the extent to which biomass burning contributes to the total concentration of suspended particles as well as the presence of carbohydrates in individual fractions of particulate matter (134). Seasonal variations of twelve carbohydrates were monitored and their interrelationship as well as possible sources were studied. Since the organic components in the particulate matter are the result of several different pollution sources, the ratios of the mass concentrations of sugar anhydrides to the concentrations of polycyclic aromatic hydrocarbons (PAH) were compared. A significant statistical correlation was obtained between anhydrosugars and benzo[a] pyrene and Σ PAH (309).

Measurements of mass concentrations anions (Cl⁻, NO₃⁻, SO₄²⁻) and cations (Na⁺, NH₄⁺, K⁺, Mg²⁺, Ca²⁺) in the fine particulate matter fraction (PM_{2.5}) continued in Zagreb city area. Furthermore, measurements were extended on monitoring mass concentrations of water-soluble organic anions in PM_{2.5}, in order to characterize different pollution sources and their contribution to overall air pollution in the western part of Zagreb (191). Also, at the coastal urban background site in Rijeka, the five-year trend of PM_{2.5} mass concentrations as well as mass concentrations of water soluble inorganic ions (Cl⁻, NO₃⁻, SO₄²⁻, Na⁺, NH₄⁺, K⁺, Mg²⁺, Ca²⁺) in its content were determined. The ratios between ions in PM_{2.5} and their contribution to the total mass of fine particulate matter was examined (280). Monitoring of the levels of acidic compounds (Cl⁻, NO₃⁻, SO₄²⁻) and the alkaline ions (Na⁺, NH₄⁺, K⁺, Mg²⁺, Ca²⁺) in the total deposited matter (TDM) content at different locations continued (124).

Measurements of metals in the PM₁₀ particle fraction and in total deposited matter at locations with different pollution sources continued. The impact of lockdown measures due to the COVID-19 pandemic on air quality in Croatia was studied. The levels of certain pollutants (nitrogen dioxide, ozone, PM₁₀, PM_{2.5}, PAH and metals in PM₁₀) were monitored during the lockdown period in the spring of 2020 and were compared with values from earlier years (48, 128, 140, 141, 218).

Scientific collaborations

Cooperation with the Biochemistry and Organic Analytical Chemistry Unit continued, and as part of the DeValApp project, the results of microwave extraction of polybrominated diphenyl ethers (PBDE) from human milk samples were published (14). PAH concentrations were determined in house dust samples collected in Zagreb, and the impact of PAH was assessed for two population groups (children up to 6 years of age and adults over 20 years of age) (33). The impact of PAHs on human health was also assessed in other environmental conditions: in the offices of various companies, kindergartens, and in the interior of cars (exposure of professional drivers) (15, 195). As part of the institutional project "Analysis of organic pollutants in biological systems and the environment" (leader S. Herceg Romanić), a method for determining PAH in sediment was developed and the collected samples were analysed.

In cooperation with the Mutagenesis Unit, research on the HUMNap project "Air pollution and biomarkers of effects in humans" (leader G. Gajski) continued. The levels of pollutants in the air at different locations (Zagreb, Slavonski Brod, Vinkovci) were monitored together with biomarkers of the effect in humans (209, 296, 297). Available data from previous years were analysed as well (19). Furthermore, the cooperation have started within the framework of the HAZU project "Assessment of the cytogenotoxic effect of pollutants from the air on human cells *in vitro*".

Cooperation with the Andrija Štampar Teaching Institute of Public Health continued within the "Ecological Map of the City of Zagreb" programme. The results of air quality measurements were uploaded to the portal https://ekokartazagreb.stampar.hr/, where the latest data on environmental measurements (soil, water, air, pollen, meteorological data) for the City of Zagreb are continuously collected. The results of measurements of PM chemical composition with the review of carbon and metals were presented as full conference papers (125, 136).

Cooperation with the Faculty of Science in Sarajevo, B&H, and Katja Džepina, PhD (University of Nova Gorica, Slovenia) on the analysis and processing of data from the SAFICA project continued. A comprehensive analysis of the PM₁₀ metal content was carried out at the city and background measuring station in Sarajevo Canton, Bosnia and Herzegovina (101). An overview of the results of organic air pollution in the Western Balkans was also made, and the results were presented at international meetings (138, 277).

In cooperation with the Faculty of Agriculture of the University of Zagreb, the concentrations of platinum, palladium and rhodium in environmental samples were determined, and the distribution of the these metals in the above-ground layers of plants (*Plantago lanceolata* L. and *Dactylis glomerata* L.) and at different soil depths was studied. The results show that there is a depth distribution of platinum group element concentrations in the soil, and that *Plantago lanceolata* L. has indicator properties, especially for Pd (163) Also, the obtained results showed that there is a seasonal and spatial distribution of platinum, palladium, and rhodium in airborne particulate matter collected at three locations with different traffic density in the city of Zagreb (132, 223).

In cooperation with the Faculty of Forestry, University of Zagreb, the effectiveness and applicability of the photometric method for determination of the mass concentration of inhalable dust from raw and dry hardwoods was studied, as well as the occupational exposure of workers in the wood factories to inhalable and respiratory fractions of wood dust (11, 122).

In cooperation with Mario Lovrić, PhD (KNOW-CENTER, Graz, Austria) data on air pollution collected in the Zagreb area were analysed. Long-term trends of the PM₁₀, PM_{2.5} and PM₁ mass concentrations and meteorological data were studied. Changes in mass concentrations of particulate matter were studied for three periods: immediately before the lockdown due to the COVID-19 pandemic, during the lockdown, and after ("new normal") and compared to previous years. Random Forest (RF) and LightGBM (LGB) models were used for meteorological normalization of PM mass concentration data (48, 139).

In-house scientific projects (Chapter 16.1.A.3.)

1. Organic content of PM₁ particle fraction

Collection of 24-hour samples of PM₁ fractions continued during the year at the IMROH location as well as the centre of Zagreb. Organic and elemental carbon, water-soluble organic carbon, levoglucose, and PAHs were analyzed in the collected samples. The obtained data were processed and systematized. The results of the research of the PM₁ organic composition and the comparison with the PM₁₀ and PM_{2.5} fractions were presented at national and international meetings in the form of posters and oral presentations. Air pollution sources of individual organic components were assessed (133, 189, 192, 227, 281, 284, 309).

2. Molecular markers of organic carbon - biomass burning indicators

In 2022, the experimental analyses of collected samples of PM₁₀, PM_{2.5}, and PM₁ particle fraction at the IMROH measuring station were completed. Two methods for sample analysis using high-performance anion exchange chromatography with pulsed amperometric detection were developed. The statistical analysis of data started with an emphasis on the correlation of carbohydrates mass concentrations and concentration of organic carbon as well as polycyclic aromatic hydrocarbons in the samples collected at the same measuring station. The results showed significant seasonal variations in the mass concentrations of carbohydrates (225). The most abundant carbohydrates are anhydrosugars, which represent one of the three groups of carbohydrates present in the particulate matter, which are associated with biomass burning. The concentrations of levoglucosan, mannosan, and galactosan were the highest in the colder part of the year, while the concentrations of other groups of carbohydrates; sugar alcohols, and primary sugars are more pronounced in the warmer part of the year. The results show that more than 90% of levoglucosan is present

in the PM_1 fraction of particulate matter (309). The mass concentrations of carbohydrates detected in the northern part of Zagreb City were compared with the concentrations determined in the southern part of the city, showing significant spatial variations (226).

RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Biochemical responses of the surface layer in the oligotrophic area of the Adriatic to atmospheric sedimentation (BiREADI, HrZZ-IP)
- 2. Air pollution and human biomarkers of effect (HUMNap, HrZZ-IP)
- 3. Ecological map of the City of Zagreb (City of Zagreb)

International research projects (Chapter 16.2.A.)

- 1. Project of extension and modernisation of the national network for continuous air quality monitoring (AIRQ, ERDF)
- 2. Development of functional beverage in sustainable packaging (JamINNO+, ERDF)
- 3. Evidence Driven Indoor Air Quality Improvement (EDIAQI, Horizon Europe)
- 4. Determining Long Term Time Trends of Air Pollution Source Tracers by Nuclear Techniques (IAEA)
- 5. Deployment of lower-cost ambient air quality sensor systems in urban environments (JRC)

PROFESSIONAL SERVICES

The monitoring of air pollution continued in Zagreb at six measuring stations of the local measuring network. At the Zagreb stations, the Unit measured different pollutants in the air: sulphur dioxide, black carbon, PM₁₀ fraction, metals arsenic (As), cadmium (Cd), nickel (Ni), lead (Pb), manganese (Mn), iron (Fe), copper (Cu), zinc (Zn), PAHs in PM₁₀ fraction, PM_{2.5} fraction, nitrogen dioxide (NO₂), ozone (O₃), carbon monoxide (CO), benzene, total deposited matter, and metals As, Cd, Ni, Pb, and Tl in the total deposited matter

According to contracts with the Ministry of Economy and Sustainable Development and the Meteorological and Hydrological Service of Croatia, following the Air Protection Act (127/19, 57/22), the Unit as a reference laboratory performs the sampling of particulate matter (PM₁₀ and PM_{2.5}) and its physical and chemical analysis at measuring sites within the Croatian State Network for Air Quality Monitoring. The Unit also carries out equivalency of non-reference methods for the determination of particulate matter mass concentration (PM₁₀ and PM_{2.5}) in the air. Similarly as in previous years, air pollutants were measured at the monitoring sites Zagreb-1, Zagreb-3, Sisak-1, Slavonski Brod-1, Slavonski Brod-2, National Park Plitvice Lakes, Ksaverska cesta, Velika Gorica, and Rijeka-2, in Croatia. In 2022, through the AIRQ project, 18 measuring stations were modernized and 5 new ones were established. The Unit started with measurements at the measuring stations Osijek-PPIPM2.5 and Polača, while the measurements at the new stations Zagreb-4 and Split-PPIPM2.5 will begin in January 2023.

Equivalence studies were performed for non-reference measuring methods of PM_{10} and $PM_{2.5}$ at measuring stations Rijeka-2 and Osijek-2, and for PM_{10} fraction at measuring site Sisak-1, as well as in Plomin, Potpićan and Našice.

The monitoring of air, water, soil, agricultural, and forest ecosystems and control of wild animals in the vicinity of the Central Gas Station (CGS) Molve continued. In 2022, in cooperation with the Institute of Public Health of the Koprivnica-Križevci County, the Institute performed measurements of hydrogen sulphide, mercaptans, and sulphur dioxide at five locations in the proximity of the CGS Molve.

The monitoring of air quality within the zone of influence of the Wastewater Treatment Plant in Zagreb continued. The monitoring of levels of hydrogen sulphide, ammonium, and total mercaptans and meteorological parameters was carried out at five measuring stations. In 2022, the measurements of these pollutants continued at two additional locations in the possible zone of influence (Resnik i Ivanja Reka, Croatia) as well.

Near the Jakuševec landfill, the levels of PM₁₀ and mercaptans are continuously measured. During different seasons, levels of metals Pb, As, Ni, Cd and PAHs in PM₁₀ fraction were also measured as well.

Measurements of PM_{10} fraction and PAHs in PM_{10} fraction were carried out at a measuring site within Zagreb International Airport, Croatia.

Special purpose measurements were carried out in Zagreb at MO Ivanja Reka and in Ogulin.

Measurements of total deposited matter were carried out at two locations at "Brezovi Rebar" sand excavation near Karlovac and in the area of the asphalt base in Našice.

List of intercomparisons

ORGANISER	TEST	AREA	DATE
LGC	LGC – AIR PT Workplace Air, Ambient Air and Stack Emissions, Round 52 (AR052); 14 – Anions on Filters	Determination of mass concentration of anions chlorides, nitrates and sulphates in particles	July/August
LGC	LGC – AIR PT Workplace Air, Ambient Air and Stack Emissions, Round 42 (AR042); 16 – Diesel Fume	Determination of mass concentration of elemental carbon in particles	August/September
EKONERG	Proficiency testing for CO and SO ₂	Determination of gaseous air pollutants – gases CO and SO ₂	December

List of accredited methods (14)

METHOD	TYPE OF TEST, RANGE
HRN EN 12341:2014 (EN 12341:2014)	Determination of mass concentration of PM_{10} and $PM_{2.5}$ particle fractions
HRN EN 14212:2012 (EN 14212:2012), HRN EN 14212:2012/Amend. 1:2014 (EN 14212:2012/AC:2014)	Determination of the concentration of sulphur dioxide in the ambient air
HRN EN 14625:2012 (EN 14625:2012)	Determination of the concentration of ozone in the ambient air
HRN EN 14211:2012 (EN 14211:2012)	Determination of the concentration of nitrogen oxide in the ambient air
HRN EN 14626:2012 (EN 14626:2012)	Determination of the concentration of carbon monoxide in the ambient air
HRN EN 14902:2007 (EN 14902:2005), HRN EN 14902/AC:2007 (EN 14902:2005/AC:2006)	Determination of the concentration of Pb, Cd, As and Ni in the $\rm PM_{10}$ fraction of suspended particulate matter
HRN EN 16909:2017 (EN 16909:2017)	Determination of the mass concentration of elemental and organic carbon in the suspended particulate matter in the ambient air
HRN EN 15549:2008 (EN 15549:2008)	Determination of the concentration of benzo(a)pyrene in the ambient air
HRI CEN/TR 16269:2017 (CEN/TR 16269:2011)	Determination of the mass concentration of anions and cations in the suspended particulate matter
VDI 4320 Part 2: 2012 (VDI 4320 Part 2:2012)	Determination of the dust deposition according to the Bergerhoff method
HRS CEN/TS 16645:2016 (CEN/TS 16645:2014)	Determination of the concentrations of benz(a)anthracene, benzo(b)fluoranthene, benzo(j)fluoranthene, benzo(k)fluoranthene, dibenz(a,h)anthracene, indeno(1,2,3-cd)pyrene and benzo(ghi)perylene in ambient air
HRN EN 15841:2010 (EN 15841:2009)	Determination of arsenic, cadmium, lead, and nickel in atmospheric deposition

In-house method OP-610-UTT-TI Edition 01 2020-01-28	Determination of thallium in atmospheric deposition
HRN EN 16913:2017 EN 16913:2017)	Determination of the mass concentration of anions and cations in $PM_{2.5}$ as deposited on filters

The Unit's quality manager: R. Godec.

PROFESSIONAL ACTIVITIES OF EMPLOYEES OUTSIDE THE INSTITUTE

I. Bešlić

Member of the Croatian Air Pollution Prevention Association's Presidency; member of the Working Group in charge of monitoring the activity plan for the national network for permanent air quality monitoring at the Ministry of Economy and Sustainable Development of the Republic of Croatia; member of the Commission for Reference Laboratory Work Monitoring at the Ministry of Economy and Sustainable Development of the Republic of Croatia; member of the Commission for the Selection of the Measuring Stations in the National Air Quality Monitoring Network; member of the Working Group for Air of the Croatian Accreditation Agency; member of the TO-146 Air Quality Committee of the Croatian Standards Institute; member of the Executive Editorial Board of the journal *Archives of Industrial Hygiene and Toxicology*.

S. Davila

Member of the Croatian Air Pollution Prevention Association's Presidency.

R. Godec

President of the Croatian Air Pollution Prevention Association; member of the TO-146 Air Quality Committee of the Croatian Standards Institute; member of Advisory Committee of EFCA International Symposium: Ultrafine Particles – Air Quality and Climate.

G. Pehnec

International coordinator and member of the Croatian Air Pollution Prevention Association's Presidency; member of the Working Group in charge of monitoring the activity plan in the national network for permanent air quality monitoring at the Ministry of Economy and Sustainable Development of the Republic of Croatia; member of the Commission for Air Quality Improvement Monitoring in the area of Slavonski Brod; member of the Working Group for Air of the Croatian Accreditation Agency; vice-president of European Federation of Clean Air and Environmental Protection Associations (EFCA); member of the Program Committee of EFCA International Symposium: Ultrafine Particles – Air Quality and Climate; member of the Scientific Board of 2. Regional symposium on Air Quality in Cities.

J. Rinkovec

Member of the Commission for Reference Laboratory Work Monitoring at the Ministry of Economy and Sustainable Development of the Republic of Croatia; member of the WHO Task Force on Health Aspects of Long-range Transboundary Air Pollution.

Z. Sever Štrukil

Treasurer and member of the Croatian Air Pollution Prevention Association's Presidency.

S. Žužul

Member of the Croatian Air Pollution Prevention Association's Presidency.



HEAD

Prim Jelena Macan, MD, PhD, permanent scientific advisor (90% of working hours and 10% in the Institute's company)

RESEARCHERS

Prof Selma Cvijetić Avdagić, PhD, MD, permanent scientific advisor Veda Maria Varnai, PhD, MD, permanent scientific advisor Željka Babić, PhD, scientific associate Assoc Prof Adrijana Bjelajac, PhD, scientific associate Jelena Kovačić, PhD, scientific associate Zrinka Franić, MD, PhD, postdoctoral researcher since 7 Feb 2022 Marija Macan, PhD student-assistant Patricia Tomac, PhD student-assistant Rajka Turk, MSc, professional advisor in science until 28 Feb 2022 Marija Kujundžić, BSc, professional associate in science Franka Šakić, MSc, professional associate in science (90% of working hours and 10% in the Institute's company)

TECHNICAL STAFF

Silvija Bošković, BSc, senior technician since 3 Jan 2022 Monika Vuletić, MSc, senior technician Jagoda Mandić, nurse, technician

PARTICIPATING RETIRED RESEARCHERS Assist Prof Biserka Ross, PhD, permanent scientific advisor

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING In-house scientific projects (Chapter 16.1.)

1. Determination of body composition and chronic stress by the method of bioimpedance

The project was completed in July 2022. A total of 730 men and women participated in the study. The results indicated the role of the autonomic nervous system and cortisol in the control of body composition in young healthy men (10). In elderly nursing home residents, a high prevalence of osteosarcopenic obesity and also a high prevalence of malnutrition and the risk of malnutrition were found (104).

2. Effects of recreational headphone noise on hearing in young adults (RecNoise)

The project started in October 2022 with the plan to examine 100-150 younger adults in the first year of the survey. In 2022, 40 participants were recruited and examined. The aims of the project are: 1) to determine the habits of recreational use of headphones in young people aged 18 to 25 years; 2) to determine the sound levels in the headphones that the participants usually use; 3) to determine the hearing level using the audiometry method; 4) to determine the relation between the headphones usage are possible hearing damage. The project is carried out in cooperation with the Department of Electroacoustics, Faculty of Electrical Engineering and Computing, University of Zagreb.

3. Prevalence and predictors of occupational contact dermatitis in apprentice nurses/medical technicians (NurseSkin)

The project was implemented according to the work plan from November 2020 to December 2022 as a cross-sectional study. In 2022, further recruitment and examination of final-year apprentices were performed. Study protocol included for all participants data collection by questionnaire, clinical examination of the skin on hands/wrists, and measurement of the skin barrier function parameters (skin pH and TEWL-transepidermal water loss, epidermal hydration and temperature on the hands and forarms). In 2022, an additional 188 apprentices were recruited from two vocational schools in Zagreb, with response rate of 90.4%. The total number of participants is now 428 for the whole study period. Results related to data collected in 2020 and 2021 on 240 participants are published (2, 90), a student of graduate course in biology performed the obligatory practical work during this project, and presentations of study results were made to the teachers and apprentices from vocational schools involved in the project. Study results were presented at the meeting of European Academy for Dermatology and Venereology Task Force for Occupational Skin Diseases. The analysis of data collected during 2022 is in progress.

4. Sleep quality in different age groups in Croatia before and during COVID-19 pandemic (CoV-Sleep)

The project has started with the implementation in 2021. Coronavirus infection and epidemiological measures introduced to control it have shown a number of adverse effects on human health and functioning. Research conducted in various countries around the world has shown an increase in sleep problems and disorders during a pandemic in all age groups. Data for our country are not known, so the aim of this study is to examine differences in sleep quality before and during the COVID-19 pandemic in Croatia in the adult and elderly population. Data for adults have been collected as part of the ongoing ICOSS-2 international epidemiological study and will be analysed during the next year in coordination with other ICOSS activities. Data for the elderly were obtained by retrospective analysis of archival data collected in projects that began before and declared a pandemic. The results showed better total sleep quality and worse self-rated health in residents of nursing homes in 2021 (244). The coronavirus pandemic contributed to more pronounced turnover and change in the structure of residents of nursing homes.

Scientific collaborations

The role of the mother and the experience of parental competence of mothers with impaired mental health (MIMOZE) (PI: E. A. Delale, Institute for Anthropological Research)

The objectives of the project were to investigate the experience of the parental role of women with mental health problems and to examine the representation of their parental role in the hospital archives and existing medical documentation. The research will be conducted with a mixed quantitative and qualitative research approach, respecting the dignity and well-being of participants, respecting their human rights, with professional and scientific responsibility of researchers, according to the highest ethical standards of the Helsinki Declaration, the Ethical Code of the Croatian Psychological Chamber and the General Data Protection Regulation. This is an internal project of the Institute of Anthropology, which will be conducted in cooperation with the Clinic of Psychiatry St Ivan, without additional funding. During 2022, informed consents have been successfully obtained to enable the beginning of the analyses of medical documentation from hospital archives has started (qualitative part of the project). Plans for further data analyses, publishing and quantitative part of the study have been revised due to the small number of obtained consents.

RESEARCH PROJECT FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

1. Exposure to pyrethroid and organophosphate insecticides in children – risk assessment for adverse effects on neuropsychological development and hormonal status (PyrOPECh, HrZZ-IP)

International research projects (Chapter 16.2.A.)

- 1. Partnership for the Assessment of Risks from Chemicals (PARC, Horizon Europe)
- 2. Network on the Coordination and Harmonisation of European Occupational Cohorts (OMEGA-NET, COST)
- 3. Genomics of MusculoSkeletal traits Translational Network (GEMSTONE, COST)
- 4. Sleep disorders related to coronavirus infection and confinement during COVID-19 Pandemic (ICOSS-2, International collaboration without founding)
- 5. Promoting the autonomous implementation of the European framework agreement on occupational health and safety in the hairdressing sector (EC: DG Employment, Social Affairs and Inclusion)

PROFESSIONAL SERVICES

Professional activities of the Unit included the organisation and implementation of teaching modules for medical doctors, residents in occupational and sport medicine, and clinical pharmacology and toxicology. A training in clinical pharmacology and toxicology over one week was conducted for three residents, and one-month training in occupational and sports medicine for 11 residents. Dr Jelena Macan was appointed as the main supervisor by the Croatian Ministry of Health for 15 residents in occupational and sports medicine.

For teachers in vocational schools, lectures were delivered in the field of health and safety at work, and actual epidemiological investigations performed in this field within the Unit.

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

Ž. Babić

Member of the Committee for safe use of medicines of the Agency for Medicinal Products and Medical Devices of Croatia; member of the commission for drafting the additional conditions for pesticides intended for professional users for professional use and non-professional users at the Ministry of Agriculture; member of the commission for drafting the law on sustainable use of pesticides at the Ministry of Agriculture; substitute member of the Biocidal Products Committee of European Chemicals Agency (ECHA); member of the Editorial Board of the journal *Public Health Toxicology*.

A. Bjelajac

Chair of the Committee for evaluation of programs for propaedeutic in psychotherapy of the Association of Psychotherapy Societies of Croatia; chair of the Committee for awarding the City of Zagreb Scholarship based on socioeconomic status; member of the Committee for propaedeutic of the Croatian Chamber of Psychotherapists; member of the Ethical Committee of the Society of Gestalt and Integrative Psychotherapists of Croatia; member of the Supervisory Board of the Croatian Chamber of Psychotherapists; member of the journal *Archives of Industrial Hygiene and Toxicology*. *J. Kovačić*

Statistical editor and Executive Committee member of the journal *Archives of Industrial Hygiene and Toxicology*; external associate of the Agency for Medicinal Products and Medical Devices of Croatia. *J. Macan*

Full member of the Croatian Academy of Medical Sciences, Collegium of Public Health; member of the Croatian Society of Occupational Health Management Committee; member of the Croatian Society of Medical Court Expertise Management Committee; member of the European Initiative for Prevention of Occupational Skin Diseases at the European Academy for Dermatology and Venereology; member of the Committee for Medical Ecology, the Working Group for developing national positions in the field of protection from electromagnetic fields, and the Working Group for climate changes and health at the Ministry of Health, Republic of Croatia; permanent court expert witness in occupational medicine; member of the Croatian Association of Court Expert Witnesses and Valuers; assistant editor and Executive Committee member of the journal *Archives of Industrial Hygiene and Toxicology*. *R. Turk*

Member of the Biocidal Products Committee of the Ministry of Health and a substitute member of the Biocidal Products Committee of the European Chemicals Agency; member of the Committee for Safe Use of

Medicines of the Agency for Medicinal Products and Medical Devices of Croatia; member of the Working group for the revision of the National Action Plan for Sustainable Use of Pesticides; substitute member of the working group for the drafting of the proposal for an ordinance on the conditions of distribution and sale of pesticides.

V. M. Varnai

Member of the Committee for Risk Assessment (RAC) at the European Chemicals Agency (ECHA).

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

Scientific degree of senior scientific associate and scientific-teaching title of an Associate Professor was gained by *A. Bjelajac* at the Faculty of Metallurgy, University of Zagreb.



HEAD

Davorka Breljak, PhD, scientific advisor

RESEARCHERS

Marija Ljubojević, PhD, senior scientific associate Ivana Vrhovac Madunić, PhD, senior scientific associate since 1 Aug 2022 Dean Karaica, PhD, scientific associate since 9 Mar 2021

TECHNICAL STAFF

Ljiljana Babić, technician

PARTICIPATING RETIRED RESEARCHER

Ivan Sabolić, MD, PhD, permanent scientific advisor

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

Scientific collaborations

We continued the long-standing national and international scientific collaborations where the scientific papers and abstracts were published in *WoS*-indexed journals, researchers' mobility was achieved as well as new project proposals were applied.

As part of the cooperation with the Veterinary Medicine and Faculty of Pharmacy and Biochemistry at the University of Zagreb, one scientific paper was published describing the protein expression of ferritin as the key intracellular iron storage in the liver and kidneys as well as emphasizing the sex-related (males *vs.* females) and age-related (young *vs.* old animals) differences in a rat aging model (65).

We continued international collaboration with Prof Mladen V. Tzvetkov (Institute for Pharmacology, Center for Drug Absorption and Transport, University of Medicine, Greifswald, Germany), conducted research within the joint Croatian-German project, and planned new research activities of studying interaction of membrane transporters OCTs and oximes/antidots in the treatment of organophosphate poisoning (Chap. 16.2.A.4.). In the frame of this bilateral project Dr Marleen J. Meyer (Institute for Pharmacology, Center of Drug Absorption and Transport, University of Medicine, Greifswald, Germany) stayed at IMROH. During this study visit, she presented the preliminary results of pharmacokinetic analysis of various drugs carried out in the completed project AGEMETAR (IP-2013-11-1481, HrZZ), and one publication is planned.

Within the frame of international collaboration with the research group led by Prof T. Weide (University Hospital of Münster, Münster, Germany), one original scientific article was published (6), describing the impact of *Pals1* gene silencing on the expression of Solute carrier (SLC) membrane transporters as well as housekeeping proteins in the mouse kidney.

In the frame of international collaboration with the research group led by Prof I. Kalajzic (Department of Reconstructive Sciences, Center for Regenerative Medicine and Skeletal Development, Farmington, USA) (Chapt. 16.2.A.5.), results were presented at the *Annual Meeting of The American Society for Bone and Mineral Research* (ASBMR) 2022 and an abstract was published in the *WoS*-indexed journal (253). In addition, one scientific article was accepted for publication in a *WoS*-indexed journal (114).

Furthermore, we continued scientific collaboration with a research group led by Prof Bojana Žegura (NIB, National Institute of Biology, Department of Genetic Toxicology, Ljubljana, Slovenia) and research was carried

out at NIB in Ljubljana during January and February 2022 in an *in vitro* 3D cell model (spheroids) under static conditions. Within this collaboration, we also submitted a joint Croatian-Slovenian project for funding.

Cooperation with the University of Zagreb constituents, including the Faculty of Science, continued; teaching activities, student practices were carried out and two diploma theses were defended through joint efforts with the Faculty of Science (165, 170). Furthermore, student practices were carried out through joint efforts with the Faculty of Food Technology and Biotechnology of the University of Zagreb as well as the Department of Biotechnology, University of Rijeka. Finally, numerous activities were carried out in order to popularize science and continue the mobility and training of researchers.

Other research activities

In the frame of current and completed national research projects funded by the *Croatian Science Foundation*, results were published in *WoS*-indexed journals as well presented at national and international scientific meetings.

Within the installation research project (CellToxTargets, UIP-2017-05-7260, HrZZ), we continued studying the mechanisms of action of newly synthesized imidazolium oximes (they have numerous pharmacological properties) in prostate cancer cells (PC-3) *in vitro*. The results of this research were presented at the international scientific conference of the Croatian Society for Biochemistry and Molecular Biology, HDBMB22 "From Science to Knowledge", published in the Book of Abstracts (232), as well scientific paper with these results is in preparation.

In the frame of research project "Age-dependent expression of membrane transporters in rats" (AGEMETAR, IP-2013-11-1481, HrZZ), one scientific paper was published concerning the long-term effects of melatonin and resveratrol on oxidative parameters, sex hormones, and DNA integrity in the rat blood, emphasizing the sex-related (male *vs.* female) as well as age-related (young *vs.* old) differences in the rat aging model (8). Additional results of the same project (AGEMETAR, IP-2013-11-1481, HrZZ) were presented at the scientific meeting "HDIR-6 Targeting Cancer – The 6th Meeting of the Croatian Association for Cancer Research with International Participation" and was published in the Book of Abstracts (205).

In the frame of completed research project "Adverse effects of single and combined mycotoxins produced by *Aspergilli*" (MycotoxA, IP-09-2014-5982, HrZZ), one scientific paper was published describing the combined and individual effects of mycotoxins (ochratoxin A and/or citrinin) and resveratrol on the expression of membrane transporters for organic cations (Oct1/Slc22a1 and Oct2/Slc22a2) in rat kidneys (39). Additional results of the same project (MycotoxA, IP-09-2014-5982, HrZZ) were presented at the international meeting "Power of Fungi and Mycotoxins in the Midst of Climate Change (PoFMy)" and were published in a *WoS*-indexed journal (182).

RESEARCH PROJECT FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Molecular mechanisms underlying the toxicity of antidotes and potential drugs (CellToxTargets, HrZZ-UIP)
- 2. Oximes as potential inhibitors of glucose transfer in prostate cancer cells (HAZU Foundation)
- 3. Understanding the (eco)toxicological role of selected SLC and MATE transport proteins in zebrafish (*Danio rerio*) using functional genomics tools (DANIOTRANS, HrZZ-IP)

International research projects (Chapter 16.2.B.)

- 1. Pharmaceutical Open Innovation Test Bed for Enabling Nano-pharmaceutical Innovative Products (Phoenix, Obzor 2020)
- 2. Evidence Driven Indoor Air Quality Improvement (EDIAQI, Obzor Europa)
- 3. Correlated Multimodal Imaging (COMULIS, COST)
- 4. Modelling immunotherapy response and toxicity in cancer (IMMUNO-model, COST)
- 5. 3Rs concepts to improve the quality of biomedical science (IMPROVE, COST)
- 6. Personalized medicine in chronic kidney disease: improved outcome based on Big Data (PerMediK, COST)

- 7. Changes in the muscle cell viability under the influence of oxime analogues (Bilateral CRO-SI)
- 8. Identifying Interactions of Renal and Hepatic Organic Cation Transporters (OCTs) with Oximes, Antidotes in Treatment of Organophosphate Poisoning (Bilateral CRO-DE)
- 9. Generating new RGS5 mouse model for lineage tracing (University of Connecticut, Farmington, USA)

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

D. Karaica

Management Committee Member and member of Board for Inclusiveness Target Countries (ITC) grants for the COST Action CA17121 COMULIS; Management Committee member for the COST Action CA21135 IMMUNO-model.

I. Vrhovac Madunić

Member of the Executive Committee of the Croatian Society of Biochemistry and Molecular Biology (HDBMB); member of the Organizing Committee for organizing conference of the HDBMB; editor of the Book of Abstracts of the International conference by HDBMB "From Science to Knowledge"; Program Committee member of the workshop "Better skills for better jobs: Excellent lab book for an excellent career"; Management Committee member, coordinator of Board for Inclusiveness Target Countries (ITC) grants and Grant Awarding coordinator for the COST Action CA17121 COMULIS; Management Committee member for the COST Action CA21139; Management Committee member for the COST Action CA21165; Secondary proposer COST Action "Human metal exposure and health – in present and in the past".

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

Scientific degree of permanent scientific advisor was gained by *D. Breljak.* Scientific degree of scientific advisor was gained by *M. Ljubojević.* Scientific degree of senior scientific associate was gained by *D. Karaica.*



HEAD

Nevenka Kopjar, PhD, permanent scientific advisor

RESEARCHERS

Vilena Kašuba, PhD, permanent scientific advisor Prof Davor Želježić, PhD, ERT, permanent scientific advisor Mirta Milić, PhD, scientific advisor since 15 Dec 2022 Goran Gajski, PhD, senior scientific associate Marko Gerić, PhD, scientific associate Katarina Matković, PhD student-assistant

TECHNICAL STAFF

Maja Nikolić, senior technician

PARTICIPATING RETIRED RESEARCHER Prof Vera Garaj Vrhovac, PhD, permanent scientific advisor

SCIENTIFIC RESEARCH

Scientific collaborations and in-house projects founded by the Institute's resources (own funds and with institutional financing)

In vitro models

Antioxidative, genoprotective and anti-inflammatory effects of probiotics were investigated (44, 111, 290). The effects of strawberry tree honey on reducing levels of DNA damage caused by ultraviolet radiation were investigated on human peripheral blood lymphocytes (35). Research on harmful chemicals on different types of cells also continued. The internalization of silver nanoparticles was investigated on the PK-15 cell line (pig kidney) and their genotoxic effects were tested using the comet assay (102). On the HepG2 cell model, the genotoxic potential of procedures for the processing of raw leather was investigated, using vegetable, synthetic, and chrome tanning (16). Cytotoxic properties of compounds that could be used for contrast in computed tomography diagnostics were investigated (275). Genotoxic effects of dental implants were evaluated on gingival epithelial cells (75). Cyto/genotoxic effects and the level of oxidative stress were investigated on bisphenol A treated root meristem cells of *Allium cepa* L. (188).

Animal studies

During 2022, the results of research regarding the harmful effects of pesticides on various animal models were published. Toxic effects of α -cypermethrin were investigated in plasma/whole blood and liver, kidney, and brain tissues of Wistar rats, using markers of oxidative stress, cholinesterase activity (ChE), and levels of primary DNA damage. Oral administration of pesticides at daily doses of 2.186, 0.015, 0.157, and 0.786 mg/kg body weight for 28 days caused a significant increase in the level of reactive thiobarbituric acid species in the rat brain, accompanied by a significant increase in glutathione peroxidase (GPx) activity. This study showed that, even at very low doses, exposure to α -cypermethrin has genotoxic effects and triggers antioxidant cellular defense mechanisms (41). Another study (40) examined the genotoxic potential of low doses of chlorpyrifos (CPF) on blood and bone marrow cells in adult male Wistar rats using the *in vivo* micronucleus (MN) test and the alkaline comet assay. CPF was administered orally at daily doses of 0.010, 0.015, and 0.160

mg/kg body weight for 28 consecutive days. Significant differences were found in the number of reticulocytes per 1000 erythrocytes between all control groups and groups exposed to CPF in daily doses of 0.015 and 0.160 mg/kg body weight. CPF treatment did not significantly increase the levels of primary DNA damage in bone marrow cells compared to the negative control. However, the damage to the bone marrow cells of rats exposed to CPF was much greater than that reported in previous studies on rat leukocytes. The results of a study of the effects of low doses of the pesticide imidacloprid on the levels of primary damage in the blood and brain cells of male Wistar rats were also published (287). The difference in the sensitivity of these two types of cells to the same treatment has been proven, whereby the degree of DNA damage in nervous tissue points to the need for further clarification of the mechanisms of action of imidacloprid in mammals in order to better characterize the risk of its exposure.

Research on DNA damage and morphological changes caused by the herbicide norflurazon and ultraviolet B radiation was carried out on an experimental model of a symbiotic and free-living hydra (200).

Research on the harmful effects of mycotoxins continued, and it was determined that ochratoxin A promotes the accumulation of citrinin in rat kidney and liver cells (80).

Investigations of the effects of inhalation anesthetics isoflurane, sevoflurane and halothane alone or in combination with radiotherapy doses of ionizing radiation (1 Gy and 2 Gy) on various organs of the Swiss albino mouse confirmed the different potential of the tested compounds for synergistic effects on increasing the level of DNA damage. For example, the results of comet assay show that single anesthetics can cause DNA damage in kidney cells (5), but that combined exposure to anesthetics and radiation did not cause synergistic effects. Among the three anesthetics investigated, halothane had the greatest potential for DNA damage and the least protective effect on the kidneys after co-exposure to radiation. Possible protective effects were observed on brain cells of mice exposed to the same combinations of anesthetics and radiation, especially for isoflurane (267).

The results of research on the beneficial effects of melatonin and resveratrol – natural compounds with antioxidant properties – on aging processes in rats have been published (8). Sex- and age-related changes in the expression of metallothionein in kidney and liver cells under the influence of antioxidants, depending on the levels of essential and toxic elements, were also investigated (205).

Research on human populations (biomonitoring)

Research and meta-analysis of biomarkers for assessing the state and degree of chronic obstructive pulmonary disease and dementia using cognitive tests and by measuring the level of DNA damage using the comet assay were carried out. It was established that genomic instability represents the first neuropathological event in the preclinical phase of cognitive disorders and that the degree of DNA damage correlated well with the degree of dementia. Oxidative damage was only associated with temporal orientation category I. (disorientation) and these subjects had 12% higher levels of DNA damage than other subjects. The obtained results can be applied in the adjustment of rehabilitation procedures for patients with such findings (28).

Using a previously established database comprised of more than 19,000 individuals, we analysed publications that included terms DNA repair, the comet assay, and base excision repair (BER). The results showed that BER was significantly higher in the female population, but this influence was significant only in the subjects older than 61 years. Smoking did not affect BER, and a body mass index greater than 25 was associated with higher levels of BER. However, at a BMI greater than 35, BER activity suddenly decreased significantly. Increased BER activity correlated with a lower level of DNA damage, which also resulted in a lower level of damage measured by the Fpg comet assay (61).

The impact of a three-week low-calorie diet of 567 kcal in controlled hospital conditions on 22 patients with a body mass index (BMI) greater than 35 kg/m² on changes in anthropometric and biochemical parameters and on the levels of oxidative DNA damage (Fpg comet assay) and total levels of primary DNA damage (alkaline comet assay) in leukocytes. It was established that such a diet can reduce BMI by 3–4 units, significantly reduce body weight, on average of 9 kg (4.8–14.4 kg), that the loss in percentage of excess body weight can be 10-35%, and that the diet can significantly reduce the level of glucose, insulin, urea, cholesterol, especially LDL, and significantly contribute to genome stability (62).
Using an online survey, we examined to what extent the Croatian population adheres to the Mediterranean diet. The investigated population moderately practiced the Mediterranean diet. Greater attention in promoting the healthy aspects of this diet should be directed towards men, people living in the continental part of Croatia, adolescents and young adults, as well as towards people with incomes below the national median (22). At the international conference, the results of the research on the levels of DNA damage and oxidation and inflammatory status in vegetarians compared to omnivores were presented (278).

Research on biological risks and monitoring of exposure to chemical and physical agents was also carried out (152). Cytogenetic indicators of exposure to low doses of ionising radiation in medical personnel were studied (24). An overview of cytogenetic methods that can be used to assess the harmful effects of exposure at workplaces was given (143).

Other investigations

Part of the findings published during 2022 was focused on studying the toxicity of secondary metabolites of marine organisms. The toxicological profile of secondary metabolites of three species of *Pseudo-nitzschia* diatoms sampled at different locations in the northern Adriatic was investigated and their effects on human leukocytes under *in vitro* conditions were studied (84). The effect of domoic acid, a known toxin from marine organisms, was investigated on the HepG2 cell model (50). The effects of anisaxins, antimicrobial peptides from marine parasites, on bacterial growth were also investigated (81).

A review article focused on the new approaches and insights into modern toxicological methods was also published (93). Research continued on application of biomarkers in the detection of various diseases, exposure to toxins, and assessment of DNA damage and repair. A literature review and analysis of experimental and epidemiological data *in vitro* and *in vivo* showed which micro RNAs (miRNAs) as specific stable and sensitive biomarkers of chemical exposure change their expression during exposure to most fungicides (miR-363 and miR-9), herbicides (let-7, miR-30, miR-126, miR-181 and miR-320) and insecticides (let-7, miR-155, miR-181 and miR-21), which are currently in use. Common changes in miRNA could be used as biomarkers of exposure to pesticides and their effects on biological and genetic material.

At the international scientific meeting, the results of research on the harmful effects of heavy metals were presented (279).

In the field of regulatory toxicology, a paper was published on the safety and efficacy of a feed additive consisting of endo-1,4- β -xylanase produced by the yeast species *Komagataella phaffii* DSM 33574 (Xylamax) (3).

In-house scientific projects

1. Investigation of toxic effects of new psychoactive substances by biochemical and molecular-biological methods

The levels of oxidative stress and the cytotoxic and genotoxic effects of ketamine were evaluated on cell model SH-SY5Y (human neuroblastoma cell line) (270, 313), codeine and morphine (306) and synthetic opioids (252). The harmful effects of ketamine were further investigated on HepG2 cells (286). The obtained results indicate an imbalance of the oxidation-antioxidation events in the cells, and the induction of cyto/genotoxic effects caused by the investigated new psychoactive substances.

2. Investigation of interactions between irinotecan and tetrahydocannabinols on laboratory rodents using integrated biochemical, molecular biology, pathohystologic and analytical methods

The final processing of the data collected within the project resulted in the publication of a congress report (314). Data referred to the levels of biochemical markers in male BALB/C mice with colorectal tumors induced by initiation of the CT26 cell line. Mice were exposed to Δ 9-tetrahydrocannabinol (THC) *per os* (7 mg/kg i.e.m.; for 7 days) and cytotoxic drug irinotecan (IRI, 60 mg/kg i.e.m.; i.p., day 1 and 5 experiments). Interactions between TCH and IRI were observed, which changed the levels of measured biomarkers

compared to the single compound's exposure, resulting in increased toxicity. Comprehensive analyses of data on Δ^9 -tetrahydrocannabinol and irinotecan, based on various experimental models and the results of own experiments, resulted with an overview of evidence about their possible interactions and the harmful effects that result from them (271).

RESEARCH PROJECT FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Air pollution and human biomarkers of effect (HUMNap, HrZZ-IP)
- 2. Evaluation of cytogenetic effects of air pollutants towards human cells in vitro (HAZU Foundation)

International research projects (Chapter 16.2.A.)

- 1. Evidence Driven Indoor Air Quality Improvement (EDIAQI, Horizon Europe)
- 2. European Venom Network (EUVEN, COST)
- 3. Acetylcholinesterase Inhibitors as Potential Anti-Alzheimer Drugs: Prooxidative and Cytogenotoxic Properties (SafeAChE, Bilateral CRO-RS)
- 4. Toxicological profile and interactions of bisphenol A and its analogues (BPAnalogInteract, Bilateral CRO-SI)
- 5. Distribution of antibiotic resistance genes in waste water treatment plants and receiving environments of China and Croatia (Bilateral CRO-CN)

Educational and science popularization projects (Chapter 16.2.B.)

1. Toxicology Innovative Learning for Europe (ToxLearn4EU, Erasmus+)

PROFESSIONAL SERVICES

The Unit provides five expert services: chromosomal aberration analysis, micronucleus assay, sister chromatid exchange (SCE) analysis, comet assay, and cell viability assay. Professional activities include cooperation with occupational health practitioners, polyclinics that carry out previous and/or periodic health examinations of employees occupationally exposed to physical mutagens (ionising and non-ionising radiation) and/or chemical mutagens (cytotoxic drugs and other genotoxic agents) and other institutions that need our services.

As part of the professional services in 2022, one analysis of chromosomal aberrations was performed for the ZVD d. o. o. (Ljubljana, Slovenia). Furthermore, in cooperation with the Teaching Institute for Public Health of Brod-Posavina County (Health Ecology Department), biomonitoring study on 22 subjects using comet- and micronucleus assays was carried out.

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

G. Gajski

Chair of International Comet Assay Working Group (ICAWG) within European Environmental Mutagenesis & Genomics Society (EEMGS); Supervisory board member of Croatian Society for Cancer Research (HDIR); member of Editorial board of magazine Medicine; member of a Working group for "Biotechnology" of the Board for applied genomics at The Croatian Academy of Sciences and Arts (HAZU); member of Working groups: Working Group on Communications (WGC), Working Group on Sustainability (WGS)) of International Society of Radiation Epidemiology and Dosimetry (ISORED).

M. Gerić

Chair of the New Investigators group within European Environmental Mutagenesis and Genomic Society (EEMGS); Work group member (Awards) at the International Society of Radiation Epidemiology and Dosimetry (ISORED); Scientific committee member ICAW/EEMGS 2022; Council member International Association of Environmental Mutagenesis and Genomics Societies (IAEMGS); Supervisory board member Croatian Radiation Protection Association.

N. Kopjar

Member of the Presidency of the Croatian Toxicological Society; member of the Governing Board of the Institute for Anthropological Research.

M. Milić

Member of the Advisory Board of journal *Helyion*; member of the Editorial Board of the journal *Mutation Research – Genetic Toxicology and Environmental Mutagenesis*; member of the Editorial and Advisory Board of journal *Toxics*; member of the Editorial Board of journal *Frontiers in Public Health* (associate editor for Radiation and Health Section); member of the Presidency of the Croatian Toxicological Society. *D. Želiežić*

Member of the Editorial Board of the journal *BioMed Research International*; President of the Croatian branch of the Register of European Toxicologists EUROTOX; expert on biological methods of testing substances in the Member State Committee; member of the Risk Assessment Committee – European Chemicals Agency (ECHA); expert in Toxicology and Clinical Research of the Food Committee of the Food Unit – European Food Safety Authority (EFSA).

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

Scientific degree of scientific advisor was gained by *M. Milić*. Scientific degree of senior scientific associate was gained by *M. Gerić*.



EMPLOYEES OF THE UNIT

HEAD

Assist Prof Irena Brčić Karačonji, PhD, ERT, scientific advisor since 15 Dec 2022, head since 1 Feb 2022, Deputy Director

RESEARCHERS

Prof Ana Lucić Vrdoljak, PhD, permanent scientific advisor (Director) Ivana Novak Jovanović, PhD, scientific advisor since 1 Jun 2022 Dubravka Rašić, PhD, senior scientific associate Blanka Tariba Lovaković, PhD, senior scientific associate since 1 Aug 2022 (in Unit since 1 Feb 2022) Suzana Žunec, PhD, senior scientific associate Anja Katić, PhD, scientific associate (in Unit since 1 Feb 2022) Andreja Jurič, PhD, postdoctoral researcher since 7 Feb 2022 (in Unit since 1 Feb 2022)

TECHNICAL STAFF

Jasna Mileković, senior technician Lea Stančin, technician

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

In-house scientific projects (Chapter 16.1.A.3.)

1. Investigation of toxic effects of new psychoactive substances by biochemical and molecular-biological methods

The effects of exposure to clinically relevant levels of ketamine, morphine and codeine on the occurrence of oxidative and DNA damage were examined on human neuroblastoma (SH-SY5Y) and hepatocellular carcinoma (HepG2) cell lines (252, 270, 286, 306, 313).

2. Assessment of the effects of prenatal exposure to α -cypermethrin on epigenetic programming and endocrine disruption of reproduction and development in experimental rats

Epigenetic, histopathological and stereological, and immunohistochemical analyses were performed on maternal and offspring samples of Wistar rats at the School of Medicine of the University of Zagreb and at the Faculty of Veterinary Medicine of the University of Zagreb. Hormone levels in the serum of female and male offspring were assessed by the immunochemical method ELISA (242, 288, 294).

3. Bioactive potential, metal and nicotine content in edible boletes regarding the toxic metal burden of soil

The development of the method for quantification of mass concentration of nicotine in edible boletes is in progress. Concentration of nicotine will be determined by solid phase microextraction (HS-SPME) followed by gas chromatography-mass spectrometry (GC/MS).

4. A relationship of resveratrol administration in cardiac surgery patients with reduction of oxidative stress and systemic inflammatory response

In corroboration with the Department of Cardiac and Transplant Surgery, at the Clinical Hospital Dubrava, blood samples of 34 patients undergoing heart valve surgery were collected. Parameters of oxidative stress were measured in plasma samples of patients receiving placebo or resveratrol. Plasma samples were collected before, during, and after the surgical procedure. Results of analysis were calculated. A review article was published (72).

Other research activities

We continued to investigate the cyto-/genoprotective and antioxidative properties of strawberry tree (*Arbutus unedo* L.) honey on effects induced by UVB radiation in human peripheral blood lymphocytes *in vitro* (35). We investigated the cytotoxic and pro-oxidative effects of strawberry tree honey, its phenolic extract and the main bioactive compound homogentisic acid (HGA) on three human cell lines: tongue squamous cell carcinoma (CAL 27), hepatocellular carcinoma (HepG2), and epithelial colorectal adenocarcinoma cells (Caco-2) cells (36).

In collaboration with the Faculty of Chemistry of the University of Belgrade, the phenolic profile of the strawberry tree leaves and fruits was determined (7), as well as potential of arbutin and its derivatives to inhibit tyrosinase activity *in silico* (273).

In collaboration with the Faculty of Food Technology and Biotechnology of the University of Zagreb, the concentrations of arbutin and hydroquinone were detemined in leaf extracts of bearberry (*Arctostaphylos uva-ursi*), a traditional plant used for therapeutic purposes in the treatment of acute urinary infections, and its antiseptic properties can be attributed to the hydroquinone that is formed by arbutin hydrolysis. The aim of this study was to determine the toxicological profile of hydroquinone on bladder cells (T24) (27, 194).

The application of 3D-printing in the production of functional products based on the strawberry tree fruits and its nutritional and biological potential were investigated in collaboration with the Faculty of Food Technology and Biotechnology of the University of Zagreb (4, 185, 266).

We evaluated the antioxidant activity of flavonoids against electrochemically generated superoxide radical anion using cyclic voltammetry (32).

Resuts of common treatment with ochratoxin A and citrinin on kidneys and liver of rats and accumulation of citrinin in both organs were published (80).

In corroboration with the Molecular Toxicology Unit, ageing effect, and effects of treatment with melathonine and resveratrol on oxidative stress parameters and expression of metallothionein in Wistar rats were published (8, 205). Results of ochratoxin A and citrinin treatment on organic cation transporters in kidneys of adult Wistar rats were also published (39).

We have continued our research on the toxicity of the pyrethroid insecticide α -cypermethrin on male Wistar rats. Evaluations were performed using markers of oxidative stress, cholinesterase activities, and levels of primary DNA damage in plasma/whole blood and liver, kidney, and brain tissue (41). The results of the investigation of the genotoxic potential of low doses of chlorpyrifos on blood and bone marrow cells in adult male Wistar rats after 28-day exposure have been published (40).

In collaboration with the Unit for Biochemistry and Organic Analytical Chemistry, we conducted research on the structure and activity relationship of *N*-alkyl quaternary quinuclidines on cholinesterase activity and selected human cell lines (229, 235).

The concentrations of 7 polybrominated diphenyl ether congeners (PBDEs), 11 polycyclic aromatic hydrocarbons (PAHs) (15) and 18 trace elements (91, 289) were measured in dust samples obtained from 10 kindergartens, 11 workplaces and 25 cars from the city of Zagreb. Based on dust analysis data, possible internal sources of PBDEs/PAHs/elements and human health risks associated with the intake of PBDEs/PAHs/elements were assessed.

In collaboration with colleagues from the Faculty of Pharmacy, University of Belgrade, we evaluated the potential role of toxic elements (As, Cd, Cr, Hg, Ni and Pb) in the development of prostate cancer based on

the results of two cohorts of subjects from Croatia and Serbia (71). The possible effect of blood As, Cd, Pb, and Hg on serum PSA levels due to environmental exposure to these elements was also evaluated (220).

As part of the collaboration with the Mutagenesis Unit (HUMNap project, IP-2020-02-1192), the association of exposure to benzene, toluene, ethylbenzene, and xylene isomers with primary DNA damage in peripheral blood cells was examined (209, 296, 297).

In cooperation with the Faculty of Medicine of the University of Rijeka, we investigated the combined biocidal effect of ozone and citric acid on *Acinetobacter baumannii* biofilm formed on ceramic tiles and polystyrene (70) and the combined inhibitory effect of fir (*Abies alba* Mill.) honeydew honey and *Lactiplantibacillus plantarum* on the growth of salmonella (53).

RESEARCH PROJECT FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

- 1. Development of Bioactive Molecules for Neurodegenerative Diseases Treatment (BioMol4ND, HrZZ-IP)
- 2. Assessment of daily exposure to metals and maternal individual susceptibility as factors of developmental origins of health and disease (METALORIGINS, HrZZ-IP)
- 3. Analysis of Butyrylcholinesterase Interactions with Novel Inhibitors and Reactivators (AnalyseBChE, HrZZ-IP)
- 4. Exposure to Pyrethroid and Organophosphate Insecticides in Children–Risk Assessment for Adverse Effects on Neuropsychological Development and Hormonal Status (PyrOPECh, HrZZ-IP)
- 5. Development, validation and application of analytical methods for PBDE determination (DeValApp, HrZZ-UIP)
- 6. Application of Nanobiotechnology for Nutritional Supplementation with Selenium (NutriNTENSe, HrZZ-IP)
- 7. Exploring the antioxidative potential of benzazole scaffold in the design of novel antitumor agents (AntioxPot, HrZZ-IP)

International research projects (Chapter 16.2.A.)

1. Development of functional beverage in sustainable packaging (JamINNO+, EFRR)

Educational projects and science popularization (Chapter 16.2.B.)

1. Meet toxicity – live safely (MeeTox, Erasmus+)

PROFESSIONAL SERVICES

Drugs of abuse from the amphetamine and opiate groups, methadone, and cocaine were determined in 16 hair samples (27 analyses in total). THC-COOH (1 sample) and buprenorphine (1 sample) were analysed in urine. A total of 53 queries were received regarding the analysis of drugs of abuse via the e-mail address infodroge@imi.hr.

ORGANISER	TEST	AREA	DATE
Society of Hair Testing, Strasbourg, France	Proficiency Test 2022	Analysis of drugs of abuse in hair	6/2022 and 12/2022 (two times per year, on three hair samples)

Participation in intercomparison programmes

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

A. Lucić Vrdoljak

Member of the Working Group in charge of monitoring the activity plan for the National Network for Permanent Air Quality Monitoring of the Meteorological and Hydrological Service at the Ministry of Economy and Sustainable Development of the Republic of Croatia.

I. Brčić Karačonji

Member of the Presidency of the Croatian Society of Toxicology; member of the Working Group on the Early Warning System on New Psychoactive Substances in the Republic of Croatia at the Croatian Institute for Public Health; member of the Strategic Board for Research Infrastructure at the Ministry of Science and Education of the Republic of Croatia; Croatian delegate of the European Research Infrastructure Consortium (ERIC) Committee.

A. Jurič

Member of the Working Group on the Early Warning System on New Psychoactive Substances in the Republic of Croatia at the Croatian Institute for Public Health.

D. Rašić

Member of the Presidency and secretary of the Croatian Society of Toxicology; member of Scientific and Organizning Committee and secretary of the symposium "Power of Fungi and Mycotoxins in the Midst of Climate Change".

S. Žunec

Member of the Court of Honour of the Croatian Society of Toxicology.

SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

Scientific degree of scientific advisor were gained by *I. Brčić Karačonji* and *I. Novak Jovanović.* Scientific degree of senior scientific associate was gained by *B. Tariba Lovaković.* Scientific degree of scientific associate was gained by *A. Jurič.*



EMPLOYEES OF THE UNIT

HEAD

Assoc Prof Branko Petrinec, PhD, senior scientific associate

RESEARCHERS

Assist Prof Dinko Babić, PhD, permanent scientific advisor Tomislav Bituh, PhD, senior scientific associate since 19 May 2022 Gina Branica Jurković, PhD, senior scientific associate until 31 Dec 2022 Davor Rašeta, PhD, postdoctoral researcher Božena Skoko, PhD, postdoctoral researcher until 24 Jun 2022 Iva Franulović, MSc, senior professional associate in science Milica Kovačić, MSc, senior professional associate in science since 25 Oct 2022 Tea Čvorišćec, MSc, professional associate in science 1 Jun 2022

TECHNICAL STAFF

Mak Avdić, MSc, senior technician Jasminka Senčar, senior technician Ljerka Petroci, technician

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

Radiation protection unit is continuously researching radioactive contamination of the environment with natural and fission radionuclides.

We continued to analyse the data acquired during the internal project "Kopački rit". We have found that Kopački Rit Nature Park is an area of very low Cs-137 concentration, meaning that the moss growing in the Park and around it is suitable for detecting even small additional Cs-137 concentration in the air, which is of great importance at the location considered representative of the middle of Danube River basin, close to the agricultural land, to a major city, and to a nuclear power plant (66).

We also analysed the radiological impact of a NORM activity – a stone quarry – in the Papuk Nature Park on the environment (67).

The influence of the gas field Molve on the metal(oid)s (including uranium and thorium) in the soil was also analysed (47).

The sediments in lakes on the island Pag were characterized and analysed, as a historical overview of deposition of radioactive and non-radioactive elements (31).

We continued long-term analysis of metals and radionuclides in brown bears in Croatia and Poland (116).

Radiochemical and measurement methods for monitoring radioactivity in various media are still being developed. Through monitoring, new knowledge in the field of radiation science and radiation protection, as well as in metrology and sampling, procedures, were standardized and methods coordinated through the implementation of quality assurance procedures. Appropriate radiation protection measures are being developed in the event of a nuclear/radiological accident, with an emphasis on the role of mobile radiological measurement laboratories in order to achieve better and faster response to such situations by collecting data timely.

Special attention in the Unit was paid to quality control. Accreditation in accordance with the international General Requirements for the Competence of Testing and Calibration Laboratories (HRN EN ISO/IEC 17025 standard) has become a widely accepted method of quality management and objective evidence of technical

competence, knowledge, and skills of testing and calibration laboratories. This year's audit was performed by the Croatian Accreditation Agency on November 7, 2022. Radiation protection Unit did not have any nonconformities.

In-house scientific projects (Chapter 16.1.A.3.)

Development and implementation of hybrid gamma-ray spectrometry methods for enhancing the capacity of environmental radiological monitoring around nuclear power plants (RAINSTORM)

RESEARCH PROJECT FUNDED BY EXTERNAL SOURCES

National research projects (Chapter 16.1.)

Sediments between source and sink during a Late Quaternary eustatic cycle: The Krka and the Mid Adriatic Deep System (QMAD, HrZZ-IP)

International research projects (Chapter 16.2.B.)

Improving Environmental Monitoring and Assessment for Radiation Protection in the Region (IAEA)

List of international intercomparisons

ORGANISER	TEST	AREA	DATE
IAEA	IAEA-TERC-2022-01/02 Proficiency test on determination of anthropogenic and natural radionuclides in water, soil (gamma-ray spectrum analysis exercise) and simulated swipe samples	Determination of radioactivity in water, soil (spectrum analysis) and swipe samples	6/2022 – 11/2022
IAEA	IAEA-RML-2022-01 Proficiency Test for Tritium, Strontium and Gamma emitters in Seawater	Determination of radioactivity in sea water	5/2022 on-going
IAEA	IAEA RER9155 Interlaboratory comparison on natural radionuclides in phosphate ore and phosphogypsum	Determination of radioactivity in phosphate ore and phosphogypsum	7/2022 on-going

List of accredited methods (3)

TEST METHOD	TYPE OF TEST, RANGE
RU-602-5.4-1 (In-house method)	Determination of radionuclides by high-resolution gamma-ray spectrometry in the energy range 40–2000 keV
RU-602-5.4-4 (In-house method)	Determination of Sr-90 activity concentration
RU-602-5.4-5 (In-house method)	Determination of Ra-226 activity concentration

The Unit's quality manager: *T. Bituh*.

PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

T. Bituh

Partner (Deputy Representative of the Republic of Croatia) on the IAEA project RER7014 Improving environmental monitoring and assessment for radiation protection in the region; member of the Management Board of the Croatian Radiation Protection Association; member of the Editorial Board of the Journal Archives of Industrial Hygiene and Toxicology.

D. Babić

Member of the Radon action plan 2019–2024 committee (Ministry of the Interior of the Republic of Croatia, The Civil Protection Directorate, Zagreb).

I. Franulović

Member of the Management Board and treasurer of the Croatian Radiation Protection Association. *B. Petrinec*

Member of the Education, Science and Culture Committee of the Croatian Parliament; Vice-president and member of the Management Board of the Croatian Radiation Protection Association; member of the TO-45 (Nuclear instrumentation) of the Croatian Standards Institute; member of the Editorial Board of the journal *Vatrogastvo i upravljanje požarima;* quality manager of the Firefighters Community of the Town of Ivanić-Grad; Senior firefighting officer 1st class; firefighter with special authorizations and responsibilities; member of the Croatian Nuclear Society; member of the Editorial Board of the Journal Archives of Industrial Hygiene and Toxicology; Deputy Member of the working group Smart Croatia.

D. Rašeta

Member of the Croatian Nuclear Society; member of the IAEA Nuclear Safety Standards Committee IAEA NUSSC.

15.10. Independent researchers



Aleksandra Fučić, PhD permanent scientific advisor until 6 Jun 2022

SCIENTIFIC RESEARCH

RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES International projects (Chapter 16.2.)

- 1. Scientific Centre of Excellence for Reproductive and Regenerative Medicine: Reproductive and Regenerative Medicine Exploring New Platforms and Potentials (CERRM, ERDF)
- 2. Relationship of the respiratory microflora composition with the human genome activity and integrity in the residents of coal industrial region (Kemerovo State University, Russia)



Jasmina Sabolović, PhD scientific advisor

RESEARCHER

Jelena Pejić, MSc, PhD student-assistant

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

Scientific collaborations

During 2022, the quantum-chemical investigations of physiologically important bis(amino acidato)copper(II) coordination compounds in aqueous media continued. In general, experimental studies of the bis(amino acidato)copper(II) compounds do not provide reliable results about their complete structures in solutions, while the structural properties can be reliably predicted by molecular modeling methods. By applying the density functional theory and the B3LYP functional, the lower-energy conformers of bis(L-glutaminato)copper(II) and (L-histidinato)(L-glutaminato)copper(II) were predicted in implicitly modelled aqueous solution. For those conformers, the effect of additionally accounted dispersion correction on the relative stability of the conformers was investigated. Reliability of predicted lower-energy conformers was examined by benchmarking the relative electronic energies as well as Gibbs free energies at 298.15 K against the corresponding values obtained by the DPLNO-CCSD(T) method. The binding affinities of different conformations of Gln⁻ and His⁻ with Cu²⁺ in (L-histidinato)(L-glutaminato)copper(II) for six coordination modes (i.e., six possible combinations of glutamine and histidine donor atoms) were predicted, and the most stable coordination modes and conformations in aqueous solution were determined. For predicted conformers with low Gibbs free energies, magnetic parameters were calculated, and the influence of apical Cu(II) bonding on

the parameters' values was investigated as well. The reliability of predicted lower-energy aqueous conformers was tested by comparing the calculated magnetic parameters with experimental electron paramagnetic resonance parameters measured in solutions and available in the literature (322).

Doctoral student J. Pejić, employed on the project for career development of young researchers – training of new doctors of science, DOK-2015-10-4185 (funded by the Croatian Science Foundation) was on maternity leave during 2022 with her work on the dissertation put on hold.



Ante Miličević, PhD permanent scientific advisor since 1 Jun 2022

SCIENTIFIC RESEARCH

RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

Scientific collaborations

In cooperation with the Biochemistry and Organic Analytical Chemistry Unit, two papers on cholinesterase activity were published, in which simple models were developed based on simple structural parameters (topological and constitutional descriptors) to predict enzyme inhibition constants, K_i . In one paper we presented a model made on 75 potential acetylcholinesterase inhibitors (55), while in the other we made a model for butyrylcholinesterase inhibition on 289 compounds (56). All the inhibition constants were taken from the literature, and all the models proved the importance of the descriptors from the class of connectivity indices (${}^n\chi^{\nu}$). The more branched and larger the molecule is, the more it is generally a better inhibitor of cholinesterases.

In-house scientific projects (Chapter 16.1.A.3.)

1. Investigation of electrochemical properties and antioxidant activity of polyphenolic compounds and their complexes with essential elements (project ended in 2021)

Two original papers were published. In the first paper, beside the model for the estimation of oxidation potentials based on the difference of atom charges between cation and the neutral form of a flavonoid, we developed the models based on the difference of atom charges between a radical and an anion, and a radical and neutral form of a flavonoid, and, also, a model based on the mean values of these three parameters was introduced (54). The parameters were derived from three possible mechanisms of flavonoid oxidation: single electron transfer-proton transfer (SET-PT), sequential proton loss electron transfer (SPLET), and hydrogen atom transfer (HAT). As the model based on the mean values yielded significantly better result than any of the models using separate parameters it could be concluded that all three mechanisms are equally important, i.e. electrochemical oxidation of the flavonoids takes place via all three mechanisms. In the second paper we measured, electrochemically, the antioxidant activities of 17 flavonoids toward superoxide anion radical, O_2^{\bullet} , and explained their relation to the first oxidation potentials (32). Six out of 17 flavonoids we did not electrochemically analyzed before, so, for this purpose we also measured their oxidation potentials.

16. PROJECTS



16.1. NATIONAL PROJECTS

16.1.A. RESEARCH PROJECTS LED BY IMROH RESEARCHERS

16.1.A.1. CROATIAN SCIENCE FOUNDATION PROJECTS



Research projects (5 projects)

LEADER (IMROH)	PROJECT	DURATION
Anita Bosak	Development of bioactive molecules for neurodegenerative diseases treatment (BioMOl4ND, IP-2020-02-9343)	2021–2024
	×	

IMROH ASSOCIATES: S. Žunec, A. Matošević, A. Zandona, M. Bartolić, Z. Kovarik EXTERNAL ASSOCIATES: D. Opsenica, K. Komatović, S. Šegan (Institute of Chemistry, Technology and Metallurgy, University of Belgrade, Serbia)

Research continued according to the work plan of the project. It has been shown that newly synthesized biscarbamates are a promising structural basis for the design of new drugs intended for use in the middle and late stages of Alzheimer's disease. Two compounds have been identified as possible multi-target drugs in the treatment of Alzheimer's disease that strongly and preferentially inhibit BChE, are non-toxic with the potential to pass through the BBB, and have the ability to chelate biometals (52, 210, 298, 299). Twenty-two 4-aminoquinoline derivatives with structurally different side chains as links between the 4-aminoguinoline and adamantyl parts of the structure were synthesized. The tested compounds proved to be very strong inhibitors of both cholinesterases with inhibition constants in the low micro to nanomolar range that could pass the blood-brain barrier by passive transport and generally moderate antioxidant activity. Two compounds were highlighted for further evaluation as possible drugs for the treatment of Alzheimer's disease (43, 199). A series of hydrazone derivatives was synthesized as a pilot study of the possibility of using compounds with such a structural basis as possible multi-targeted drugs that preferentially act as cholinesterase inhibitors (184), and whose additional targets are BACE 1 inhibition and chelation of biometals that accumulate in the brain as part of complex pathophysiology Alzheimer's disease (264). Also, a pilot study of the use of 4-aminoquinolines as multi-targeted drugs, one of the targets of which is BACE1 inhibition, was conducted (265). The inhibitory activity of a series of chloroquine derivatives against human cholinesterases was tested. Members of the project team held four public lectures where the results of the research so far were presented; two invited lectures at international meetings (186, 268) and one lecture for the scientific public at a domestic scientific meeting (211) and one at an international advanced course (299).

LEADER (IMROH)	PROJECT	DURATION
Goran Gajski	Air pollution and human biomarkers of effect (HUMNap, IP-2020-02-1192)	2021–2025

IMROH ASSOCIATES: M. Gerić, M. Milić, V. Kašuba, K. Matković, G. Pehnec, S. Davila, I. Jakovljević EXTERNAL ASSOCIATES: A. Cvitković, M. Sanković, A. Šumanovac, A-M. Domijan, I. Guseva Canu, P. Wild, N. Hopf

Clean air is crucial to our health and the environment. Rising industrial and energy productions, the burning of fossil fuels and biomass, as well as the rise in road traffic contribute to air pollution in our cities. Hence, air pollution leads to serious health and environmental problems. Urban air is a complex and variable mixture of many different chemicals whose exact mechanisms of action is not known, although oxidative stress and inflammation are suspected. Human biomonitoring is an essential tool for assessing whether and to what extent environmental substances affect the human population and as such can provide valuable data on environmental exposure and to help identify potential health risks. Therefore, HUMNap will determine possible associations between the air

pollutants and biomarkers of exposure and early biological effect. The project will start with investigations at multiple locations with different air pollution levels and origin followed by measurement of various environmental airborne pollutants. The next step will be a detailed assessment of different biomarkers of exposure and early biological effects (genomic instability and oxidative stress) in human populations living in those locations. HUMNap will promote stateof-art techniques and research approaches to develop risk assessments of human exposure to airborne pollutants. The results from HUMNap will demonstrate how airborne pollutants affect early molecular events important for disease development in different human cells. It will also provide an assessment of cancer risk among human populations affected by polluted urban areas. Moreover, HUMNap aims to draw the attention of many stakeholders such as leading scientists, policy makers, industry, and the public in order to raise awareness regarding air pollution and to develop monitoring regimes. Finally, HUMNap will provide new datasets necessary for scientifically based risk assessments of human populations exposed to urban air pollution. The project activities carried out during 2022 resulted in the publication of one scientific paper (19) and three presentations at scientific meetings (209, 296, 297).

LEADER (IMROH)	PROJECT	DURATION
Jasna Jurasović	Assessment of Daily Exposure to Metals and Maternal Individual Susceptibility as Factors of Developmental Origins of Health and Disease (METALORIGINS, IP-2016-06-1998)	2017–2022

IMROH ASSOCIATES: M. Piasek (leader until 31 Dec 2020), T. Orct, A. Pizent, M. Lazarus, I. Brčić Karačonji, N. Brajenović, A. Katić, B. Tariba Lovaković, A. Sekovanić, A. Sulimanec Grgec, Z. Kljaković-Gašpić, J. Kovačić EXTERNAL ASSOCIATES: D. Pašalić (School of Medicine, University of Zagreb), S. Stasenko (Merkur University Hospital, Zagreb), K. Branović Čakanić (Croatian Veterinary Institute, Zagreb), L. Škrgatić, I. Miškulin (University Hospital Centre, Zagreb)

By the analysis of the degree of methylation of the *MT2A* gene, we completed all of the planned research activities on the project involving health risk assessment after birth to adulthood due to prenatal exposure to the main toxic metals (Cd, Pb, Hg), maternal intake of essential elements (Fe, Zn, Cu, Se, Ca), and gene polymorphisms *MT2A* together with possible metal-induced disruptions of steroid hormones (progesterone and estradiol) in the fetoplacental unit caused by epigenetic mechanisms and oxidative stress.

We evaluated the associations of maternal cigarette smoking with Cd and Pb levels and the expression of candidate miRNA (miR-1537, miR-190b, miR-16, miR-21 i miR-146a) in the placenta and maternal and umbilical cord blood/serum as well as biochemical parameters in maternal urine. Preliminary results have been presented at the congress of the Croatian Society of Medical Biochemistry and Laboratory Medicine (177) and the final data integrated in an original scientific article (82). A manuscript was prepared on the effects of exposure to toxic metals through cigarette smoking on essential elements and stereoidogenesis in mother-child pairs assessed after term vaginal delivery of healthy women.

The results of related research on the assessment of the environmental exposure of metals and their health effects have been published in research papers and presented at a scientific conference. Exposure to Hg, intake of Se and omega-3 fatty acids by consumption of fish from the Adriatic and/or available on the HR market was assessed, focusing on the well-being and health risks for women of reproductive age (120). Metal(loid)s in the aquatic environment (water, sediment, and fish) of the upper and middle reaches of the Raša River were analyzed in order to assess the impact on the karst water system under the long-term anthropogenic impact of the Raša coal mine (110) and their biological availability using the European eel as a biological indicator of the environmental pollution (109). The results of research and experience gained during the implementation of the project, mainly related to the biomonitoring of metals in humans and the environment and the intake of toxic and essential elements through a diet that includes marine fish, were presented by poster and oral presentations at the national scientific-professional symposium (203, 228) as well as during the popularization activities and IMROH colloquia (Chapter 11.1., presentations by Z. Kljaković-Gašpić, T. Orct, A. Sekovanić, and A. Sulimanec Grgec).

In conclusion, all of the results of this project have been fully achieved, despite major difficult circumstances, including the relocation of equipment and researchers due to the major construction works on the adaptation and renovation of the IMROH as well as occasional work delays caused by the COVID-19 pandemic and the consequences of the devastating earthquake in Zagreb in early 2020. Since the planned goals of the research were fully met, and in some aspects achieved even more than originally planned, by the decision of the Board of Directors of the Croatian Science Foundation the project was given the highest possible final grade A.

All published results related to the activities of the research project are available on the project's official website (http://metalorigins.imi.hr/).

LEADER (IMROH)	PROJECT	DURATION
Zrinka Kovarik	Analysis of Butyrylcholinesterase Interactions with Novel Inhibitors and Reactivators (AnalyseBChE, IP-2018-01-7683)	2018–2022

IMROH ASSOCIATES: A. Bosak, T. Čadež, M. Katalinić, N. Maček Hrvat, A. Matošević, G. Šinko, T. Zorbaz, S. Žunec

EXTERNAL ASSOCIATES: V. Gabelica Marković (Faculty of Chemical Engineering and Technology, University of Zagreb), A. Knežević (Ruđer Bošković Institute, Zagreb), Z. Radić (University of California, La Jolla, USA)

Research into the mechanisms of BChE interactions with known and newly synthesized compounds continued. Inhibition of BChE with insecticides and herbicides (197, 217) highlighted fenamiphos as its potent inhibitor. Reactivation of fenamiphos-inhibited BChE, like other phosphoramides, is resistant to reactivation, but the potential of zwitterionic oxime in AChE reactivation was demonstrated (197, 201). We demonstrated the effectiveness of natural eutectic solvents in increasing its solubility (64). Pyridinium oximes with halogen substituents successfully reactivate BChE phosphorylated with sarin and cyclosarin (99). Although a large part of the research has been published, a very important part on pralidoxime analogs and the conversion of BChE from a stoichiometric to a pseudo-catalytic biocleaner, presented at several poster presentations (187, 238, 239), is being prepared for publication and relates to Tena Čadež's dissertation defended on 16 December 2022 (159). New bicarbamate selective inhibitors of BChE (in relation to AChE) have been developed and can be considered for further development of therapeutics (52). This part is part of Ana Matošević's dissertation defended on 17 January 2023.

This project had 4 research objectives whose activities, check points and results complemented each other in order to fully realize the work plan. The balance of dissemination results are 11 Q1, 7 Q2, 2 Q3 and 3 Q4 papers and two dissertations. Two papers are in final versions and at least one more is in preparation. A workshop and an international symposium were organized in 2022. In addition, there were numerous conference announcements in addition to posters, younger collaborators gave oral presntations, and of the several invited lectures (10 in total) the keynote lecture at the cholinesterase international meeting in Bologna stands out (292).

LEADER (IMROH)	PROJECT	DURATION
Veda Marija Varnai	Exposure to pyrethroid and organophosphate insecticides in children – risk assessment for adverse effects on neuropsychological development and hormonal status (PyrOPECh, IP-2019-04-7193)	2020–2024

IMROH ASSOCIATES: J. Macan, Ž. Babić, A. Bjelajac, J. Bobić, S. Cvijetić Avdagić, A. Jurič, J. Kovačić, M. Macan, R. Turk, A. Sulimanec Grgec, P. Tomac

EXTERNAL ASSOCIATES: M. Jergović, G. Jurak, T. Petričević Vidović i M. Posavec ("Andrija Štampar" Teaching Institute of Public Health, Zagreb), B. Krnić (Institute for the Public Health of the Zagreb County, Zaprešić), E. A. Delale (Institute for Anthropological Research, Zagreb), I. Bebek (Solvias AG, Kaiseraugst, Switzerland), K. Dumić Kubat and S. Kralik Oguić (University Hospital Centre Zagreb), J. Garvey (Backweston Laboratory Campus – the Pesticide Control Laboratory, Ireland), R. Gjergja Juraški (Srebrnjak Children's Hospital, Zagreb), I. Keser (Faculty of Food Technology and Biotechnology, University of Zagreb), M. Matek Sarić (Department of Health Studies, University of Zadar), B. McNulty (UCD Institute of Food & Health – University College Dublin, Ireland), B. Murray (Department of Agriculture, Food and the Marine, Irish Ministry for Agriculture, Ireland), V. Musil (School of Public Health "Andrija Štampar", Zagreb), A. Nugent (Institute for Global Food Security, Queens University Belfast, UK), S. Sekušak Galešev (Faculty of Education and Rehabilitation Sciences, University of Zagreb)

The main objective of the project is to assess inadequately explored risks of pyrethroid (PYR) and organophosphate (OP) insecticide exposure to neuropsychological development and hormonal status in prepubertal and pubertal boys in a 2-year cohort study, while controlling for potential confounders, and using only non-invasive methods. In the second project period, as part of the Total Diet Study, the measurement of pesticide residues in food samples was continued in a collaborating laboratory in Ireland (the Backweston Laboratory Campus, Celbridge; Department of Agriculture, Food and the Marine), and the first part of the 1st wave of an epidemiological cohort study in fifth-grade elementary school students in Zagreb and the surrounding area was performed. The preliminary results of the Total Diet Study were presented at one international and one national scientific meeting with international participation, in two oral presentations (230, 295) and at one poster presentation (291). The research is expected to increase the knowledge on possible risks of PYR and OP insecticides' exposure for neurodevelopment and hormonal status in pubertal boys; help to recognise deficiencies and assess available methodology for evaluation of developmental

neurotoxicity and endocrine disruption within the framework of regulatory toxicology; improve insufficient methodology for exposure assessment of non-bioaccumulative pesticides; and contribute to a better characterisation of pesticide exposure in the Croatian population.



Installation research projects (2 projects)

LEADER (IMROH)	PROJECT	DURATION
Maja Katalinić	Molecular mechanisms underlying the toxicity of antidotes and potential drugs (CellToxTargets, UIP-2017-05-7260)	2018–2023
IMROH ASSOCIATES: AM. Lulić, J. Madunić, N. Maraković, I. Vrhovac Madunić, A. Zandona		

EXTERNAL ASSOCIATE: S. Pirkmajer (Institute for Pathophysiology, Ljubljana, Slovenia)

During the fifth and final project year, we evaluated effects on the cell level of 3 new series of compounds synthesised as potential anticholinesterase drugs. Effects were evaluated in dose and time-dependant manner utilising specific methods in order to determine in example, mechanism of cell death (apoptosis and/or necrosis), induction of reactive oxygen species, activation of antioxidative defence, activation of specific caspases and effects on the mitochondrial potential. Furthermore, research has been round up by in silico structure-cell-based activity analysis, resulting in guidelines for future compounds design (21, 97, 99). In addition, cell-based assay battery for detection of compounds action has been utilised for evaluation of possible negative cell effects of polibroilated diphenyl ethers, known as persistant organic pollutants present in the environment (96), than of evaluation of effects of ketamine, morphine, codeine, and synthetic opioids as well as selected herbicides.

Second project theme was linked to the investigation of the NRE enzyme (PNPLA7) (204, 248). During the fifth project year, we continued to investigate physiological role of NRE in the human cells and the possibility of this enzyme to be considered as a new pharmacological target in organophosphorus compound poisoning.

Results obtained were presented in this year on numerous conferences (17 abstracts) as well as in 4 published scientific papers.

LEADER (IMROH)	PROJECT	DURATION
Darija Klinčić	Development, validation and application of analytical methods for PBDE determination (DeValApp, UIP-2017-05-6713)	2018–2023
INPOLIASSOCIATES NA Duoršánk K Josić A Juriž		

IMROH ASSOCIATES: M. Dvoršćak, K. Jagić, A. Jurič

Research continued regarding the presence of selected congeners of polybrominated diphenyl ether (PBDE) in dust samples from different indoor spaces and the assessment of their impact on human health (15, 276). Additionally, 18 trace elements and 11 polycyclic aromatic hydrocarbons (PAHs) were analysed in collected dust samples, their daily intake was estimated, and it was investigated whether they pose a health risk to people in this area (15, 33, 91, 195, 289). Research related to the presence of PBDE compounds in the environment was extended to samples of eels collected in the area of the Raša River (109, 283). The toxicity of PBDEs was also tested in *in vitro* conditions (96).

The optimization of the microwave-assisted extraction conditions of PBDEs from human milk samples was completed, as well as the extract purification procedure. The reliability of the selected analytical procedure was also verified by analyzing commercial infant formula as a related matrix, and very good agreement of the analytical recoveries with the previously obtained results of the validation method was obtained (14). The developed methods were applied to the analysis of comparative samples of human milk and dust samples from the homes of milk donors, and by applying statistical techniques, correlations of the measured mass fractions of PBDE compounds with collected data on mothers and their lifestyle habits and potential sources of PBDE compounds present in their households were investigated (161, 282). The doctoral dissertation "Trace analysis of polybrominated diphenyl ethers in household dust and human milk for human health risk assessment" was prepared and defended (161).



16.1.A.2. CROATIAN ACADEMY OF SCIENCE AND ART FOUNDATION (5 projects)

LEADER (IMROH)	PROJECT	DURATION
Antonio Zandona	Establishment of a cellular model of the blood-brain barrier for <i>in vitro</i> assessment of the passage of potential drugs into the brain	2022–2023
IMROH ASSOCIATES: AM. Lulić, M. Katalinić		
EXTERNAL ASSOCIATES: M. Cavaco, V. Neves (Institute of Molecular Medicine, Lisbon, Portugal)		

The aim of research is to establish an *in vitro* model of the blood-brain barrier and to assess whether such a model based on HBEC-5i cells can be used to assess the passage of drugs to their target site of action. Therefore, the establishment of a new model would contribute to the understanding and evaluation of the possibility of new compounds passing through the blood-brain barrier in general, and thus to the reduction of compounds to be applied *in vivo* with the aim of reducing the number of animals in experiments.

LEADER (IMROH)	PROJECT	DURATION
Karla Jagić	Polybrominated diphenyl ethers in the dust of public spaces – do they pose a risk to human health?	2022–2023

Suradnice iz IMI-ja: D. Klinčić, M. Dvoršćak

The aim is to investigate the impact of persistent, lipophilic, and toxic polybrominated diphenyl ethers (PBDEs) on the health of children and adults to whom they are exposed via dust from indoor spaces. Indoor spaces where they spend part of their time, and which are not their living space are included. On the one hand, there are schools, kindergartens, and workplaces where children and adults spend about a third of their time per day, and on the other hand, public spaces such as pharmacies, libraries or theaters where stays are short-term. The results of research within the framework of this project will provide the first information on the burden of public indoor spaces with compounds of interest.

LEADER (IMROH)	PROJECT	DURATION
Ana Matošević	Synthesis and biological evaluation of carbamates as potential cholinesterase inhibitors in the treatment of Alzheimer's disease	2022-2023

IMROH ASSOCIATES: A. Bosak, M. Bartolić

Alzheimer's disease is a complex and progressive neurodegenerative disease characterized by a loss of memory and reasoning abilities and personality changes. This disease represents the most common form of dementia that requires timely recognition and treatment, and due to its frequency, it has been declared a global public health priority. Today, almost 50 million people live with this disease worldwide, with the number of sufferers tending to grow as the average life expectancy of people increases. Drugs that act as cholinesterase inhibitors or *N*-methyl-D-aspartate receptor (NMDA) antagonists are currently used for the treatment of Alzheimer's disease. Medicines from both groups are effective in the initial and/or middle phase of disease progression and act mainly to alleviate the symptoms of the disease. Although great efforts have been made in recent decades to find new, more effective drugs, where hundreds of new potential cholinesterase inhibitors have been synthesized that can significantly alleviate the symptoms of the disease and affect their course or outcome, from 2003 until today, not one of them approved for use by the European Medicines Agency.

This research is focused on the synthesis of new carbamate compounds and their biological evaluation as potential cholinesterase inhibitors in the treatment of Alzheimer's disease. As part of the biological evaluation, the inhibitory potential of the newly synthesized carbamates against human cholinesterases will be determined, the ability to pass through the blood-brain barrier (BBB) and the effect on cells representing brain, liver, and kidney models will be evaluated.

LEADER (IMROH)	PROJECT	DURATION
Marko Gerić	Evaluation of cytogenetic effects of air pollutants towards human cells <i>in vitro</i>	2021–2022
IMROH ASSOCIATES: G. Gajski, I. Jakovljević, G. Pehnec, J. Rinkovec EXTERNAL ASSOCIATE: AM. Domijan		

Air pollution is a growing environmental and public health problem. Leading world organizations associate polluted outdoor air with the occurrence of numerous diseases and premature mortality. This project will evaluate the modal solutions that represent air pollution for winter and summer on human cells *in vitro* for their toxic effects and mechanisms of action. The results of this project will contribute to the understanding of the mechanisms of harmful effects of compounds that pollute the air and the development of scientific research abilities of scientists at an early stage of their careers.

LEADER (IMROH)	PROJECT	DURATION
Ivana Vrhovac Madunić	Oximes as potential inhibitors glucose transfer in prostate cancer cells	2021–2022

IMROH ASSOCIATES: D. Karaica, A.-M. Lulić, M. Katalinić, J. Madunić, A. Zandona

The aim of this project was to determine whether newly synthesized oxime compounds inhibit glucose uptake and thus the growth of human prostate cancer cells and as such can be considered as candidates for antitumor drugs. The cytotoxic effect of oximes in vitro on prostate cancer cells was tested and the inhibitory concentration for 50% of the cells (IC₅₀) was determined. The determination of IC₅₀ enabled the selection of non-toxic concentrations of oxime compounds that were further used within the project. Cell viability (survival) was determined by MTS test for 24 and 48 hours. Experiments are underway to determine glucose uptake in untreated and oxime-treated human prostate cancer cells using a colorimetric reagent kit (Glucose Uptake Assay), which had to be tested and optimized in the laboratory.

16.1.A.3. IN-HOUSE SCIENTIFIC PROJECTS (16 projects)

LEADER (IMROH)	PROJECT	DURATION	
Adrijana Bjelajac	The role of the mother and the experience of parental competence of mothers with impaired mental health (MIMOZE)	2021-2025	
Principal investigator: E. A. Delale (Institute for Anthropological Research) EXTENAL ASSOCIATES: S. Missoni, V. Pribačić, N. Fuchs, T. Carić (Institute for Anthropological Research), I. Filipčić, D. Šmida (University Psychiatric Hospital St. Ivan), J. Seferović (Faculty of Arts, University of Ljubljana, Slovenia), A. L. Korajlija (Faculty of Humanities and Social Sciences, University of Zagreb)			
Adrijana Bjelajac	Sleep quality in different age groups in Croatia before and during COVID-19 pandemic (CoV-Sleep)	2021–2023	
IMROH ASSOCIATES: J. Macan, S. Cvijetić Avdagić, P. Tomac, J. Mandić, B. Ross EXTERNAL ASSOCIATES: E. A. Delale (Institute for Anthropological Research), D. Lučanin (University of Applied Health Sciences)			
lrena Brčić Karačonji	Investigation of toxic effects of new psychoactive substances by biochemical and molecular-biological methods	2020–2023	
IMROH ASSOCIATES: N. Brajenović, A. Jurič, M. Katalinić, N. Kopjar, A. Lucić Vrdoljak, J. Madunić, K. Nekić, M. Nikolić, A. Pizent, D. Rašić, L. Stančin, B. Tariba Lovaković, V. Triva, A. Zandona EXTERNAL ASSOCIATES: I. Canjuga, G. Kozina, M. Neuberg (University North, Koprivnica), N. Benco, I. Hižar, J. Leniček Krleža, J. Obuljen, A. Rešić, M. Zrilić (Children's Hospital Zagreb), M. R. Meyer (Saarland University, Homburg, Saar, Germany)			

Selma Cvjetić Avdagić	Determination of body composition and chronic stress by bioimpedance method	2018–2022	
IMROH ASSOCIATES: A. Bjelajac, J. Macan, Ž. Babić, J. Jurasović, Zr. Franić, T. Orct, F. Šakić EXTERNAL ASSOCIATES: I. Colić Barić, I. Keser (Faculty of Food Technology and Biotechnology, University of Zagreb), J.Ilich Ernst (Florida State University, Talahasee, SAD)			
Ranka Godec	Organic content of PM ₁ particle fraction	2018–2023	
IMROH ASSOCIATES: G. Pe	hnec, I. Bešlić, I. Jakovljević, Z. Sever Štrukil, I. Šimić, S. Sopčić		
Snježana Herceg Romanić	Analysis of organic pollutants in biological systems and the environment	2021–2024	
IMROH ASSOCIATES: G. Me G. Pehnec, I. Jakovljević, I. EXTERNAL ASSOCIATES: M Karlovac), G. Jovanović i T. Faculty of Chemistry, Serbi	endaš Starčević, S. Fingler Nuskern, S. Stipičević, D. Klinčić, M. Dvoršć Šimić . Matek Sarić (University of Zadar Department of Health Studies), G. Milićević (Institute of Physics Belgrade, Serbia), A. Popović (Universi ia), D. Stanković (Vinča Institute of Nuclear Sciences, Serbia)	ćak, N. Medved, Jakšić (AQUATIKA, ty of Belgrade	
Anja Katić	Assessment of the effects of prenatal exposure to α - cypermethrin on epigenetic programming and endocrine disruption of reproduction and development in experimental rats	2020–2023	
IMROH ASSOCIATES: A. Luc EXTERNAL ASSOCIATES: M G. Kozina, M. Neuberg, R. I	cić Vrdoljak, V. Micek, A. Sulimanec Grgec, S. Žunec . Himelreich Perić, A. Katušić Bojanac, D. Krsnik (School of Medicine, Ribić (University North, Koprivnica)	Zagreb), I. Canjuga,	
Marija Kujundžić	Effects of recreational headphone noise on hearing in young adults (RecNoise)	2022–2024	
IMROH ASSOCIATES: S. Cvijetić Avdagić, J. Macan, Zr. Franić, S. Bošković, J. Mandić EXTERNAL ASSOCIATES: S. Fajt (Faculty of Electrical Engineering and Computing, University of Zagreb), D. Šušković (Microton LtD)			
Maja Lazarus	Bioactive potential, metal and nicotine content in edible boletes regarding the toxic metal burden of soil	2021–2022	
IMROH ASSOCIATES: I. Brčić Karačonji, A. Jurič, S. Mataušić, B. Petrinec, D. Rašeta, A. Sekovanić, J. Senčar, S. Stipičević EXTERNAL ASSOCIATES: D. Šamec (University North, Koprivnica), I. Širić and N. Šprem (Faculty of Agriculture, University of Zagrap)			
Jelena Macan	Prevalence and predictors of occupational contact dermatitis in apprentice nurses/medical technicians (NurseSkin)	2020–2022	
IMROH ASSOCIATES: S. Cvijetić Avdagić, Zr. Franić, Ž. Babić, A. Bjelajac, J. Kovačić, F. Šakić, J. Mandić			
Branko Petrinec	Development and implementation of hybrid gamma-ray spectrometry methods for enhancing the capacity of environmental radiological monitoring around nuclear power plants - RAINSTORM	2022–2025	
IMROH ASSOCIATES: L. Pav	velić, J. Šiško, M. Jurdana, D. Babić, D. Rašeta, I. Pavičić, T. Meštrović		
Ivica Prlić	Development of UV radiation sensors	2015-2024	
IMROH ASSOCIATES: J. Mac EXTERNAL ASSOCIATES: M	can, L. Pavelić , J. Šiško, M. Jurdana . Hajdinjak (Haj-kom d. o. o.), Z. Cerovac (ALARA d. o. o.), KBC Zagreb)	
Ivica Prlić	Thermometry, thermography and sensory evaluation of electromagnetic radiation in medicine (TTSem3)	2014-2024	
IMROH ASSOCIATES: L. Pavelić, I. Bešlić, J. Šiško, S. Kobešćak, M. Jurdana, Martina Dragičević EXTERNAL ASSOCIATES: KBC Zagreb, Zagreb Children's Hospital (A. Antabak), Plastic Surgery Clinic (K. Bulić), OB Karlovac, M. Hajdinjak (Haj- kom d. o. o.), Z. Cerovac (ALARA d. o. o.)			

Dubravka Rašić	Development, validation and application of analytical methods for PBDE determination (DeValApp, UIP-2017-05-6713)	2021–2023	
IMROH ASSOCIATE: M. Per EXTERNAL ASSOCIATE: M.	aica Planinc (Dubrava University Hospital, Zagreb)		
Ankica Sekovanić	Assessment of the effects of <i>MT2A</i> + 838 G/C and <i>MT2A</i> – 209A/G gene polymorphisms on the levels of toxic and essential elements at childbirth	2021–2022	
IMROH ASSOCIATES: J. Jurasović, T. Orct, M. Piasek EXTERNAL ASSOCIATE: D. Pašalić (School of Medicine, University of Zagreb)			
Suzana Sopčić	Molecular markers of organic carbon – biomass burning indicators	2021–2023	
IMROH ASSOCIATES: G. Pehnec, I. Jakovljević, R. Godec			

16.1.B. COLLABORATION ON RESEARCH PROJECTS OUTSIDE THE INSTITUTE

16.1.B.1. CROATIAN SCIENCE FOUNDATION



Research projects (8 projects)

LEADER	PROJECT	DURATION
I. Šola, Faculty of Science, University of Zagreb	Indirect effect of global warming on mammals physiological parameters via high temperature-stressed plant diet (TEMPHYS, IP-2020-02-7585)	2021–2025

IMROH ASSOCIATE: M. Lazarus

The chain interactions between temperature shift, plant biochemical traits, and physiology of the mammals fed with those plants will be assessed employing targeted specific metabolomics approach for plant analyses, biosafety and bioactivity tests on mammals, and statistical data analyses and modelling in order to construct a model showing a tentative pattern of environment temperature indirect (through plant diet) effect on mammal physiology. Results showed high temperature (simulation of global warming) changes nutritive value of broccoli seedlings. Plant ability to adapt to temperature variation is reflected on the phytochemicals, micro- and macroelements, antioxidant capacity and *in vitro* cytotoxic potential of broccoli extracts tested on five different cell lines (106).

LEADER	PROJECT	DURATION
V. Filipović-Marijić, Ruđer Bošković Institute, Zagreb	Integrated evaluation of aquatic organism responses to metal exposure: gene expression, bioavailability, toxicity and biomarker responses (BIOTOXMET, IP- 2020-02)	2020–2024

IMROH ASSOCIATE: Z. Kljaković-Gašpić

The objectives of this project were to determine the concentration of metals in the water and sediment of the Krka River and its tributaries, assess seasonal trends and long-term exposure to metals, study biological responses of organisms to metal exposure, assess the bioavailability and toxicity of metals, and determine the binding mechanisms and efficiency of the accumulation of metals in intestinal parasites of fish. All the activities planned for the second year were carried out according to the schedule and all planned goals were achieved. Associate from IMROH determined the concentrations of metal(loid)s in sediments, different tissues (muscle, intestines, gut content) of the brown trout and in intestinal parasites (acanthocephalans) from eight locations of different levels of pollution in the upper Krka River watercourse. In combination with the results of other project participants, the state of the aquatic environment in the upper course of the Krka River, which is under the influence of municipal wastewater discharges (city of Knin) and industrial wastewater from the former screw factory, and the effects of exposure to metals on biological markers (metallothioneins) in brown trout were assessed. The results of this research were presented at three international scientific meetings (300, 311, 317).

LEADER	PROJECT	DURATION
T. Smital, Ruđer Bošković Institute, Zagreb	Identification and functional characterization of (eco)toxicologically relevant polyspecific membrane transport proteins in zebrafish (<i>Danio rerio</i>) (DANIOTRANS, IP-2019-04-1147)	2020–2024

IMROH ASSOCIATE: D. Karaica

Following the project research plan, one paper was published in a top *WoS*-indexed journal describing the optimization of techniques for tissue samples preparation and antigen retrieval protocols in zebrafish tissues/organs for (immuno)histochemical analyses (108). Specific binding of designed antibodies for Oatp1d1 and Oci1 was confirmed using Oatp1d1 and Oct1 KO zebrafish models. In addition, results were presented at two international scientific conference including the 25th IUBMB Congress, 46th FEBS Congress The Biochemistry Global Summit (Lisbon, Portugal) and International Congress of the Croatian Society of Biochemistry and Molecular Biology "From Science to Knowledge", HDBMB 2022 (Brela, Croatia), and abstracts were published in the Book of Abstract (196) as well in the *WoS*-indexed journal (241). Furthermore, two graduation theses were completed and defended (165, 170), and five laboratory practices were provided under the mentorship of D. Karaica. D. Karaica successfully completed an international zebrafish course at the Karlsruhe Institute of Technology (Karlsruhe, Germany).

Role of blood-brain barrier, innate immunity, and tau	LEADER	PROJECT	DURATION
G. Simic, Croatian Institute for Brain Research, Zagrebprotein oligomerization in the pathogenesis of Alzheimer's disease (ALZ-BBB-STOPINNATETAU, IP-2019-04-3584)2020–2024	G. Šimić, Croatian Institute for Brain Research, Zagreb	Role of blood-brain barrier, innate immunity, and tau protein oligomerization in the pathogenesis of Alzheimer's disease (ALZ-BBB-STOPINNATETAU, IP-2019-04-3584)	2020–2024

IMROH ASSOCIATE: A. Sekovanić

We assess the relationship between cerebrospinal fluid (CSF) biomarkers of Alzheimer's disease (AD) and element levels in plasma and CSF of patients with Alzheimer's disease, patients with mild cognitive impairment and healthy individuals. We used three different statistical methods (simple correlation and two machine learning algorithms; redescription mining and principal component analysis) to test the association of element levels with CSF biomarkers of AD (180).

LEADER	PROJECT	DURATION
S. Miko, Croatian Geological Institute, Zagreb	Sediments between source and sink during a Late Quaternary eustatic cycle: The Krka and the Mid Adriatic Deep System (QMAD, IP-04-2019-8505)	2019–2023

IMROH ASSOCIATE: B. Petrinec

The proposed project aims to improve the knowledge of the thus far poorly explored submerged landscapes of the eastern Adriatic shelf, as well as late Quaternary sediments deposited along the eastern part of the Central Adriatic Basin (MAD). The study of the Pleistocene floodplain of the Krka River will provide insight into the stratigraphic sequence of sediments with the development of the delta system and estuaries, which were formed by the interaction of eustatic sea level changes and local factors such as sediment yield and tectonic activity. Continuous marine sedimentation during the late Quaternary and the yield of material from the Krka River Basin will be investigated in the eastern part of the MAD. By applying high-resolution geophysical methods and sedimentological, petrophysical, geochemical, micropaleontological and aDNA methods on samples from sediment cores, it will for the first time be possible to monitor paleoenvironmental evolution from rivers/lakes to deep-sea environments on a profile shorter than 100 km. Appropriate climatic and environmental indicators will be identified and insight will be gained into the migration and environmental adaptation of hunters and gatherers who lived on the eastern Adriatic coast during the late Palaeolithic, where the Krka River floodplain probably existed. The obtained results on sea level and landscape changes will enable an understanding of the possible interaction among people from the wider study area during the time of systemic tracts of falling, low and rising sea levels. This will explore the possible role of the Krka River as a land/floodplain "bridge" for human migration. Special attention will be paid to the assessment of the new sedimentation rate, the recognition of the characteristics of submerged landscapes and the calculation of the rate of accumulation of organic carbon and terrestrial components of sediments, as well as potentially toxic elements.

LEADER	PROJECT	DURATION
T. Vinković, Faculty of Agriculture, Osijek	Application of Nanobiotechnology for Nutritional Supplementation with Selenium (NutriNTENSe, IP-2018-01-8119)	2019–2022

IMROH ASSOCIATES: A. M. Marjanović Čermak, B. Tariba Lovaković, I. Vinković Vrček (advisor)

Selenium (Se) is an essential chemical element that plays an important role in the metabolism and other vital functions. The main source of Se for humans and animals are plants and different strategies such as biofortification and the use of plant extracts are used to develop dietary supplements based on Se. In the form of nanoparticles, selenium shows greater biological effectiveness and less toxicity than inorganic selenite. As part of this project, the effect of olive pomace extract in the biogenic synthesis of selenium nanoparticles was tested. The obtained nanoparticles were characterised by determining the size, shape, zeta potential, and stability in different media as well as the gastrointestinal bioavailability and biocompatibility. Spherical particles with a diameter of 53.3-181.7 nm were obtained. The resulting system proved to be sensitive to gastrointestinal conditions and the bioavailability of nanoparticles increased in the presence of olive pomace extract. The obtained nanoparticles were less toxic compared to sodium selenite.

LEADER	PROJECT	DURATION
S. Frka Milosavljević, Ruđer Bošković Institute, Zagreb	Biochemical responses of oligotrophic Adriatic surface ecosystems to atmospheric deposition Inputs (BiREADI, IP-2018-01-3109)	2018–2022
IMROH ASSOCIATES: I. Bešlić, R. Godec, S. Žužul, I. Šimić, G. Pehnec (advisor)		

The aim of the project was to assess the impact of atmospheric deposition on complex biochemical responses of oligotrophic systems, considering the importance of promotion and inhibition effects on phytoplankton, and the consequent altering of the surface water chemistry, including the sea surface microlayer at the air-water interface. Within the project, the concentrations, sources and deposition fluxes of atmospheric constituents are evaluated as well as the nature of enrichments of macro-nutrients, trace metals and organic pollutants within the sea surface layers. All activities were carried out according to schedule and all planned goals have been achieved. Associates from IMROH analysed the results of measurements of airborne particulate matter and atmospheric deposition, collected at the location of Martinska near Šibenik (137, 301, 316). The input of nitrogen and phosphorus through airborne particulate matter and atmospheric deposition on the surface layer of the sea was studied in detail, and a significant impact of fire events was found (58). The data on total deposition matter and its composition were processed, including a comprehensive analysis of 23 metals in the total deposition samples (137).

LEADER	PROJECT	DURATION
M. Hranjec, Faculty of Chemical Engineering and Technology, Zagreb	Exploring the antioxidative potential of benzazole scaffold in the design of novel antitumor agents (AntioxPot, IP-2018-01-4379)	2018–2022
IMPOH ASSOCIATE: L Novak Jovanović		

IMROH ASSOCIATE: I. Novak Jovanović

We evaluated the electrochemical oxidation mechanisms of synthetic amino/amidino-substituted benzothiazole derivatives and their reactivity toward electrochemically generated superoxide radical anion (305).

16.1.B.2. UNIVERSITY PROJECTS

PROJECT	DURATION	
Toxicological profile of the phytoplankton Ostreopsis in the northern Adriatic Sea	2021–2022	
IMROH ASSOCIATE: G. Gajski		
	PROJECT Toxicological profile of the phytoplankton Ostreopsis in the northern Adriatic Sea	

The aim of the project is the isolation of Adriatic phytoplankton species and their cultivation for the purpose of further research. As part of the project, morphological and genetic identification of the species and the isolation of associated toxins and their characterization will be carried out. Furthermore, the project will examine the effect of

toxins on nasal epithelial cells and how the toxin affects their permeability. Also, a detailed toxicological characterization will be performed on human peripheral blood lymphocytes as sensitive biomarkers of exposure in this type of research.

16.1.C. PROFESSIONAL PROJECTS

PROJECT	CONTRACTOR	LEADER		
Service provider: Environmental Hygiene Unit				
Monitoring air pollution in the City of Zagreb (from 1963)	City of Zagreb, City Office for Energy, Environmental Protection and Sustainable Development	G. Pehnec		
Monitoring of the Total Effects of CPS Molve on the Ecosystem (from1998)	INA-Naftaplin and Institute for Public Health of the Koprivnica-Križevci County	G. Pehnec		
Monitoring Air Quality at the CWWTP Construction Site in Zagreb (from 2003)	Zagrebačke otpadne vode	G. Pehnec		
Monitoring Air Pollution at National Network Stations for the Purpose of Continued Air Quality Monitoring (from 2015)	Ministry of Economy and Sustainable Development and Meteorological and Hydrological Service of Croatia	G. Pehnec		
Drafting Equivalency Studies at Measurement Stations of the National Network for Continued Air Pollution Monitoring (from 2015)	Ministry of Economy and Sustainable Development and Meteorological and Hydrological Service of Croatia	I. Bešlić		
Ecological Map of the City of Zagreb	City of Zagreb	G. Pehnec, S. Davila		
Service provider: Radiation Protection Unit	'			
Background Radioactivity Monitoring in the Republic of Croatia, IMI-CRZ-96 (since 1959)	Civil protection directorate of the Republic of Croatia Ministry of the Interior	B. Petrinec		
Radioactivity measurements of zero state at the location of the Center for Radioactive Waste Disposal and in the area of the Dvor municipality S-RAO-Z	Decommissioning and Disposal of Radioactive Waste and Spent Nuclear Fuel of the Krško Nuclear Power Plant Fund	B. Petrinec		
Results of Monitoring of Environmental Radioactivity in Vicinity of Plomin Coal- Fired Power Plant, IMI-P-491	HEP proizvodnja, Thermal power plant Plomin I, Plomin	B. Petrinec		
Results of Radioactivity Measurements at Gas Fleld Molve, IMI-P-493	Koprivnica-Križevci County, Koprivnica	B. Petrinec		
Service provider: Radiation Dosimetry and Radiobiology Unit				
Determination of the radiological status of the working environment in IPNP (Phase III)	INA Group	I. Prlić		
Determination of the radiological status of production tubing during maintenance processing (Phase IV)	INA Group and STSI	I. Prlić		
Study on meeting the test conditions of particular basic requirements related to ionising and non-ionising radiation during experimental work for the purpose of permits for the reconstruction and expansion of IMROH's buildings	IMROH	I. Prlić		



16.2.A. SCIENTIFIC RESEARCH PROJECTS

16.2.A.1. EUROPEAN UNION PROGRAMS

EUROPEAN REGIONAL DEVELOPMENT FUND Operational Program Competitiveness and Cohesion (4 projects)



European Union European Regional Development Fund

INSTITUTION (Leader)	PROJECT	DURATION
Jamnica plus, Zagreb (S. Lovković)	Development of functional beverage in sustainable packaging (JamINNO+, KK.01.2.1.02.0305)	2020–2023

IMROH ASSOCIATES: J. Jurasović (coordinator), I. Bešlić, N. Brajenović, I. Brčić Karačonji, S. Davila, G. Pehnec, I. Jakovljević, A. Jurič, Z. Kljaković-Gašpić, T. Orct, A. Sekovanić, A. Sulimanec Grgec, I. Šimić, B. Tariba Lovaković, S. Žužul

PARTNERS: Faculty of Pharmacy and Biochemistry University of Zagreb, IMROH and Ruđer Bošković Institute

In the second year of experimental activities, we continued testing the air sampling system for the collection of microplastic particles in the air and our work on airborne microplastic particles analysis method implementation. The ICP-MS method was optimized and the analysis of metals (Al, Ba, Cd, Co, Cu, Fe, Li, Mn, Ni, Pb, Sb, Sn, and Zn) was performed in pure (virgin) PET resins and 100% recycled (rPET) pellets, their bottle preforms and blow-moulding products. Analyses of metals in water samples from the spring, before treatment and before and after bottling. We developed a GC-MS method for determination of selected 7 phthalates in mineral and spring water samples in different types of packaging. Different extraction conditions were tested (different solvent types, manufacturers, solvent mixtures and their ratios, extraction time, and methods). Concentrations of 12 polycyclic aromatic hydrocarbons (PAHs) were determined in water samples from the source and before filling in packaging in Sveta Jana and Pisarovina. Also, the influence of temperature, sunlight, and product storage time on the migration of metals, phthalates, and PAHs from different types of packaging in water was evaluated.

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (A. Lucić Vrdoljak)	Research and Educational Centre of Environmental Health and Radiation Protection – Reconstruction and Expansion of the IMROH (ReC-IMI, KK.01.1.1.02.0007)	2017–2023

IMROH ASSOCIATES: S. Barbarić, M. Herman, B. Roić, S. Stankić

The project grant of 232,602,280.72 HRK is intended for the implementation of the project during whose implementation the Institute will be expanded with a new building of 6,785.15 m², while its existing building of 2,067.41 m² will be renovated. The Institute will also increase its capacities with modern research and IT equipment for all of its units.

During 2022, regular work began in the larger phase of construction, the expansion of the Institute, whereas the renovation of the older building was largely completed. Apart from construction works, the Institute also finished all of the required public procurement procedures. Due to delays caused by the earthquakes in Zagreb and Petrinja, the implementation period was extended to late 2023.

INSTITUTION (Leader)	PROJECT	DURATION
Meteorological and Hydrological Service of Croatia (J. Škevin Sović)	Project of extension and modernisation of the national network for continuous air quality monitoring (AIRQ, KK.06.2.1.02.0001.)	2017–2023
IMROH ASSOCIATES: G. Pehnec (coordinator), R. Godec, I. Bešlić, S. Žužul, S. Stankić, B. Roić, S. Barbarić, M. Herman		

The purpose of the project is to improve and optimize the system for managing and monitoring air quality in urban areas, zones, and agglomerations. The project aims to support the implementation of the legislative

framework for air quality and environmental protection. The project will receive a grant in the amount of 125.1 million HRK (85% funded by the ERDF OP Competitiveness and Cohesion, 15% by the Environmental Protection and Energy Efficiency Fund). The project will result in: 5 new and 19 modernized measuring stations at full functionality; a developed and functional model for the assessment of ground level concentrations of pollutants; additional equipment for DHMZ and IMROH chemical laboratories for measurements in accordance with the National Programme for measuring the level of air pollution in the national network for continuous air quality monitoring; with additional equipment for a laboratory for calibrating air quality measures and related measurement sizes. In 2019 and 2020 IMROH finished in full all planed procurements and all equipment have been put into operation. Two advanced trainings planned in the laboratory of equipment manufacturers abroad were postponed due to the COVID-19 pandemic for the first possible date. By the end of 2022, 5 new measuring stations were built and 18 stations were modernized. Due to delays in the implementation and completion of certain public procurement procedures, the competent authorities were requested to extend the duration of the entire project until September 2023.

INSTITUTION (Leader)	PROJECT	DURATION
School of Medicine, Zagreb (D. Ježek)	Scientific Center of Excellence for Reproductive and Regenerative Medicine, Reproductive and Regenerative Medicine – Exploring New Platforms and Potentials (CERRM, KK.01.1.1.01.0008)	2014–2022

IMROH ASSOCIATE: A. Fučić

Within the EU human biomonitoring initiative (HBM4EU), a targeted multi-national study on occupational exposure to hexavalent chromium (Cr(VI)) was performed. A survey performed to evaluate the policy relevance of the HBM4EU chromates study findings supports the usefulness of the study results. According to the responses received from the survey, the HBM4EU chromates study was able to demonstrate the added value of the human biomonitoring (HBM) approach in assessment and management of occupational exposure to Cr(VI). For future occupational studies, the need for engagement of policy makers and regulators throughout the whole research process to ensure awareness, relevance and uptake of the results in future policies was suggested (92, 115). The number of unsolved issues on infertility etiology, especially potential environmental causes, in couples demonstrates the need for further investigations into infertility biomarkers. For the first time seminal plasma Nglycosylation as a biomarker of environmental exposure in semen samples from 82 normozoospermic men and 84 men with abnormal semen parameters was compared with genome damage measured by DNA fragmentation. Results show that the selected seminal plasma N-glycans were significantly associated with smoking, exposure to pesticides, air pollution, agents emitted during photocopying, alcohol consumption, and obesity. Some N-glycans showed a simultaneous association with DNA fragmentation, semen parameters, and environmental stressors. These subgroups of N-glycans are new potential candidates for biomonitoring of exposure to different environmental factors in men with semen abnormalities (51).

EUROPEAN UNION SOLIDARITY FUND (2 projects)



INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (M. Herman)	Strengthening and Renovation of the Earthquake- damaged Central Building of the Institute for Medical Research and Occupational Health (FSEU.2021.MZO.038)	2021–2023

IMROH ASSOCIATES: S. Barbarić, A. Lucić Vrdoljak, B. Roić, S. Stankić

Following the earthquake that took place in Zagreb on 22 March 2020, the Croatian Ministry of Science and Education opened a call to fund the strengthening and renovation of infrastructure damaged by the earthquake. Within this call, the Institute submitted a project to fully strengthen and renovate its central building. The project grant of 13,212,021.60 HRK will go toward repairing and strengthening the central building, built in 1947, for the purpose of increasing its resilience against earthquakes. During 2022, all construction on the renovation of the Institute's central building was completed, but due to administrative reasons the project's implementation was extended to March, 2023.

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (M. Herman)	Strengthening and Renovation of the Northern Building of the Institute for Medical Research and Occupational Health (FSEU.2021.MZO.071)	2021–2023

IMROH ASSOCIATES: S. Barbarić, A. Lucić Vrdoljak, B. Roić, S. Stankić

Following the earthquake that took place in Zagreb on 22 March 2020, the Croatian Ministry of Science and Education opened a call to fund the strengthening and renovation of infrastructure damaged by the earthquake. Within this call, the Institute also submitted a project to fully strengthen and renovate its northern building. The project grant of 6,687,750.00 HRK will go toward repairing and strengthening the northern building, built in 1961, for the purpose of increasing its resilience against earthquakes. The project grant was officially awarded on 5 Nov 2021 and during 2022, the Institute prepared all of the documentation necessary for construction, which is set to begin in the first months of 2023.

EUROPEAN RESEARCH AND INNOVATION PROGRAMME Horizon 2020/Horizon EUROPE/Euroatom (5 projects)

HORIZON 2020

INSTITUTION (Leader)	PROJECT	DURATION
French Agency for Food, Environmental and Occupational Health & Safety (ANSES)	Partnership for the Assessment of Risks from Chemicals, (PARC, Grant agreement ID: 101057014)	2022–2029

IMROH ASSOCIATES: V. M. Varnai, J. Jurasović, I. Vinković Vrček, J. Kovačić, G. Pehnec, G. Gajski

PARC aims to bring together a broad community of research establishments and health agencies to advance, share knowledge and improve skills in chemical risk assessment. PARC brings together Ministries and national public health and risk assessment agencies, research organisations, and academia from almost all EU Member States, as well as Representatives of Directorates-General of the EC and EU agencies involved in the monitoring of chemicals and the assessment of risks. Specific objectives are: an EU-wide sustainable cross-disciplinary network to identify and agree on research and innovation needs and to support research uptake into regulatory chemical risk assessment; joint EU research and innovation activities responding to identified priorities in support of regulatory risk assessment for chemicals; strengthening existing capacities and building new transdisciplinary platforms to support chemical risk assessment.

INSTITUTION (Leader)	PROJECT	DURATION
Institute for Radiological Protection and Nuclear Safety – IRSN, Fontenay- aux-Roses, Francuska (JC. Gariel)	European Partnership for Radiation Protection Research (PIANOFORTE, Grant Agreement ID 101061037)	2022–2027

IMROH ASSOCIATES: I. Prlić (coordinator for CRO, WP3T2 Coordinator, PoM-Program manager Contact Point, member of the Consortium Management Board), L. Pavelić, N. Kopjar, I. Brčić Karačonji, A. Lucić Vrdoljak, J. Macan, B. Petrinec, M. Herman

Partner: University of Zagreb Faculty of Mining, Geology and Petroleum Engineering (Ž. Veinović) Consortium: 22 EU Member States and Norway, 7 associations from the field of radiation protection: MELODI, ALLIANCE, EURAMED, NERIS, EURADOS, SHARE, MEENAS

The PIANOFORTE research partnership aims to improve knowledge and promote innovation in the field of radiation protection for the benefit of better protecting the public, patients, workers and the environment in all scenarios of exposure to ionising radiation. The European Partnership for Radiation Protection Research will contribute to improving the protection of the public, workers, patients and the environment from environmental, occupational and medical exposure to ionising radiation. It brings together 58 partners representing 22 EU countries as well as the United Kingdom and Norway, and is coordinated by the French Institute for Radiation Protection and Nuclear Safety (IRSN). It is co-financed by the European Union's EURATOM program and the governments of the participating countries. Through the research activities that will be carried out within its framework, PIANOFORTE

will contribute to the implementation of European policies such as the European plan to combat cancer, the green pact for growth, and the implementation of the roadmap for reducing industrial and natural risks.

INSTITUTION (Leader)	PROJECT	DURATION
The Lisbon Council for Economic Competitiveness and Social Renewal, Brussels, Belgium (F. Mureddu)	Evidence Driven Indoor Air Quality Improvement (EDIAQI, 101057497)	2022–2026

IMROH ASSOCIATES: G. Gajski (koordinator za WP5), M. Gerić, K. Matković, M. Milić, V. Kašuba, G. Pehnec, D. Karaica, I. Vrhovac Madunić

Indoor air pollution, an emerging threat recognized by European society, is claiming millions of lives annually. In the heat of current COVID-19 pandemic, elevated exposure to indoor air pollutants due to increased time spent indoors further faces a significant increase in negative effect on both physical and mental health and well-being not only in Europe, but also worldwide. When it comes to indoor air quality itself, serious knowledge gaps remain in understanding complex nature of indoor-outdoor pollution relationships, pollution sources and exposure pathways, health effects of emerging pollutants, ventilation of indoor spaces on wide spatial and long temporal scales. This is mainly because air quality monitoring in European Union (EU) is primarily focused on outdoor air quality, which paradoxically is a result of regulatory target compliances, which is lacking for indoor environments. To increase the resilience of EU for emerging threats of indoor air pollution and to promote living and working in healthy environments, project EDIAQI aims at conducting characterization of sources and routes of exposure and dispersion of chemical, biological, and emerging indoor air pollution in multiple cities in EU. Quantification of the main properties of pollutants and processes that governs its fate in indoor environments will be investigated on two levels: a) the-state-of-the-art, small-scale, high-intensity scientific focus measurement campaigns; and b) long-term, large-scale monitoring of target indoor air pollutants. The chosen project strategy for developing, characterization, and deployment of cost-effective/user-friendly monitoring solutions, together with the-state-of-the-art scientific instrumentation will allow to create new knowledge on sources, routes of exposure, and body burdens of indoor multipollutant.

INSTITUTION (Leader)	PROJECT	DURATION
MyBiotech (N. Günday- Türeli) and Luxembourg Institute for Science and Technology (T. Serchi)	Pharmaceutical Open Innovation Test Bed for Enabling Nano-pharmaceutical Innovative Products (Phoenix, Grant Agreement ID 953110)	2021–2025

IMROH ASSOCIATES: I. Vinković Vrček (coordinator), I. Pavičić, I. Capjak, N. Peranić, Ž. Babić Consortium: 12 EU Member States

Nanopharmaceuticals have the potential to stimulate the scientific and technological development of EU Member States, offering major clinical and socioeconomic benefits to society as a whole, industry and key stakeholders, and ultimately to patients. Affordable and advanced testing, manufacturing facilities and services for new nano-medicines are the main prerequisites for the successful implementation of these developments to further strengthen growth and innovation capacities. The establishment of current good manufacturing practice (GMP) in nano-pharmaceutical production is a key step for the successful transfer of nano-medicines from the laboratory to the industrial level, and clinical practice. Due to the lack of resources to implement GMP production, the development and production of innovative nano-medicines continues to be a challenge for the main players in the nanomedicine market in the EU, start-ups and SMEs. In order to enable the successful application of nanomedicines in the field of medicine, it is urgently necessary to establish an Open Innovation Test Bed (OITB) based on scientific achievements and regulatory rules. The goal of the PHOENIX project is to enable the smooth, timely and cost-effective transfer of nano-medicines from the laboratory to clinical trials by providing an advanced, affordable and easily accessible PHOENIX platform. The PHOENIX platform will offer a consolidated network of laboratories, manufacturing facilities, technologies, services, and expertise for all aspects of technology transfer, from characterization, testing, verification to final products compliant with GMP manufacturing and regulatory guidelines. The PHOENIX platform will develop and establish new facilities and upgrade existing ones to make them available to SMEs, start-ups and research laboratories for scale-up, GMP manufacturing, and nano-medicine testing. Services and expertise provided by OITB will include manufacturing and characterization under GMP conditions, safety assessment, regulatory compliance and commercialization enhancement.

INSTITUTION (Leader)	PROJECT	DURATION
Norwegian Institute for Air Research (NILU), Kjeller, Norway (M. Dusinska)	Science-Based Risk Governance of Nanotechnology (RiskGONE, Grant Agreement ID 814425)	2019–2023
IMROH ASSOCIATES: I. Vinković Vrček (coordinator), I. Pavičić, Z. Franić, B. Pem. K. Ilić, L. Božičević		

Consortium: 15 EU Member States and USA, and Iran

RiskGONE (Science-Based Risk Management of Nanotechnology) is an EU H2020 project that aims to provide robust procedures for consistent risk management of manufactured nanomaterials. The project started on January 1, 2019 and will end on February 28, 2023. During that time, the project partners will develop new tools or modify existing ones to identify with greater certainty the environmental and human health impacts of a range of nanomaterials. These tools and the test results using them will then be integrated into the work of the European Risk Management Council (ERGC), a group of individuals with different areas of nanomaterials expertise tasked with making management decisions about the safety of specific materials. A risk management framework, composed of tools and the ERGC, will be developed to manage the safety of nanomaterials in a coherent and scientifically sound manner.

EUROPEAN SOCIAL FUND

Operational Programme Efficient Human Resources

Croatian Science Foundation – Scientific Cooperation Programme (2

European Union European

2 projects)		***	Social Fund	
INSTITUTION (Leader)	PROJECT		DURATION	
IMROH, Zagreb (I. Vinković Vrček)	Safe-by-Design Approach for Development of Nano- Enabled-Delivery Systems to Target the Brain (SENDER, HrZZ-PZS-2019-02-4323)		2019–2023	

IMROH ASSOCIATES: I. Pavičić, B. Pem, K. Ilić, N. Kalčec, M. Beus, R. Barbir, N. Peranić PARTNER: University of Melbourne, Victoria, Australia

Nanotechnology enables innovative and effective therapeutic and diagnostic means and tools. Nevertheless, the treatment of neurodegenerative disorders still represents a great challenge due to the existence of the blood-brain barrier (BBB), which hinders the efficient delivery of drugs to the brain. Multifunctional nanoparticles (NPs) represent a new and improved platform for increased efficacy, bioavailability, and targeted delivery of drugs across the BBB. Therefore, the main goal of the proposed project is to develop a multifunctional nanosystem that will enable the delivery of drugs into the brain (BRaiND) for the effective and safe treatment of brain abnormalities associated with aging and degeneration. For this purpose, specific activities will be carried out: - design, preparation and characterization of BRaiND; - assessment of the stability and fate of BRaiND in biological media; - mechanical and quantitative assessment of the interaction of BRaiND with the BBB; - profiling the efficacy and safety of BRaiND using a combined in vitro and in vivo approach. BRaiND will be based on selenium or gold nanoparticles, stabilized with polyethylene glycol and functionalized with proteins that target brain receptors. Model neuroactive drugs will be attached to such a multifunctional system to demonstrate the effectiveness, guality and safety of the BRaiND system. Careful in vitro and in vivo studies will be conducted including stability and interactions of BRaiND in different biological media, permeability through the BBB, efficacy of targeting specific brain sites, neuroprotective activity and evaluation of the safety of their application. The work plan of the project is based on validated and standardized methodologies, as well as on innovative experimental techniques. Considering the main challenges of translational research of neurodegenerative diseases, the SENDER strategy is based on the Safe-by-Design approach, and is enabled by nanotechnological tools that analyse and manipulate biological processes on the nanoscale, where diseases arise and progress.

INSTITUTION (Leader)	PROJECT	DURATION
Department of Physics, Faculty of Science, Zagreb (M. Makek)	Single layer gamma-ray polarimeter for medical imaging applications and fundamental physics research (SiLGaP, HrZZ-PZS-2019-02-5829)	2019–2023
IMROH ASSOCIATE: L. Paveli	ć	

PARTNER: University of Sydney, New South Wales, Australia

Information about the polarization of gamma radiation is important in many areas of modern physics research. In the field of fundamental research, an example is the phenomenon of quantum coupling, which can be studied by analysing the relative polarizations of three gamma-photons from the decay of ortho-positronium. In the field of applications, an important case is biomedical imaging using positron emission tomography (PET), where simulation studies have shown that the polarization information not used in PET systems has the potential to improve image quality. The polarization of the gamma photon can be determined via Compton scattering, which results in a scattered electron and a scattered gamma particle. To reconstruct the Compton scattering, position and energy sensitive detectors are needed, which usually consist of two layers: the first one for the detection of electrons and the second one for the detection of the scattered photon. However, in many applications, where the detectors are highly segmented and contain a large number of channels, as in PET, a system based on two-layer detectors would have a relatively high cost. The plan of this project is to create a new, modular system for measuring the polarization of gamma-photons, based on single-layer detectors for measuring Compton scattering. Individual modules will consist of a matrix of scintillation detectors, read by silicon photomultipliers. Compared to two-layer systems, this concept offers the possibility of constructing more affordable, compact, and multifunctional devices. In the project, we will set up a system of sixteen modules that will then be applied through two studies. In the first research, the possibility of using information about the polarization of gamma radiation in PET will be tested experimentally for the first time, as an important step towards a new generation of efficient devices for medical imaging. In the second, azimuthal correlations of three gamma-photons from ortho-positronium decay will be analysed in order to investigate quantum coupling as a fundamental physical concept.

EUROPEAN COMMISSION DG EMPLOYMENT, SOCIAL AFFAIRS AND INCLUSION

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	European Commission	

INSTITUTION (Leader)	PROJECT	DURATION
University of Osnabrück, Germany (S. Malte John)	Promoting the autonomous implementation of the European framework agreement on occupational health and safety in the hairdressing sector (VS/2019/0440)	2021–2022
IMROH ASSOCIATES: J. Macan, Ž. Babić, R. Turk, Zr. Franić, M. Macan		

Consortium: Germany, Denmark, Nederlands, Croatia

The specific aims of the project are to: 1) identify and prioritize hazardous and harmful substances contained in cosmetic products used by hairdressers by means of a systematic review; 2) adopt two Medical Reference Documents, which identify and prioritize different substances and ingredients (including reprotoxic substances); 3) draft a Methodological Note showcasing the difference in exposure between a consumer and a professional hairdresser; 4) participate in the Technical Working Group at the level of the CEN on the hairdressing glove standardisation process. In 2022, eight systematic reviews about health effects of the most common hairdressing chemicals, and exposure in hairdressers via skin and respiratory system were published (1,25,42,49,87-89,117). Medical reference document was published as a summary of scientific data about the toxicity of hairdressing chemicals and prevention of these effects in hairdressers (158). Results of the project were presented and discussed at two meetings of social partners in hairdressing organized by European Commission in March and October 2022.



EUROPEAN COMMISSION, JOINT RESEARCH CENTRE (JRC)

INSTITUTION (Leader)	PROJECT	DURATION
VITO, Flemish Institute for Technological Research, Belgium (M. Van Poppel)	Deployment of lower-cost ambient air quality sensor systems in urban environments (ENV.C3/SER/2019/0010)	2020–2022

IMROH ASSOCIATES: S. Davila (coordinator for Croatia), I. Bešlić, M. Mihaljević

This project aims to help evaluate the performance and potential of low-cost sensor systems for air quality and make comparisons with conventional measurement methods. To achieve this, the sensors are used under different environmental and meteorological conditions in three different European cities, Antwerp, Oslo and Zagreb. In May 2020, measurements of pollutants began in Zagreb using 17 sensor boxes owned by the JRC. In the first phase of the project, from early June to early July, all 17 instruments were placed at IMROH for calibration. At the beginning of July 2020, the second phase of measurement began, in which the devices were installed at an additional 16 locations in the city of Zagreb. The location of the automatic measuring station at the Institute was selected as the reference location for monitoring the air quality of the city of Zagreb, and two sensor measuring devices were installed at the automatic station. In 2021, sensor measurements were completed at assigned locations and all sensors were returned to IMROH for calibration with reference data from IMROH station (123). As the second phase of the project was completed, 7 sensor sets were returned to the JRC, while the other sensor sets were left to IMROH for further research, after which they will be returned to the JRC. In 2022, part of the sensors left at IMROH was placed on the bicycles of volunteers cycling through the streets of Zagreb, and the other part was placed at locations in Zagreb where air quality measurements had not been carried out yet. During 2022, the project research group consolidated all sensor data collected during the project into a database that can be used for publications (https://zenodo.org/record/7256406). Furthermore, in 2022 the JRC published two reports: Guidance on low-cost sensors deployment for air quality monitoring experts based on the AirSensEUR experience and Guidance on lowcost air quality sensor deployment for non-experts based on the AirSensEUR experience, which were both created as part of the project. In 2023, there is a plan to publish a set of data in which the methodology of sample collection will be explained, as well to publish a scientific paper in which the results of the whole project would be presented. In 2023, the JRC also plans to publish a third report that would deal with sensor calibration and the proposals of the research group in the project.

EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY COST ACTION Programme (10 projects)



INSTITUTION (Leader)	PROJECT	DURATION
The Germans Trias i Pujol Research Institute (IGTP), Badalona, Spain (E. Martinez-Balibrea)	Modelling immunotherapv response and toxicity in cancer (IMMUNO-model, CA21 135)	2022–2026

IMROH ASSOCIATE: D. Karaica (Management Committee Member)

The aim of the Action is to foster research and innovation in the field of preclinical immuno-oncology models with the ultimate goal of advancing the treatment of cancer patients and their quality of life. Therefore, the first meetings of the Management Committee and Working groups (1, 2, and 5) were held in Brussels (1– 3 October 2022) and all planned project activities were initiated within the "Memorandum of Understanding" document.

INSTITUTION (Leader)	PROJECT	DURATION
AIT-Austrian Institute of Technology GmbH, Vienna, Austria (W. Neuhaus)	3Rs concepts to improve the quality of biomedical science (IMPROVE, CA21139)	2022–2026
IMPOH ASSOCIATE: L. Vrhouze Madunić (Management Committee Member)		

IMROH ASSOCIATE: I. Vrhovac Madunić (Management Committee Member)

The aim of the Action is to establish a network of scientists who will work on improving and promoting the 3Rs (Replacement, Reduction and Refinement) concepts, data and documents, in order to improve the quality of

biomedical sciences. The project brings together a unique network of scientists from basic and biomedical sciences, regulatory authorities and the education sector. The IMPROVE action will be implemented and support the implementation of the EU directive 2010/63/EU on the protection of laboratory animals used for scientific purposes. On October 21, 2022, the first meeting of the Management Committee was held in Brussels, which appointed the heads of the working groups and elected the heads of the ITC (Inclusiveness Target Countries) and STSM (Short-term scientific missions) committees. At the meeting, the proposed action plan was approved and the next hybrid meeting in Sarajevo and the Training school in the WG3 Dissemination Working Group in Milan were announced.

INSTITUTION (Leader)	PROJECT	DURATION
GENyO, Pfizer-University of Granada, Granada, Spain (K. Benabdellah)	Genome Editing to Treat Humans Diseases (GenE-Humdi, CA21113)	2022–2026

IMROH ASSOCIATE: J. Madunić

Recent advances on genome editing (GE) technologies opened up the possibility of treating diseases through precise modifications of patients' genomes. Impressive results have been achieved on animal models of several genetic disorders, infectious diseases as well as cancer and several clinical trials are already on going. However, the inadequate integration of the results of academic research into the research development strategy of pharmaceutical companies, the insufficient interest of academic institution in regulatory science and the absence of established standards to well acceptable risk-benefit ratio by regulatory agencies, preclude its general application for treating human diseases. Therefore, the translation of the GE technologies to address public health needs, require a strong collaboration between basic and clinical research, regulatory bodies and the different stake holders involved for each application. There are several networks to improve or analyse GE technologies for different applications, however, no one cover all the actors involved in gene therapy translation. The principal aim of the GenE-HumDi Action is to bring together pharmaceutical companies, academic institution, science and regulatory agencies, biotechnology firms, patient advocacy association and information technology, in order to tackle knowledge fragmentation with the aim to accelerate the translation of GE technologies to the treatment of human diseases.

INSTITUTION (Leader)	PROJECT	DURATION
University of Ferrara, Ferrera, Italy (E. Adinolfi)	P2X receptors as a therapeutic opportunity (PRESTO, CA21130)	2022-2026

IMROH ASSOCIATE: J. Madunić

P2X receptors (P2XRs) are ATP-gated ion channels involved in intercellular communication with an established role in neurodegeneration, infection, inflammation, cancer growth, and progression. In vitro and in vivo evidence, generated mainly by leading Europe-based laboratories, shows that P2XRs might be an ideal pharmacological target in these diseases and many others. Over the years, highly selective agonists and antagonists have been synthesized, and therapeutic antibodies targeting the P2XRs have been raised. However, the transfer of this wealth of knowledge from research laboratories to the patients' bed has been slow, and clinical trials so far carried out have been unsatisfactory. This was due to a noticeable lack of coordinated effort by basic research, clinical and industry-based investigators. The PRESTO Action aims at accelerating the transition of P2XRs knowledge to clinical applications. PRESTO will be accomplishing these goals by 1) promoting a coordinated effort by leading basic and clinical science experts and Industry-based investigators aimed at the selection of the most appropriate pathologies amenable to P2XR-targeted therapy; 2) identifying the best-suited P2XR-directed drugs to take through the clinical pipeline; 3) establishing validated experimental protocols and tools; 4) setting criteria for the validation of P2XRs as diagnostic and prognostic biomarkers; 5) promoting dedicated clinical trials; 6) training a new, multicultural, transdisciplinary, generation of young researchers skilled in the P2XR field; 7) disseminating in the scientific community, biomedical students, charities, local and national health authorities and the general public, the awareness of the importance of P2XR-based research.

INSTITUTION (Leader)	PROJECT	DURATION
University Hospital RWTH Aachen, Aachen, Germany (J. Jankowski)	Personalized medicine in chronic kidney disease: improved outcome based on Big Data (PerMediK, CA21165)	2022–2026
IMPOH ASSOCIATE: L. Vrhouse Madunić (Management Committee Member)		

IMROH ASSOCIATE: I. Vrhovac Madunić (Management Committee Member)

The aim of this Action is to support the development of a path towards personalized medicine in chronic kidney disease (CKD), based on multidimensional -omics data (Big Data). This field is mature enough (through the existence of ample molecular data, promising therapeutic targets, and markers) to move to the next step of clinical implementation. On October 13, 2022, the first meeting of the Management committee was held in Brussels, which appointed the heads of the working groups and elected the heads of the ITC (Inclusiveness Target Countries) and STSM (Short-term scientific missions) committees. At the meeting, the proposed work plan of the action was approved and the location of the next meeting of the COST action in Cyprus was agreed.

INSTITUTION (Leader)	PROJECT	DURATION
Stazione Zoologica Anton Dohrn, Napoli, Italy (M. V. Modica)	European Venom Network (EUVEN, CA 19144)	2020–2024
INADOLLASSOCIATELS, C. Coiclei (Nanagament Committee member substitute)		

IMROH ASSOCIATE: G. Gajski (Management Committee member substitute)

Partners: 27 European countries, Tunisia, Armenia, Belarus, Russia, and Morocco

The overarching aim of the EUVEN COST Action is to foster venom investigation at the European level. The Action will identify priority targets and promising innovative approaches, develop best practice pipelines ensuring consistency across Europe and providing international standards in venom research. Further, it provides a novel platform to promote synergistic interactions between academia, industry and society, and to nurture a new generation of venom researchers with a multidisciplinary expertise. Building a gender, age and geographically balanced network involving all the relevant stakeholders will be the fundamental prerequisite to leverage the extraordinary biochemical warfare enclosed in animal venoms, with an enduring scientific, technological and socioeconomic impact. As part of the project collaboration, a review paper was published in which current insights, new methods and future perspectives in biological and applied research on animal poisons are presented (94).

INSTITUTION (Leader)	PROJECT	DURATION
Erasmus University Medical Center, Rotterdam, Netherlands (F. Rivadeneira)	Genomics of MusculoSkeletal traits Translational Network (GEMSTONE, CA18139)	2019–2023

IMROH ASSOCIATE: S. Cvijetić Avdagić

The project work continued in the area of the major membrane trafficking pathways in osteoclasts, bone phenotyping approaches in humans and monogenic forms of low and high rare bone mass disorders.

INSTITUTION (Leader)	PROJECT	DURATION
University of Lodz, Poland (B. Klajnert-Maculewicz)	Cancer Nanomedicine – from the bench to the bedside (Nano2Clinic, CA17140)	2018–2023

IMROH ASSOCIATE: I. Vinković Vrček (Management Committee member, WP2 leader)

Finding effective cancer therapies is an urgent and still unsolved problem, and in the fight against this disease, scientists are investing enormous efforts in the application of nanomedicines. Nanotherapeutics show major advantages over unmodified drugs, including improved half-life, more efficient tumor targeting, and reduced side effects. However, only a few nanotherapeutics have reached the commercial level, most of them are still in the research phase. Accordingly, this activity aims to develop and strengthen the relationship between industry and the academic community with the ultimate goal: encouraging the clinical transfer of nanomedicine from the bench to the bedside. This will be achieved by creating the first, pan-European interdisciplinary network of representatives of academic institutions and small and medium-sized enterprises, including clinical research organizations (CROs) dedicated to the development of nanosystems that carry anticancer drugs from their initial design, preclinical testing of efficacy, pharmacokinetics and toxicity to the preparation of the detailed protocols required for their first phase clinical studies. By promoting scientific exchange, technological implementation and innovative solutions,

the Action will provide a timely instrument for rationalizing and focusing research efforts at the EU level in facing the great challenge of translating nanomedicine in cancer, one of the main human pathologies burdening society. Thanks to its quality, the Action network will also generate key research teams of excellence for funding applications, patent fulfillment and discoveries of high scientific impact. The network will also be actively dedicated to raising awareness of the great potential of nanomedicine through publications in international peer-reviewed journals and presentations at open events.

INSTITUTION (Leader)	PROJECT	DURATION
Vienna BioCenter Core Facilities, Vienna, Austria (A. Walter)	Correlated Multimodal Imaging in Life Sciences (COMULIS, CA 17121)	2018–2022

IMROH ASSOCIATES: D. Karaica (Management Committee Member, Member of Board for ITC grants) and I. Vrhovac Madunić (Management Committee Member, Coordinator of Board for ITC grants, Grant Awarding Coordinator)

The last meetings of the Management committee and working groups were held, which concluded all project activities, and the Conference Correlated Multimodal Imaging - enabling discoveries from atoms to anatomy was held (September 20–22, 2022, Nicosia, Cyprus). During 2022 four virtual mobilities and four Short-Term Scientific Missions were approved. Furthermore, with collaborators from this project, the COST action (as a secondary proposer) "Human metal exposure and health - in the present and in the past" was submitted.

INSTITUTION (Leader)	PROJECT	DURATION
National Institute of Occupational Health, Oslo, Norway (I. S. Mehlum)	Network on the coordination and harmonisation of European occupational cohorts (OMEGA-NET, CA16216)	2017–2022

IMROH ASSOCIATES: J. Macan and A. Bjelajac (Management Committee members), Zr. Franić

Action was closed in April 2022. The main accomplished aim is established network of scientists to optimize the usage of cohorts from working and general population in Europe. The databases with joint data from various European cohorts from working and general populations were formed, and they are available for further research to European scientists. Associates of this Unit were involved in working groups focused on prevention of occupational skin diseases, mental disorders related to work, and occupational exposure to COVID-19 infection. The work of the expert group for the creation of job-exposure matrix for occupational exposure to UV radiation in Europe were presented in 2022 (254).

16.2.A.2. Other european and international collaborations

EUROPEAN SLEEP RESEARCH SOCIETY
International collaboration without founding



ESRS with European Sleep Research Society Sleep Research and Sleep Medicine in Europe

INSTITUTION (Leader)	PROJECT	DURATION
International COVID-19 Sleep Study Collaboration Group (ICOSS-2)	ICOSS 2 nd Survey: Sleep disorders related to coronavirus infection and confinement during COVID-19 Pandemic (ICOSS-2)	2021–2022

IMROH ASSOCIATES: A. Bjelajac (leader for Croatia), J. Macan, S. Cvijetić Avdagić, P. Tomac, J. Mandić, B. Ross Partners: 31 coordinators from 19 states worldwide

The purpose of launching the ICOSS research collaboration was to harmonize the instruments and methods of gathering knowledge on various aspects of sleep and adult health during the COVID-19 pandemic, to allow a valid comparison of results collected in different countries. The goal of the ICOSS-2 study was to determine the prevalence and incidence of sleep disorders and coronavirus-related symptoms and to analyse the effects of infection independently of other effects of the COVID-19 pandemic. Data of 15,813 adult participants have been collected through online survey in 17 countries throughout the world. The results have been systematically analysed under different hypotheses in a coordinated way within the collaboration. Two papers have been published in 2022: one analysing the relationship between sleep symptoms and long COVID (113) and the other analysing increased risk of severe COVID-19 in shiftworkers (103). The study has no additional financial support.

16.2.A.3. UNITED NATIONS ENVIRONMENT PROGRAMME (UNEP) International Atomic Energy Agency (IAEA) (3 projects)



INSTITUTION (Leader)	PROJECT	DURATION
Department of Nuclear Sciences and Applications (C. E. Jimenez Velasco)	Improving Environmental Monitoring and Assessment for Radiation Protection in the Region (TC RER7014)	2020–2024

IMROH ASSOCIATES: I. Prlić (leader), T. Bituh

The objectives of the project are to contribute to the radiological protection of the public and environment in different exposure settings in the region. Project activities: 1. Building technical and managerial expertise in analytical and sampling techniques for radionuclide analysis. 2. Review the status of environmental radiation monitoring programmes and technical capabilities. 3. Increasing awareness, visibility and outreach. 4. Drafting country project action plans to establish or optimize environmental radiation monitoring programmes. 5. Develop capacities in designing and implementing environmental monitoring programmes. 6. Participate in IAEA Proficiency Tests (PT) on radionuclide measurement. 7. Develop and apply QA/QC procedures. 8. Conduct data analysis, interpretation, reporting and communication. 9. Develop recommendations for improving the legal framework and regulations for environmental radiation monitoring.

INSTITUTION (Leader)	PROJECT	DURATION
Department of Nuclear Sciences and Applications, IAEA Laboratories Seibersdorf, Austria (R. Padilla Alvarez)	Determining Long Term Time Trends of Air Pollution Source Tracers by Nuclear Techniques (TC RER/7/012)	2020–2022

IMROH ASSOCIATES: I. Bešlić, S. Davila, R. Godec

Project RER/7/012 "Determining long term time trends of air pollution source tracers by nuclear techniques (RER/7/012)" started as a continuation of the previous three-year project "Enhancing the Inventory of Aerosol Source Profiles Characterized by Nuclear Analytic Techniques in Support of Air Quality Management" (RER/7/011). The project started in 2020 and officially ended in 2022 with the final meeting in Vienna on 21–25 November 2022. The collection of the PM_{2.5} fraction of particulate matter for the RER/7/012 project started at the IMROH air quality monitoring station on 1 April 2020. Since then, daily PM_{2.5} samples had been collected on Teflon filters every third day (121). Filters and Petri dishes were distributed by IMROH as in previous projects. In 2021 and 2022, IMROH also provided elemental analysis of over 2000 samples collected in participating countries, including Portugal, Bulgaria, Lithuania, Cyprus, Tajikistan, Moldova, Slovenia, Montenegro, Bosnia and Herzegovina, Serbia, and North Macedonia. The conclusion of the final meeting in Vienna was to extend sample collection until April 2023. Data collection and processing for airborne particle content (black carbon, elemental and organic carbon, elemental composition) will continue until mid 2023. The obtained results will be used to compare the differences in the dominant contributions of air pollution between participating countries and will be published as scientific papers.

INSTITUTION (Leader)	PROJECT	DURATION
Environmental Radioactivity Monitoring Department Greek Atomic Energy Commission, Athens, Greece (K. Karfopoulos)	Enhancing Regulatory and Metrological Infrastructures Needed to Ensure Radiation Safety in Naturally Occurring Radioactive Materials Industry (TC RER9155)	2019–2024
IMROH ASSOCIATE: I. Prlić		

The objectives of the project are to enhance the MS regulatory and metrological infrastructures in reference to industries involving NORM ensuring the radiation protection of the workers and the environment in compliance with the IAEA BSS.

16.2.A.4. GOVERNMENT PROJECTS



National Institutes of Health (NIH), USA

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (Z. Kovarik) University of California at San Diego, La Jolla, USA (Z. Radić)	<i>In vivo</i> efficacy of novel uncharged bis-oximes in OP poisoning treatment	2022–2024

IMROH ASSOCIATES: D. Kolić, N. Maček Hrvat

Biochemical characterization of neutral bisoximes as reactivators of cholinesterase inhibited by organophosphorus compounds (OP) has begun. Due to their physico-chemical properties, three oximes are expected to be effective reactivators in the central nervous system and contribute to the protection of the nervous system from the long-term consequences of OP poisoning.

Ministry of Science and Education, Republic of Croatia Scientific and Research Bilateral Cooperation in Science and Technology (9 projects)

MINISTARSTVO ZNANOSTI I OBRAZOVANJA REPUBLIKE HRVATSKE

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (I. Vrhovac Madunić) Institute for Pharmacology, University Medicine Greifswald, Germany (M. V. Tzevtkov)	Identifying interactions of renal and hepatic organic cation transporters (OCTs) with oximes, antidotes in treatment of organophosphate poisoning (Bilateral CRO-DE)	2022–2023

IMROH ASSOCIATES: T. Čadež, M. Katalinić, Z. Kovarik, J. Madunić, A. Zandona

We planned new research activities of studying interaction of membrane transporters OCTs and oximes/antidots in the treatment of organophosphate poisoning. According to the project plan, we selected 2 known and 3 newly synthesized oximes for detailed evaluation of transport experiments in HEK293 kidney cells. At the Institute of Pharmacology in Greifswald (Germany), an LC-MS/MS method was modified and established for precise quantification of relatively small amounts of oxime, which is crucial for transport and inhibition experiments. In July 2022, Dr Marleen J. Meyer (Institute for Pharmacology, Centre of Drug Absorption and Transport, University Medicine Greifswald, Germany) stayed at IMROH, where she introduced us to methods of oxime transport and inhibition in OCT1 transfected HEK293 cells with the aim of introducing the method at the Institute. At the end of September 2022, we held the 1st kick-off meeting in Croatia where we discussed the obtained results. All details of processing the obtained results, planning future experiments, and writing scientific publications were agreed upon.

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (M. Katalinić) Institute for Pathophysiology, University of Ljubljana, Ljubljana, Slovenia (S. Pirkmajer)	Effect of oxime analogues on skeletal muscle cell viability (Bilateral CRO-SI)	2020–2023

IMROH ASSOCIATES: A. Bosak, A. Matošević, N. Maraković, I. Vrhovac Madunić, A. Zandona

This project was extended due to the specific situation caused by Sars-Cov2 pandemic and other unexpected circumstances and during this year we finalised planned research and visits. We evaluated the effects of newly synthesised oxime analogues (antidotes to toxic organophosphorus compounds poisoning) on muscle cells and effects on the specific cell targets. We tested several groups of oxime analogues on different stages of muscle tissue development, to perform a wider analysis of potential effects. Furthermore, we determined the structural characteristics of these compounds triggering certain effects. The obtained results were presented in 2022. on several conferences (207, 233) and in one published scientific paper (97).

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (Z. Kovarik) Research Center for Eco- environmental Sciences, Chinese Academy of Sciences, Beijing, China (Q. Xie)	Effects of selected pesticides on neuronal acetylcholinesterase expression (Bilateral CRO-CN)	2020–2022

IMROH ASSOCIATES: T. Čadež, M. Katalinić, A. Zandona

Our collaboration focused on several pesticides (metamidophos and fenamiphos) and their toxicity and whether their toxicity depends on the interaction with acetylcholinesterase or depends on its expression. The paper is in preparation with the first research results. Due to the pandemic, it was not possible to hold the planned visits, so the meetings were held via Zoom.

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (I. Vinković Vrček) Faculty of Electrical Engineering and Computer Science, University of Maribor, Slovenia (S. Gorgieva)	Modified bacterial cellulose as artificial biomimetic membrane for biological blood-brain barrier (Bilateral HR-SI)	2020–2022

IMI: R. Barbir, K. Ilić, B. Pem, I. Pavičić, N. Peranić, N. Kalčec

The blood-brain barrier (BBB) plays a major role in maintaining homeostasis within the central nervous system, as it acts as a dynamic barrier to the brain, protecting it from toxic substances coming from the bloodstream. Its complex function is made possible by tight junctions between microvascular endothelial cells of the brain, which inhibit the passage of specific molecules physically on the one hand and inactivate some drugs and neurotransmitters by enzymatic action on the other. In addition to these protective functions, the BBB limits the penetration of some drugs that target the brain, for example during the treatment of neurodegenerative diseases and brain tumors. During the development of such drugs, it is necessary to evaluate their quality, efficacy and safety using different in vitro and in vivo approaches. One of the important steps during such testing is the application of a relevant in vitro mimetic BBB model. So far, extensive research has been carried out in the development of such models as a drug permeability testing platform to reduce costs and use animals. Ideally, an in vitro model can speed up the entire assessment process. However, the existing (commercial) system model has several obstacles. One of the biggest, but not the least, obstacles in the application of in vitro models for the BBB is the adsorption and/or permeability of tested compounds such as various nano-enabled materials, when material sticking and membrane clogging may occur during the transport process. The proposed project aims to develop a new and more efficient in vitro BBB system based on the inclusion of bacterial cellulose (BC) as a basement membrane. The main output of the project will be a detailed strategy for the development of an effective in vitro BBB model that can be applied to test nano-enabled drug delivery systems. This bilateral project also represents the beginning of joint research activities between both groups in the field of bio- and nano-medical research that rely on the continuation of the "proof of concepts" already established within both groups. The results obtained are expected to complement the initiated FET OPEN project (which is in the preparation phase), as well as to serve as a background in the upcoming call for research, linked to the Health, Well-being and Demographic Change program under Horizon 2020, as well as after Horizon EUROPA, not excluding other grant schemes, such as M.Era.Net and COST actions. Dissemination channels (conference presentation, workshops) will be used as a formal tool for data exchange, as well as a critical review of the obtained results. Nevertheless, the project is also a great opportunity for the early-stage researchers involved to develop their careers within an international collaborative environment, together with people from different cultural, socioeconomic, and educational backgrounds.
INSTITUTION (Leader)	PROJECT	DURATION
Faculty of Pharmacy and Biochemistry, Zagreb (AM. Domijan) National Institute of Biology, Ljubljana, Slovenia (M. Filipič)	Toxicological profile and interactions of bisphenol A and its analogues (BPAnalogInteract, Bilateral CRO-SI)	2020–2022

IMROH ASSOCIATES: G. Gajski, M. Gerić, K. Matković

The aim of the project is to examine the toxicity and toxicity mechanisms of BPA and its analogues, BPS, BPF and BPAF individually, but also in combination on a human cell model. Primary human peripheral blood lymphocytes and human liver cancer cells (HepG2) will be used in *in vitro* studies. Cytogenetic, molecular biological and biochemical methods will be applied in the research, in order to monitor cell damage, cell genome damage, changes in gene expression, effect on the cell cycle, and oxidative stress parameters.

INSTITUTION (Leader)		DURATION
IMROH, Zagreb (I. Vinković Vrček) Chinese Academy of Sciences, Beijing, China (S. Liu)	Endocrine disrupting mechanism of typical environmental pollutants (EmergeTox, Bilateral CRO-CN)	2020–2022
IMROH ASSOCIATES: I. Pavičić, R. Barbir, K. Ilić Partner: KBC Osijek (Ž. Debeljak)		

Nanopharmaceuticals have the potential to stimulate the scientific and technological development of EU Member States, offering major clinical and socioeconomic benefits to society as a whole, industry and key stakeholders, and ultimately to patients. Affordable and advanced testing, manufacturing facilities and services for new nano-medicines are the main prerequisites for the successful implementation of these developments to further strengthen growth and innovation capacities. The establishment of current good manufacturing practice (GMP) in nano-pharmaceutical production is a key step for the successful transfer of nano-medicines from the laboratory to the industrial level, and clinical practice. Due to the lack of resources to implement GMP production, the development and production of innovative nano-medicines continues to be a challenge for the main players in the nanomedicine market in the EU, start-ups and SMEs. In order to enable the successful application of nanomedicines in the field of medicine, it is urgently necessary to establish an Open Innovation Test Bed (OITB) based on scientific achievements and regulatory rules. The goal of the PHOENIX project is to enable the smooth, timely and cost-effective transfer of nano-medicines from the laboratory to clinical trials by providing an advanced, affordable and easily accessible PHOENIX platform. The PHOENIX platform will offer a consolidated network of laboratories, manufacturing facilities, technologies, services and expertise for all aspects of technology transfer, from characterization, testing, verification to final products compliant with GMP manufacturing and regulatory guidelines. The PHOENIX platform will develop and establish new facilities and upgrade existing ones to make them available to SMEs, start-ups and research laboratories for scale-up, GMP manufacturing, and nano-medicine testing. Services and expertise provided by OITB will include manufacturing and characterization under GMP conditions, safety assessment, regulatory compliance, and commercialization enhancement.

IMROH, Zagreb (G. Gajski) Vinča Institute of Nuclear Science, University of Belgrade, Serbia (M. Čolović)Acetylcholinesterase Inhibitors as Potential Anti- Alzheimer Drugs: Prooxidative and Cytogenotoxic Properties (SafeAChE, Bilateral CRO-RS)2019-	2022

IMROH ASSOCIATES: M. Gerić, M. Milić

SafeAChE will evaluate pro-oxidative and toxic effect of newly synthesized polyoxometalate compounds exhibiting an inhibitory effect on AChE; a targeted enzyme of drugs used as symptomatic therapy in patients with Alzheimer's disease.

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (S. Herceg Romanić) Institute of Physics, University of Belgrade, Serbia (G. Jovanović)	Persistent organochlorine compounds in human milk and their potential effect on the level of primary DNA damage in human cells (Bilateral CRO-RS)	2019–2022

IMROH ASSOCIATES: D. Želježić, D. Klinčić, G. Mendaš Starčević

The planned research was completed, and the results were published in five publications (scientific paper, two book chapters, extended summary, master's thesis) in 2020 and 2021. New research started with the aim of assessing the risk to human health by researching the resorption of persistent organochlorine compounds, macroand micro-elements in the human body (infant formula) with samples of mother's milk. The results are in the process of evaluation, and the first publication on the development of *in vitro* method is being prepared

INSTITUTION (Leader)	PROJECT	DURATION
Ruđer Bošković Institute, Zagreb (S. Orlić) Chinese Academy of Sciences (A. Hu)	Distribution of antibiotic resistance genes in waste water treatment plants and receiving environments of China and Croatia (Bilateral CRO-CN)	2019–2022

IMROH ASSOCIATE: G. Gajski

The project goal is to evaluate the types and concentrations of typical new organic pollutants in the coastal cities and the receiving environment and their temporal and spatial distribution characteristics, migration patterns and country differences. The abundance and community composition of typical antibiotic resistance genes in sewage plants and receiving environments in the two countries and their temporal and spatial distribution characteristics, migration patterns and country differences. Besides, the project will clarify the coupling relationship between new organic pollutants and antibiotic resistance genes and assess ecological risk.

16.2.A.5. UNIVERSITY PROJECTS (2 projects)

INSTITUTION (Leader)	PROJECT	DURATION
UConn Health, University of Connecticut, Farmington, USA (I. Kalajzic)	Generating new RGS5 mouse model for lineage tracing	2019–2023

IMROH ASSOCIATE: I. Vrhovac Madunić

The project started in 2019/2020 during the postdoctoral training of I. Vrhovac Madunić in the Laboratory of prof. I. Kalajzić in Connecticut, USA. Generating a new transgenic mouse (RGS5-CreERT2) suitable for lineage tracing in bone remodeling and regeneration is important for determining cell origin and fate. The aim of the project is to assess whether the RGS5 mouse model is suitable for defining mesenchymal progenitor cells, i.e. to identify perivascular cells within the periosteum *in vitro* and *in vivo*. Some of the results of this project were presented at the *Annual conference The American Society for Bone and Mineral Research (ASBMR)* 2022 and abstract was published in the *WoS*-indexed journal (253). The results of this study were also summarized in the scientific article accepted for publication in 2023 (114).

INSTITUTION (Leader)	PROJECT	DURATION
Department of Genetics, Kemerovo State University, Kemerovo, Russia (V. Druzhinin)	Relationship of the respiratory microflora composition with the human genome activity and integrity in the residents of coal industrial region	2018–2023

IMROH ASSOCIATE: A. Fučić

The susceptibility for lung cancer (LC) is modified by genetic variations in xenobiotic detoxification and DNA repair capacity The aim of the study was to investigate the association between *GSTM1* (deletion), *APEX1* (*rs1130409*), *XPD* (*rs13181*) and *NBS1* (*rs1805794*) gene polymorphisms and LC risk in patients who worked in coal mines. The

study included 395 underground miners and 244 healthy men who do not work in industrial enterprises. The results show that polymorphisms of *APEX1* (recessive model: $OR_{adj} = 1.87$; CI 95%: 1.01-3.48) and *XPD* (log additive model: $OR_{adj} = 2.25$; CI 95%: 1.59-3.19) genes were associated with increased LC risk. *GSTM1* large deletion I was linked with decreased risk of LC formation ($OR_{adj} = 0.59$, CI 95%: 0.36-0.98). The multifactor dimensionality reduction method for 3-loci model of gene-gene interactions showed that the *GSTM1* (large deletion)-*APEX1* (*rs1130409*)-*XPD* (*rs13181*) model was related with a risk of LC development (59).

16.2.B. EDUCATIONAL AND SCIENCE POPULARIZATION PROJECTS

European Union programs

European Social Fund

INSTITUTION (Leader)	PROJECT	DURATION
Croatian Judo Federation, Zagreb (R. Kerep)	About science through sport (STEMsport, UP.04.2.1.10.0160)	2022–2024

European Union

European Social Fund

IMROH ASSOCIATES: S. Stipičević (coordinator), I. Vrhovac Madunić, M. Kujundžić, Zr. Franić, S. Žunec, V. M. Varnai, L. Božičević; consultants: J. Macan, I. Brčić Karačonji, I. Vinković Vrček

Partners: IMROH, Zagreb; Institute for Popularization of Science, Zabok; Professor Baltazar Association, Zagreb; Elementary school of Dr. Ante Starčević, Zagreb

Project grant: 322.867.45 EUR

The STEMsport project aims to strengthen the capacities of civil society organizations through cooperation with higher education institutions for their active participation in informal STEM education of society. As part of the project, 35 trainers and popularizers of science will be educated, who will promote and promote STEM knowledge and skills through sport (judo) to children and young people and the general population during multi-day and one-day popularization events throughout the Republic of Croatia. Educators will perform activities in an innovative and interactive way using exhibits that will be produced for the needs of this project and by conducting a series of useful workshops. During 2022, several meetings of partner coordinators and promotional activities were held: "Science show" as part of the Scientific Picnic in Gornja Stubica, (Sep 2022), kick-off conference in Zagreb (Oct 2022), CARNet Users Conference CUC 2022 in Šibenik (Oct 2022). IMROH is in charge of designing and preparing educational materials for the education of STEMsport educators, which include the creation of STEMsport curriculum, manuals and presentations. Six topics from the field of IMROH's research activities have been selected for training of the STEMeducators, covering toxicology, biochemistry, ecology, nutrition and public health. More about the project: https://judo.hr/stemsport/.

INSTITUTION (Leader)	PROJECT	DURATION
Croatian Society of Natural Sciences, Zagreb (N. Bilić)	Rivers of knowledge (UP.04.2.1.10.0112)	2021–2023

IMROH ASSOCIATES: S. Stipičević (coordinator) and other researchers according to their availability Partners: IMROH, Croatian Chemical Society, Association for Nature, Environment and Sustainable Development Sunce, Docendo discimus Association, Science Factory, Klikeraj Association, Association for the Promotion of Natural Sciences, Mediterran Institute – Association for the Cultural and Scientific Study of the Mediterranean, Croatian Association for Information, Communication and Electronic Technology – MIPRO, Karlovac Mixed Industrial and Craft School (until June 2022), Duga Resa High School (since June 2022)

Project grant: 387,308.57 EUR

The objectives are to strengthen the capacities of nine civil society organizations in order to implement science popularization activities and to raise awareness of the impact of science on everyday life, especially among children and young people. The project is planned to educate 36 popularizers of science in the fields of physics, chemistry, and environmental protection to conduct more than 100 workshops and hold about 50 professional lectures for children, young people and the general public, and to create a permanent display of interactive content at Duga Resa High School. The project will be implemented throughout Croatia. During the year, the partner school was changed, where permanent interactive exhibits for STEM workshops has to be set up, and the training of new popularizers of science began. IMI prepared a dozen expert topics from the field of its research for the implementation of one-day workshops for the education of new popularizers and the general public. More about the project: https://www.rijekeznanja.info/



Erasmus+

INSTITUTION (Leader)	PROJECT	DURATION
Institut National Polytechnique de Toulouse, Toulouse, France (B. Pourrut)	Toxicology Innovative Learning for Europe (ToxLearn4EU, ref. 2021-1-FR01-KA220-HED-000030081) Cooperation partnerships in higher education	2022–2025

IMROH ASSOCIATES: G. Gajski, M. Gerić, M. Milić, K. Matković

Partners: 11 partners from Europe

Project grant: 399,998.00 EUR

The Erasmus ToxLearn4EU project aims to modernize of Toxicology and Ecotoxicology teaching in Europe and has several objectives and target audiences: - develop and use innovative and free educational resources (interactive courses, online PBL) in order to develop high quality digital education; - provide innovative content on current hot topics in the field of toxicology/Ecotoxicology to fit with recent evolution of European Policy (Action Plan: "Towards Zero Pollution") and with job market needs;- stimulate interest of students for those fields and limit school dropout by putting students back at the centre of teaching through the use of active pedagogies adapted to digital practice to recreate interactions between students, between students and teachers, and by stimulating their motivation through playful approaches (156).

INSTITUTION (Leader)	PROJECT	DURATION
Serbian Society of Toxicology, Belgrade, Serbia (D. Đukić-Ćosić)	Meet the Toxicity – Live Safely (MeeTox, ref. 2022-1-RS01-KA210-ADU-000083718)	2021–2023

IMROH ASSOCIATES: S. Stipičević (coordinator), D. Rašić (coordinator), IMROH's Poison Control Center and other CST members (M. Peraica, I. Brčić Karačonji, M. Dvoršćak, Zr. Franić, M. Gerić, K. Jagić, A. Jurič, A. Katić, D. Klinčić, N. Kopjar , M. Lazarus, A. Sulimanec Grgec, B. Tariba Lovaković, A. Pizent, S. Žunec, A. Katić) Partners: IMROH, Faculty of Pharmacy, University of Belgrade, Serbia, Croatian Toxicoogical Society (CTS)

Project grant: 60,000.00 EUR

The goal of the project is to create online, self-learning materials about toxicity, to hold webinars, and, if possible, to organize also live lectures. Since basic knowledge about toxicity properties is not included in school plans and programs and the knowledge of the general public is deficient, and the progress of technology and the wide availability of information through social networks often leads to inaccurate information about the toxicity of chemicals and potential risk, it is important to examine the understanding of the general public about knowledge of toxicity chemicals from everyday use (medicines, cosmetics, hygiene and cleaning products, pesticides) and those that we often encounter when reading declarations. Education regarding such chemicals will be mainly aimed at pregnant and lactating women and teachers. The kick-off meeting was held virtually in November and the next one was held live in mid-December in Zagreb, where partners exchanged their experience in public opinion research and adult education. The activity plan was adopted and the first mini-symposium of the MeeTox project was announced to be held during the 13th congress of the Association of Toxicologists of Serbia and the 1st TOXSEE regional conference (Mav 10-12. 2023. Belgrade. Serbia). More about the project: https://www.imi.hr/hr/2023/06/02/meetox-meet-the-toxicity-live-safely-erasmus/

16.2.C. PROFESSIONAL PROJECTS

PROJECT	CONTRACTOR	LEADER	
Service provider: Radiation Dosimetry and Radiobiology Unit			
ENA – European NORM association. A joint project between EAN NORM & European ALARA Network. Continuation of TREN/H4/51/2005 of the European Commission (EC) (since 2017)	IAF-Radioökologie GmbH, Dresden, Germany https://ena-norm.eu/	I. Prlić (for CRO) L. Pavelić	

17. PROFESSIONAL UNITS



17.1. LABORATORY ANIMAL UNIT

EMPLOYEES OF THE UNIT

HEAD Vedran Micek, DVM, professional associate

TECHNICAL ASSOCIATES

Kata Šmaguc, technician until 31 Aug 2022 Patricija Topol, veterinary technician since 1 Dec 2022

PROFESSIONAL WORK

The Laboratory Animal Unit of the Institute breeds laboratory rats, strain HsdBrlHan: Wistar, in accordance with the Animal Welfare Act (OG 102/17) and other applicable laws, guidelines, and policies. Animals are bred under strictly controlled conditions, under surveillance of authorised personnel (DVM), and then used as a model in scientific and experimental research. The Unit has facilities that are consistent with legislation and guidelines concerning the breeding and housing of laboratory animals. From 2016, the Laboratory Animal unit is authorized for performing *in vivo* experiments for a ten-year period. The living conditions of animals are appropriate and contribute to their health and welfare. The housing, feeding, animal care and experimental procedures are managed by a veterinarian in accordance with contemporary veterinary practices. The animals are kept in steady-state micro environmental conditions and fed with standard GLP certified laboratory food and water *ad libitum* with altering 12 h light and dark cycles. Sanitation of facilities is performed on a weekly basis in order to reduce the possibility of any external contamination. Breeding colony health monitoring is provided by the Croatian Veterinary Institute Zagreb.



17.2. POISON CONTROL CENTRE

EMPLOYEES OF THE CENTRE

HEAD

Željka Babić, PhD, research associate Prof Selma Cvijetić Avdagić, MD, PhD, acting head since 1 Jun 2022

ASSOCIATES

Rajka Turk, MSc, professional advisor in science until 28 Feb 2022, as external associate since 1 Mar 2022 Researchers of the Occupational and Environmental Health Unit (Chapter 15.5.). Researchers of the Analytical Toxicology and Mineral Metabolism Unit (Chapter 15.1.)

PROFESSIONAL WORK

During 2022, the telephone information service of the Croatian Poison Control Center (CPCC) was consulted for 3086 cases of poisoning and suspected poisoning, by health professionals and the general public. Following requests from the industry, 63 toxicological evaluations were prepared for the registration of pesticides according to the Plant Protection Products Act and Regulation (EU) No. 1107/2009 on placing of plant protection products on the market. Following enquiries from the industry, 8 evaluations for the purpose of biocidal products registration and 4 for the authorization according to the Biocidal products Act and Regulation (EU) No. 528/2012 concerning the placement on the market and use of biocidal products were prepared.

Collaboration with the Agency for Medicinal Products and Medical Devices of Croatia in monitoring of drug poisonings (pharmacovigilance) was continued. Further work on the revision of the National Action Plan for sustainable use of pesticides and on the draft proposal for an ordinance on the conditions of distribution and sale of pesticides was continued with the Ministry of Agriculture. Collaboration with the MINISTRY of Labour, Pension System, Family and Social Policy on the amendments of the Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work also continued.

Opinion on a dossier proposing harmonised classification and labelling at the EU level for cyclohex-3-ene-1-carbaldehyde derivatives (the Opinion was adopted in September 2022 but has not yet been published on the official ECHA website) was prepared for the European Chemicals Agency (ECHA) by the Committee for Risk Assessment's rapporteur.

Annual reports continued to be published in the journal *Archives of Industrial Hygiene and Toxicology* in English and Croatian (155).

A professional paper on occupational poisonings recorded at the CPCC in 2021 was published (119).

Results of the monitoring of the number and characteristics of disinfectant and antiseptic poisonings in Europe, organized by the COVID Working Group at the European Association of Poison Control Centers and Clinical Toxicologists, were published (26). The characteristics of poisonings that were treated with antidotes and for which the CPCC was consulted in 2021 were presented at the EAPCCT annual congress in the form of a poster presentation (237).

At the request of the Ministry of Agriculture of the Republic of Croatia, a contact person (Veda M. Varnai, MD, PhD) was appointed for the exchange of information in order to apply for non-refundable financial assistance from the European Commission for participation in work related to plant protection products and biocidal products.

The CPCC staff participated in the undergraduate and graduate teaching of toxicology courses at the Department of Biotechnology, University of Rijeka and the Faculty of Metallurgy, University of Zagreb, and in the courses of clinical and industrial toxicology for medical doctors. In addition, CPCC was involved in the creation of educational materials for continued education and training of exterminators, for deratisation, disinsection and disinfection (DDD), on the topic of toxicological properties and clinical picture of poisoning with the most commonly used disinfectants, insecticides, fumigants and rodenticides (142).

18. RESEARCH AREA ŠUMBAR

HEAD

Josip Tončić, DVM, MSc, professional associate in science

PROFESSIONAL WORK

The Research Area Šumbar is home to activities related to the control, preservation, and improvement of the ecosystem. During 2022, activities continued with regard to research into the quality of water, air, and soil, as well as background ionising radiation and, if needed, biological samples in correlation with natural and anthropogenic pollution, all with the fundamental goal of preserving human and animal health and maintaining a healthy habitat.

Šumbar's cooperation with the Environmental Hygiene Unit and Radiation Dosimetry and Radiobiology Unit continued through planned air quality monitoring and monthly water sampling as well as measurements of its total sediment matter and metal and polycyclic aromatic hydrocarbon content. The monitoring of background ionising radiation continued by means of the referent station installed at the Area, which measures environmental data and delivers results wirelessly to the central base.

Furthermore, Šumbar is a hunting ground where all legally prescribed measures related to the management of wildlife habitats are strictly adhered to. This includes the maintenance of hunting grounds, regular feeding of animals, and monitoring protected species according to the instructions of the Ministry of Environmental and Nature Protection. Aided by the local forestry department, we strive to preserve the wildlife habitats and implements all measures set by the Ministry of Agriculture.

19. COMPANY OF THE INSTITUTE

Occupational Health Polyclinic of the Institute for Medical Research and Occupational Health Ltd., Ksaverska cesta 2, Zagreb

DIRECTOR

Prim Jelena Macan, MD, PhD, permanent scientific advisor (90% of working hours at the IMROH, 10% at the Polyclinic)

ASSOCIATE

Franka Šakić, MSc, senior professional associate in science (90% of working hours at the IMROH, 10% at the Polyclinic)

BUSINESS RESULTS

The professional activity of the Occupational Health Polyclinic of the Institute for Medical Research and Occupational Health Ltd continued operating in 2022 providing services in the domain of occupational and sports medicine. The outpatient clinic provided a total of 160 medical services for 70 customers. An occupational medicine specialist delivered 10 judicial-medical expertises for the Administrative Courts in Zagreb and Rijeka, Municipal Courts in Šibenik, Slavonski Brod and Zlatar, and the Municipal Civil Court in Zagreb. The Psychotherapy Office led by Adrijana Bjelajac, PhD, psychologist and psychotherapist, continued working within the company. The company operated positively in 2022.

20. PUBLISHING

The Institute is the publisher of the scientific journal *Archives of Industrial Hygiene and Toxicology*; print: ISSN 0004-1254, online: ISSN 1848-6312. The *Archives* is issued four times a year.



General information about the journal

Articles from the fields of occupational health, toxicology, ecology, chemistry, biochemistry, biology, pharmacology, and psychology are edited in line with modern standards. The journal's publication is financially supported by the Ministry of Science and Education and, to a smaller extent, subscriptions.

Year	IF	5-years IF
2021	2.078	2.804
2020	1.948	2.172
2019	1.727	1.777
2018	1.436	1.606
2017	1.117	1.335
2016	1.395	1.320
2015	0.971	1.019
2014	0.932	1.120
2013	0.727	0.980
2012	0.674	-
2011	1.048	-
2010	0.826	-

The Archives is indexed in SCI-Expanded, Medline/PubMed, Scopus, and many other databases. The Impact Factor (IF) for 2022 was 2.078, which is the highest IF value since the journal was listed in InCites Journal Citation Reports (Clarivate Analytics). The 5year IF was 2.804, which is the highest value ever achieved in the journal's history. The Archives is currently ranked within the fourth Quartile (Q4), both in the Toxicology area and the Public, Environmental & Occupational Health area.

The citation of the *Archives* in 2022 was very good. As of 2 Jan 2023, the Web of Science database recorded 7,464 citations of articles published since 2008, when the journal was included in the database to date. The h-

index of the Archives for the period 2008–2022 according to the Web of Science database is 34.

During 2022, the Editorial Office of the *Archives* received 82 submissions, most of which were submitted through the journal's online system available at https://arhiv.imi.hr and the remainder by e-mail (arhiv@imi.hr). Most of the submissions covered topics from toxicology. Most of the manuscripts received (89 %) referred to original scientific papers.



Distribution of articles submitted in 2022 according to research areas

The manuscripts were submitted by authors from 22 countries. The largest number of manuscripts was submitted from Turkey (32%) and Croatia (18%), while other countries were represented by less than 5%.



Distribution of articles submitted in 2022 according to origin country

The rejection rate was 52% (43 of 82 manuscripts received were rejected). A larger proportion (64%) was rejected due to negative reviews, and the rest by the Editor-in-Chief or an Editorial Board decision because of poor quality or failure to meet the minimum criteria for review.

Each submission is screened for plagiarism by the iThenticate Plagiarism Detection Software. The contained Crossref Similarity Check is used to check the authenticity of a submission against a vast database of scientific literature published worldwide. Access to the aforementioned software system is enabled through the journal's cooperation with its online publisher Sciendo.

In 2022, four regular issues of Volume no. 73 were published, containing articles published in four categories: Original article (28), Review/Mini-Review (5), Letter to the Editor (2), Technical Paper (1). In addition to regular manuscripts, one short article in the category *In memoriam*, two project reports, three meeting reports, and one announcement for congress were also published.

In issue 2, abstracts of the symposium "Synergy at the chemistry-nanotechnology interface" (held on May 28, 2022 at the Faculty of Science, University of Zagreb) were published. In issue 4, summaries of the symposium "Power of Fungi and Mycotoxins in the Midst of Climate Change (PoFMy)" (held on September 16 and 17, 2022 at the University North, Koprivnica) were published.

In 2022, a redesign of the journal's cover page and layout was adopted, authored by the graphics editor A. Marković.



Cover pages of all regular Archives' issues published in 2022 (Volume 73)



In November 2022, a Supplement issue was published comprising abstracts from the 4th International Congress on Food Safety and Quality – "One Health", held in Dubrovnik on November 3–6, 2022. The issue was prepared for print by and M. Herman, while technical editing was done by I. Brčić Karačonji.

According to the attendance on the Portal of Scientific Journals of the Republic of Croatia (HRČAK) during 2022, the *Archives* holds a high position in relation to other journals in the fields of biomedicine and health and the natural sciences. The total number of visits to the *Archives* through the HRČAK website was 4,139,539 on 2 Jan 2023.

Throughout 2022, the journal continued to operate in accordance with high standards of editorial work comparable to foreign journals. The *Archives* is a regular member of the Committee on Publication Ethics (COPE) and the Editors are members of the Mediterranean Editors and Translators and European Association of Science Editors (EASE).

The regular publication of the journal, and its successful operation during 2022 was achieved by the enthusiasm of the Editorial Office, and due to their large number of working hours spent in daily activities such as language and technical editing, print layout preparation, maintenance of the online submission system and manuscript management, digitalization of old volumes, and other administrative affairs within the journal.

The journal is available free of charge to the foreign and domestic scientific public through the link https://hrcak.srce.hr/aiht (all regular issues published from 1946 to the present and the most important supplements are available). Full text articles in PDF format are available through Sciendo's service (https://content.sciendo.com/view/journals/aiht/aiht-overview.xml). Full text articles are also available on PubMed Central as well (https://www.ncbi.nlm.nih.gov/pmc/journals/3972/).

21. PRILOZI

A. OVLAŠTENJA INSTITUTA

- Ministarstvo zdravstva RH ovlaštenje za provođenje Programa specijalističkog usavršavanja doktora medicine u području medicine rada i sporta, u dijelu programa Profesionalne bolesti, bolesti u svezi s radom i profesionalna toksikologija. Ovlaštenje od prosinca 2018. vrijedi do izdavanja novog rješenja.
- Ministarstvo gospodarstva i održivog razvoja RH dozvola za obavljanje djelatnosti praćenja kvalitete zraka. Ovlaštenje vrijedi do 10. prosinca 2025.

Ministarstvo gospodarstva i održivog razvoja RH – dozvola za obavljanje djelatnosti osiguranja kvalitete mjerenja i podataka kvalitete zraka (referentni laboratorij) za metode:

- HRN EN 12341:2014 (EN 12341:2014): Određivanje masene koncentracije PM₁₀ i PM_{2,5} frakcije lebdećih čestica
- HRN EN 14902:2007 (EN 14902:2005), HRN EN 14902/AC:2007 (EN 14902:2005/AC:2006): Određivanje koncentracije Pb, Cd, As i Ni u PM₁₀ frakciji lebdećih čestica
- HRN EN 16909:2017 (EN 16909:2017): Određivanje masenih koncentracija elementnog i organskog ugljika u lebdećim česticama u vanjskom zraku
- HRN EN 15549:2008 (EN 15549:2008): Određivanje koncentracija benzo(a)pirena u vanjskom zraku
- HRI CEN/TR 16269:2017 (CEN/TR 16269:2011): Određivanje masenih koncentracija aniona i kationa u lebdećim česticama
- HRS CEN/TS 16645:2016 (CEN/TS 16645:2014): Određivanje koncentracija benzo(a)antracena, benzo(b)fluorantena, benzo(j)fluorantena, benzo(k)fluorantena, dibenzo(a,h)antracena, indeno(1,2,3-cd)pirena i benzo(ghi)perilena u vanjskom zraku
- HRN EN 16913:2017 (EN 16913:2017): Određivanje masenih koncentracija aniona i kationa u lebdećim česticama PM2,5 sakupljenim taloženjem na filtrima.

Ovlaštenje vrijedi do 10. prosinca 2025.

- Ministarstvo unutarnjih poslova, Ravnateljstvo civilne zaštite ovlaštenje za obavljanje poslova radiološke sigurnosti:
 - mjerenje operativnih dozimetrijskih veličina potrebnih za procjenu osobnog vanjskog ozračenja osoba
 - redovito godišnje ispitivanje zatvorenih radioaktivnih izvora i/ili električnih uređaja koji proizvode ionizirajuće zračenje u medicinskim djelatnostima i ispitivanje zatvorenih radioaktivnih izvora i/ili električnih uređaja koji proizvode ionizirajuće zračenje u nemedicinskim djelatnostima te davanje mišljenja na osnovi mjerenja i proračuna
 - radiološki nadzor mjesta rada i ispitivanje uvjeta rada te izrada dokumenata iz kojih je vidljivo udovoljava li radni okoliš, prostorije i uvjeti rada propisanim uvjetima radiološke sigurnosti
 - ispitivanje i praćenje vrste i aktivnosti radioaktivnih tvari u zraku, tlu, moru, rijekama, jezerima, podzemnim vodama, oborinama, vodi za piće, hrani i potrošačkim proizvodima i
 - ispitivanje koncentracije radona i radonovih potomaka u zraku.

Ovlaštenje vrijedi do 10. prosinca 2025.

Ministarstvo poljoprivrede RH – ovlaštenje za obavljanje analiza: hrana, hrana za životinje, prirodna mineralna, prirodna izvorska i stolna voda. Ovlaštenje od travnja 2016. vrijedi do izdavanja novog rješenja.

B. SURADNE USTANOVE

Sporazumi o suradnji

RED. BR.	NAZIV USTANOVE	GODINA POTPISIVANJA
1.	Institut za istraživanje i razvoj održivih eko sustava	2005.
2.	Medicinski fakultet Sveučilišta J. J. Strossmayera u Osijeku	2013.
3.	Sveučilište u Rijeci	2013.
4.	Sveučilište u Zagrebu	2013.
5.	Grad Zagreb	2014.
6.	Institut "Jožef Stefan"	2014.
7.	Nastavni zavod za javno zdravstvo "Dr. Andrija Štampar"	2014.
8.	Sveučilište u Mostaru	2014.
9.	Sveučilište u Zadru	2014.
10.	Veterinarski fakultet Univerziteta u Sarajevu	2014.
11.	Hemijski fakultet Univerziteta u Beogradu	2015.
12.	Hrvatski zavod za javno zdravstvo	2015.
13.	Institut za fiziku	2015.
14.	Ministarstvo unutarnjih poslova RH	2015.
15.	Agencija za lijekove i medicinske proizvode RH	2016.
16.	Ericsson Nikola Tesla d. d.	2016.
17.	Klinički bolnički centar Zagreb	2016.
18.	Rudarsko-geološko-naftni fakultet Sveučilišta u Zagrebu	2016.
19.	Sveučilište Sjever	2016.
20.	Grad Kaštela	2017.
21.	Nuklearna elektrana Krško	2017.
22.	Institut za hemiju, tehnologiju i metalurgiju, Beograd, Srbija	2018.
23.	Metalurški fakultet Sveučilišta u Zagrebu, Sisak	2018.
24.	Prirodno-matematički fakultet Univerziteta u Novom Sadu, Srbija	2018.
25.	Prirodno-matematički fakultet Univerziteta u Sarajevu, BiH	2018.
26.	Sveučilište Jurja Dobrile u Puli	2018.
27.	Javna ustanova "Park prirode Medvednica"	2018.
28.	Institut za higijenu i tehnologiju mesa, Beograd, Srbija	2018.
29.	AVANCO d. o. o.	2019.
30.	Prehrambeno-tehnološki fakultet Sveučilišta J. J. Strossmayera u Osijeku	2019.
31.	Medicinski fakultet Sveučilišta u Zagrebu	2019.
32.	Javna ustanova "Park prirode Kopački rit"	2019.
33.	Agronomski fakultet Sveučilišta u Zagrebu	2020.
34.	Fakultet medicinskih znanosti, Univerzitet "Goce Delčev", Štip, Sjeverna Makedonija	2020.
35.	Hrvatski geološki institut, Zagreb	2020.
36.	Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu	2020.
37.	Veterinarski fakultet Sveučilišta u Zagrebu	2020.
38.	Visoka škola Ivanić-Grad	2020.
39.	Institut za jadranske kulture i melioraciju krša, Split	2021.
40.	Međimursko veleučilište u Čakovcu	2021.
41.	Hrvatska agencija za poljoprivredu i hranu, Osijek	2021.
42.	Hrvatski zavod za javno zdravstvo, Zagreb	2021.
43.	Institut "Ruđer Bošković"	2021.
44.	Fakultet šumarstva i drvne tehnologije Sveučilišta u Zagrebu	2022.

Ostale znanstvenoistraživačke i stručne suradnje

USTANOVE U REPUBLICI HRVATSKOJ

- 1. Agencija za lijekove i medicnske proizvode (HALMED)
- 2. Agronomski fakultet Sveučilišta u Zagrebu
- 3. Aquatika slatkovodni akvarij Karlovac
- 4. CARNet, Zagreb
- 5. Državni hidrometeorološki zavod, Zagreb
- 6. Ekonerg d. o. o., Zagreb
- 7. Fakultet elektrotehnike i računarstva Sveučilišta u Zagrebu
- 8. Fakultet kemijskog inženjerstva i tehnologije Sveučilišta u Zagrebu
- 9. Fakultet šumarstva i drvne tehnologije Sveučilišta u Zagrebu
- 10. Fakultet zdravstvenih studija Sveučilišta u Rijeci
- 11. Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu
- 12. Fond za zaštitu okoliša i energetsku učinkovitost, Zagreb
- 13. Gekom d. o. o., Zagreb
- 14. Hrvatska agencija za poljoprivredu i hranu, Osijek
- 15. Hrvatski institut za istraživanje mozga, Zagreb
- 16. Hrvatski sindikat male privrede, obrtništva, uslužnih djelatnosti i stranih predstavništava, Zagreb
- 17. Hrvatski veterinarski institut, Zagreb
- 18. Hrvatski zavod za javno zdravstvo, Zagreb
- 19. Institut "Ruđer Bošković", Zagreb
- 20. Institut za antropologiju, Zagreb
- 21. Jamnica plus d. o. o.
- 22. Kaznionica u Lepoglavi
- 23. Klinička bolnica Merkur, Zagreb
- 24. Klinički bolnički centar Osijek
- 25. Klinički bolnički centar "Sestre milosrdnice", Zagreb
- 26. Klinički bolnički centar Zagreb (KBC Zagreb)
- 27. Klinika za dječje bolesti, Zagreb
- 28. Klinika za ženske bolesti i porode, KBC Zagreb
- 29. Medicinski fakultet Sveučilišta u Rijeci
- 30. Medicinski fakultet Sveučilišta u Zagrebu
- 31. Ministarstvo unutarnjih poslova RH, Ravnateljstvo civilne zaštite, Sektor za radiološku i nuklearnu sigurnost
- 32. Ministarstvo gospodarstva i održivog razvoja RH, Zagreb
- 33. Nastavni zavod za javno zdravstvo "Dr. Andrija Štampar", Zagreb
- 34. Nastavni zavod za javno zdravstvo Primorsko-goranske županije, Rijeka
- 35. Nezavisni sindikat znanosti i visokog obrazovanja, Zagreb
- 36. Odgojni zavod Turopolje, Velika Gorica
- 37. Odjel za biotehnologiju Sveučilišta u Rijeci
- 38. Petrokemija d. d., Kutina
- 39. Prehrambeno-biotehnološki fakultet Sveučilišta u Zagrebu
- 40. Prehrambeno-tehnološki fakultet, Sveučilište J. J. Strossmayera u Osijeku
- 41. Prirodoslovno-matematički fakultet Sveučilišta u Splitu
- 42. Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu
- 43. Sabor RH, Zagreb
- 44. Stomatološki fakultet Sveučilišta u Zagrebu
- 45. Sveučilište J. J. Strossmayera u Osijeku, Odjel za kemiju
- 46. Sveučilište u Zadru, Odjel za ekologiju, agronomiju i akvakulturu
- 47. Škola narodnog zdravlja "A. Štampar", Medicinski fakultet Sveučilišta u Zagrebu
- 48. Veterinarski fakultet Sveučilišta u Zagrebu
- 49. Zavod za javno zdravstvo Brodsko-posavske županije, Slavonski Brod
- 50. Zavod za javno zdravstvo Istarske županije, Pula
- 51. Zavod za javno zdravstvo Koprivničko-križevačke županije, Koprivnica
- 52. Zavod za javno zdravstvo Osječko-baranjske županije, Osijek
- 53. Zavod za javno zdravstvo Zadarske županije, Zadar

USTANOVE U INOZEMSTVU

- 1. Academic Medical Centre, Amsterdam, Nizozemska
- 2. Backweston Laboratory Campus, Ministarstvo poljoprivrede, hrane i pomorstva Republike Irske
- 3. Bundesamt fur Strahlenschutz, Salzgitter, Njemačka
- 4. Department of Biology and Pharmaceutical Botany, Medical University of Łódź, Łódź, Poljska
- 5. Fakulteta za kemijo in kemijsko tehnologijo Univerza v Ljubljani, Slovenija
- 6. Faculty of Science, University of Hradec Králové, Češka
- 7. Florida State University, Tallahassee, FL, SAD
- 8. Helmholtz Zentrum München Deutsches Forschungszentrum für Gesundheit und Umwelt, München, Njemačka
- 9. Hemijski fakultet Univerziteta u Beogradu, Beograd, Srbija
- 10. Hungarian Institute for Public Health, Budimpešta, Mađarska
- 11. Institut de Recherche Biomédicale des Armées, Brétigny-sur-Orge cedex, Francuska
- 12. Institut für Chemie, Universität Graz, Austrija
- 13. Institut für Physikalische und Theoretische Chemie, Technische Universität Graz, Graz, Austrija
- 14. Institut für Soziale Ökologie, Alpen-Adria-Universität Klagenfurt, Austrija
- 15. Institut za fiziku Univerziteta u Beogradu, Beograd, Srbija
- 16. Inštitut za biokemijo, Medicinska fakulteta, Univerza v Ljubljani, Ljubljana, Slovenija
- 17. Institut za hemiju, tehnologiju i metalurgiju, Univerzitet u Beogradu, Beograd, Srbija
- 18. Inštitut za patološko fiziologijo, Medicinska fakulteta, Univerza v Ljubljani, Ljubljana, Slovenija
- 19. Institute for Nuclear Research, Hungarian Academy of Sciences, Debrecen, Mađarska
- 20. Institute of Basic Medical Sciences, University of Oslo, Oslo, Norveška
- 21. Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic, Prag, Češka
- 22. Institute of Nature Conservation of Polish Academy of Sciences, Krakow, Poljska
- 23. Institute of Organic Chemistry and Biochemistry of the CAS, Prag, Češka
- 24. International Atomic Energy Agency, Beč, Austrija
- 25. Joint Research Centre of the European Commission, Bruxelles, Belgija
- 26. Max Planck Institute for Chemistry, Njemačka
- 27. Nacionalni inštitut za biologijo, Ljubljana, Slovenija
- 28. NILU Norwegian Air Research Institute, Norveška
- 29. NMR laboratórium, Pannon Egyetem, Veszprém, Mađarska
- 30. Paul Scherrer Institute, Švicarska
- 31. Prirodno-matematički fakultet, Univerzitet u Kragujevcu, Srbija
- 32. Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Peking, Kina
- 33. The Scripps Institute of Science, CA, SAD
- 34. Umweltbundesamt (UBA), Langen, Njemačka
- 35. UHasselt University Belgium, Campus Diepenbeek, Agoralaan Gebouw H, Diepenbeek, Belgija
- 36. Universidad Autónoma de Tlaxcala, Universidad Nacional Autónoma de México, Meksiko
- 37. Universität Osnabrück, Osnabrück, Njemačka
- 38. Universitätsklinikum Hamburg-Eppendorf (UKE), Hamburg, Njemačka
- 39. University of California at San Diego, La Jolla, CA, SAD
- 40. University of Melbourne, Melbourne, Victoria, Australia
- 41. University of Rouen, Mont-Saint-Aignan, Francuska
- 42. University of Strasbourg, Strasbourg, Francuska
- 43. Univerzita Hradec Králové, Hradec Králové, Češka
- 44. VITO Flemish Institute for Technological Research, Belgija
- 45. VVM Flemish Environment Agency

C. PRIHODI INSTITUTA

RED. BR.	VRSTA PRIHODA	IZNOS (HRK)	%
Α	PRIHODI IZ DRŽAVNOG PRORAČUNA	52.349.485	31,65
1.	Plaće i rashodi za zaposlene	28.654.985	17,32
2.	Programsko financiranje Instituta	4.751.485	2,87
3.	Nacionalno sufinanciranje Projekta REC IMI i konstrukcijske obnove	14.781.588	8,94
4.	Bilateralni projekti	710.095	0,43
5.	Potpore za prijavu projekata, održavanje znanstvenih skupova,		
	popularizaciju znanosti i izdavanje časopisa	209.324	0,13
6.	Projekti i doktorandi Hrvatske zaklade za znanost	3.242.008	1,96
В	PRIHODI OD PRUŽENIH USLUGA NA TRŽIŠTU	12.351.347	7,47
7.	DHMZ - Program mjerenja razine onečišćenosti u Državnoj mreži	2.949.439	1,78
8.	Gradski ured za gospodarstvo, energetiku i zaštitu okoliša, Zagreb	1.473.518	0,89
9.	Klinički bolnički centar Zagreb	688.835	0,42
10.	Ministarstvo unutarnjih poslova RH, Zagreb	750.700	0,45
11.	Klinički bolnički centar "Sestre milosrdnice", Zagreb	461.075	0,28
12.	Zagrebačke otpadne vode d.o.o., Zagreb	408.126	0,25
13.	Klinička bolnica Dubrava, Zagreb	550.915	0,33
14.	Fond za financiranje razgradnje i zbrinjavanja radioaktivnog otpada NEK	401.700	0,24
15.	Eurofins Croatiakontrola Zagreb	316.000	0,19
16.	Hrvatski zavod za zdravstveno osiguranje, Zagreb	157.600	0,10
17.	CARnet - Hrvatska akademska i istraživačka mreža, Zagreb	800.000	0,48
10	Zavod za javno zdravstvo Koprivničko-križevačke županije,		
10.	Koprivnica	440.020	0,27
19.	Nuklearna elektrana Krško	198.769	0,12
20.	Međunarodna zračna luka Zagreb d.d.	121.560	0,07
21.	Zagrebački holding d.o.o. Zagreb	186.600	0,11
22.	Opća bolnica Varaždin	128.400	0,08
23.	Siemens Energy d.o.o. Zagreb	118.960	0,07
24.	STSI Integrirani tehnički servisi d.o.o., Zagreb	80.384	0,05
25.	Ispitivanje i mjerenje radioaktivnosti uzoraka	248.746	0,15
26.	Ocjena ekološke prikladnosti objekata	183.255	0,11
27.	Dozimetrija izvora zračenja	946.539	0,57
28.	Laboratorijske usluge - pacijenati	142.347	0,09
29.	Laboratorijske analize i toksikološke ocjene uzoraka	472.700	0,29
30.	Pretplata Arhiv, ugovori IMI	125.159	0,08
С	PRIHODI OSTVARENI IZ OSTALIH IZVORA	100.716.826	60,89
31.	Prihodi iz EFRR, FSEU i NPOO za financiranje Projekta REC IMI i konstrukcijsku obnovu	94.339.734	57,03
32.	EU projekti	5.285.802	3.20
33.	Međunarodni projekti	384.469	0.23
34.	Sveučilište Sjever	140.093	0.08
35.	Prihodi od dividendi, kamata i pozitivnih tečainih razlika	149.192	0.09
36.	Refundacije troškova	357.334	0.22
37.	Ostali prihodi i sufinanciranie troškova	60.202	0.04
A+B+C	UKUPNI PRIHOD	165.417.658	100,00

D. PUBLIKACIJE DJELATNIKA INSTITUTA U 2022. GODINI

KATEGORIJA PUBLIKACIJE	BROJ RADOVA
D.1. Znanstveni, pregledni i stručni radovi (+ prihvaćeni za objavu u 2023.)	125 (+16)
Radovi u časopisima indeksiranim u bazi WoS	101
Radovi u časopisima indeksiranim u bazi WoS prihvaćeni za objavu u 2023.	16
Radovi u časopisima indeksiranim u ostalim bazama	3
Radovi u neindeksiranim časopisima	0
Radovi u zbornicima skupova održanih u RH i virtualno	17
Radovi u zbornicima skupova održanih u inozemstvu i virtualno	4
D.2. Knjige, časopisi, zbornici	13
Autor ili urednik knjige	0
Rad ili poglavlje u knjizi	5
Urednik časopisa ili zbornika	8
D.3. Ostale publikacije	4
Tiskana izdanja	3
Elektronička izdanja	1
D.4. Kvalifikacijski radovi	18
Radovi djelatnika Instituta	3
Radovi pristupnika s mentorom/sumentorom na Institutu	15
D.5. Kongresna priopćenja na skupovima održanim u RH i virtualno	60
Sažetci u časopisima indeksiranim u bazi WoS	7
Sažetci u ostalim časopisima i knjigama sažetaka	52
Sažetci u elektroničkom izdanju	1
D.6. Kongresna priopćenja na skupovima održanim u inozemstvu i virtualno	87
Sažetci u časopisima indeksiranim u bazi WoS	21
Sažetci u elektroničkom izdanju u časopisu indeksiranom u bazi WoS	6
Sažetci u ostalim časopisima i knjigama sažetaka	52
Sažetci u elektroničkom izdanju	8
D.7. Izvještaji stručne djelatnosti	23
Nacionalni projekti, ugovori i suradnje	21
Međunarodni projekti, ugovori i suradnje	2
UKUPAN BROJ RADOVA OBJAVLJENIH U 2022. (+ prihvaćenih za objavu u 2023.)	330 (+16)

D1. ZNANSTVENI, PREGLEDNI I STRUČNI RADOVI

Radovi u časopisima indeksiranim u bazi WoS

- 1. BABIĆ Ž, MACAN M, FRANIĆ Z, HALLMANN S, HAVMOSE MS, JOHANSEN JD, JOHN SM, SYMANZIK C, UTER W, WEINERT P, VAN DER MOLEN HF, KEZIC S, TURK R, MACAN J. Association of hairdressing with cancer and reproductive diseases: A systematic review. J Occup Health 2022;64(1):e12351. (pregledni rad, Q3)
- 2. BABIĆ Ž, ŠAKIĆ F, FRANIĆ Z, MACAN J. Skin barrier function in nursing apprentices during the coronavirus disease 2019 (COVID-19) pandemic. Contact Dermatitis 2022;86:507-13. (znanstveni rad, Q1)
- 3. BAMPIDIS V, AZIMONTI G, BASTOS MDL, CHRISTENSEN H, DUSEMUND B, FAŠMON DURJAVA M, KOUBA M, LÓPEZ-ALONSO M, LÓPEZ PUENTE S, MARCON F, MAYO B, PECHOVÁ A, PETKOVA M, RAMOS F, SANZ Y, VILLA RE, WOUTERSEN R, GLANDORF B, SVENSSON K, ZELJEZIC D, ANGUITA M, BROZZI R, GALOBART J, ORTUÑO J, REVEZ J, TARRÉS-CALL J, PETTENATI E. Safety and efficacy of a feed additive consisting of endo-1,4-8-xylanase produced by *Komagataella phaffii* DSM 33574 (Xylamax) or chickens and turkeys for fattening, chickens reared for laying/breeding, turkeys reared for breeding and minor poultry species for fattening or raised to the point of lay (BioResource international, Inc.). EFSA J 2022;20(7):e07428. (znanstveni rad, Q2)
- 4. BEBEK MARKOVINOVIĆ A, BRČIĆ KARAČONJI I, JURICA K, LASIĆ D, SKENDROVIĆ BABOJELIĆ M, DURALIJA B, ŠIC ŽLABUR J, PUTNIK P, BURSAĆ KOVAČEVIĆ D. Strawberry tree fruits and leaves (*Arbutus unedo* L.) as raw material for sustainable functional food processing: A review. Horticulturae 2022;8:881. (pregledni rad, Q1)

- 5. BENKOVIĆ V, ORŠOLIĆ N, KNEŽEVIĆ AH, BOROJEVIĆ N, BROZOVIĆ G, MILIĆ M. Kidney cell DNA damage caused by combined exposure to volatile anaesthetics and 1 Gy or 2 Gy radiotherapy dose *in vivo*. Arh Hig Rada Toksikol 2022;73:62-70. (znanstveni rad, Q4)
- 6. BERGHAUS C, GROH A-C, BRELJAK D, CIARIMBOLI G, SABOLIĆ I, PAVENSTÄDT H, WEIDE T. Impact of Pals1 on expression and localization of transporters belonging to the solute carrier family (SLC). Front Mol Biosci 2022;9:792829. (znanstveni rad, Q1)
- 7. BRČIĆ KARAČONJI I, JURICA K, GAŠIĆ U, DRAMIĆANIN A, TEŠIĆ Ž, MILOJKOVIĆ OPSENICA D. Comparative study on the phenolic fingerprint and antioxidant activity of strawberry tree (*Arbutus unedo* L.) leaves and fruits. Plants 2022;11:25. (znanstveni rad, Q1)
- BRELJAK D, MICEK V, GERIĆ M, GAJSKI G, KRALIK OGUIĆ S, RAŠIĆ D, KARAICA D, VRHOVAC MADUNIĆ I, LJUBOJEVIĆ M, ORCT T, JURASOVIĆ J, NOVAK JOVANOVIĆ I, PERAICA M, NANIĆ L, RUBELJ I, SABOLIĆ I. Long-term effects of melatonin and resveratrol on aging rats: a multi-biomarker approach. Mutat Res Genet Toxicol Environ Mutagen 2022;876-77:503443. (znanstveni rad, Q3)
- CHEIMARIOS N, PEM B, TSOUMANIS A, ILIĆ K, VINKOVIĆ VRČEK I, MELAGRAKI G, BITOUNIS D, ISIGONIS P, DUSINSKA M, LYNCH I, DEMOKRITOU P, AFANTITIS A. An *in vitro* dosimetry tool for the numerical transport modeling of engineered nanomaterials powered by the Enalos RiskGONE Cloud Platform. Nanomaterials 2022;12(22):3935. (znanstveni rad, Q1)
- CVIJETIĆ S, KESER I, JURASOVIĆ J, ORCT T, BABIĆ Ž, BOSCHIERO D, ILICH JZ. Diurnal salivary cortisol in relation to body composition and heart rate variability in young adults. Front Endocrinol 2022;13:831831. (znanstveni rad, Q1)
- 11. ČAVLOVIĆ AO, BEŠLIĆ I, PERVAN S, BARLOVIĆ N, MIKŠIK M, KLARIĆ M, PREKRA S. Occupational exposure to inhalable and respirable wood dust of pedunculate oak (*Quercus robur* L.) in a furniture factory. BioResources 2022;17:5831-47. (znanstveni rad, Q2)
- 12. DEBELJAK Ž, VINKOVIĆ VRČEK I, DRINKOVIĆ N, MICEK V, GALIĆ E, GORUP D, ĆURLIN M, MANDIĆ D, BANDJAK A, PEM B, KALČEC N, ILIĆ K, PAVIČIĆ I, MIMICA S, GÜNDAY-TÜRELI N, TÜRELI E. Imaging mass spectrometry differentiates the effects of doxorubicin formulations on non-targeted tissues. Analyst 2022;147:3201-8. (znanstveni rad, Q1)
- 13. DRUZHININ VG, BARANOVA ED, VOLOBAEV VP, IVANOV VI, LARIONOV AV, MININA VI, SMAGULOVA F, LEGOFF L, TITOV VA, FUCIC A. The length of telomeres and the baseline level of cytogenetic damage in leukocytes of lung cancer patients. Russ J Genet 2022;58:73-84. (znanstveni rad, Q4)
- 14. DVORŠĆAK M, JAGIĆ K, BESEDNIK L, ŠIMIĆ I, KLINČIĆ D. First application of microwave-assisted extraction in the analysis of polybrominated diphenyl ethers in human milk. Microchem J 2022;179:107447. (znanstveni rad, Q1)
- 15. DVORŠĆAK M, JAKOVLJEVIĆ I, JAGIĆ K, TARIBA LOVAKOVIĆ B, KLINČIĆ D. Polybrominated diphenyl ethers and polycyclic aromatic hydrocarbons in dust from different indoor environments in Zagreb, Croatia: Levels and human exposure assessment. Indoor Air 2022;32:e13145. (znanstveni rad, Q1)
- 16. ERCEGOVIĆ RAŽIĆ S, KOPJAR N, KAŠUBA V, SKENDERI Z, AKALOVIĆ J, HRENOVIĆ J. Evaluation of DNA-damaging effects induced by different tanning agents used in the processing of natural leather Pilot study on HepG2 cell line. Molecules 2022;27(20):7030. (znanstveni rad, Q2)
- 17. FILIPOVIĆ V, DEFTERDAROVIĆ J, KREVH V, FILIPOVIĆ L, ONDRAŠEK G, KRANJČEC F, MAGDIĆ I, RUBINIĆ V, STIPIČEVIĆ S, MUSTAĆ I, BUBALO KOVAČIĆ M, HE H, HAGHVERDI A, GERKE HH. Estimation of stagnosol hydraulic properties and water flow using uni- and bimodal porosity models in erosion-affected hillslope vineyard soils. Agronomy 2022;12(1):33. (znanstveni rad, Q1)
- 18. FRIŠČIĆ M, PETLEVSKI R, KOSALEC I, MADUNIĆ J, MATULIĆ M, BUCAR F, HAZLER PILEPIĆ K, MALEŠ Ž. *Globularia alypum* L. and related species: LC-MS profiles and antidiabetic, antioxidant, anti- inflammatory, antibacterial and anticancer potential. Pharmaceuticals 2022;15:506. (znanstveni rad, Q1)
- 19. GAJSKI G, GERIĆ M, PEHNEC G, MATKOVIĆ K, RINKOVEC J, JAKOVLJEVIĆ I, GODEC R, ŽUŽUL S, BEŠLIĆ I, CVITKOVIĆ A, WILD P, GUSEVA CANU I, HOPF NB. Associating air pollution with cytokinesis-block micronucleus assay parameters in lymphocytes of the general population in Zagreb (Croatia). Int J Mol Sci 2022;23(17):10083. (znanstveni rad, Q1)
- 20. GALIĆ E, RADIĆ K, GOLUB N, VITALI ČEPO D, KALČEC N, VRČEK E, VINKOVIĆ T. Utilization of olive pomace in green synthesis of selenium nanoparticles: physico-chemical characterization, bioaccessibility and biocompatibility. Int J Mol Sci 2022;23(16):9128. (znanstveni rad, Q1)
- GAŠO SOKAČ D, ZANDONA A, ROCA S, VIKIĆ-TOPIĆ D, LIHTAR G, MARAKOVIĆ N, BUŠIĆ V, KOVARIK Z, KATALINIĆ M. Potential of vitamin B6 dioxime analogues to act as cholinesterase ligands. Int J Mol Sci 2022;23(21):13388. (znanstveni rad, Q1)
- 22. GERIĆ M, MATKOVIĆ K, GAJSKI G, RUMBAK I, ŠTANCL P, KARLIĆ R, BITUH M. Adherence to Mediterranean diet in Croatia: Lessons learnedtoday for a brighter tomorrow. Nutrients 2022;14(18):3725. (znanstveni rad, Q1)

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- 161.JAGIĆ K. Analiza tragova polibromiranih difenil-etera u kućnoj prašini i ljudskome mlijeku radi procjene rizika za ljudsko zdravlje / Trace analysis of polybrominated diphenyl ethers in household dust and human milk for human health risk assessment [disertacija]. Zagreb: Sveučilište u Zagrebu, Prirodoslovno-matematički fakultet; 2022. Mentorica: D. Klinčić

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