

**INSTITUTE FOR MEDICAL RESEARCH AND OCCUPATIONAL HEALTH**

# **Annual Report**



**ZAGREB, 2020**

## 14. ORGANISATION OF THE INSTITUTE

*Date and place of founding:* 27 Dec 1947 in Zagreb.

*Founder:* Prof Andrija Štampar, PhD, 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:* general, genetic, and molecular toxicology, allergotoxicology, 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 such exposures, as well as various psychogenic factors.

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

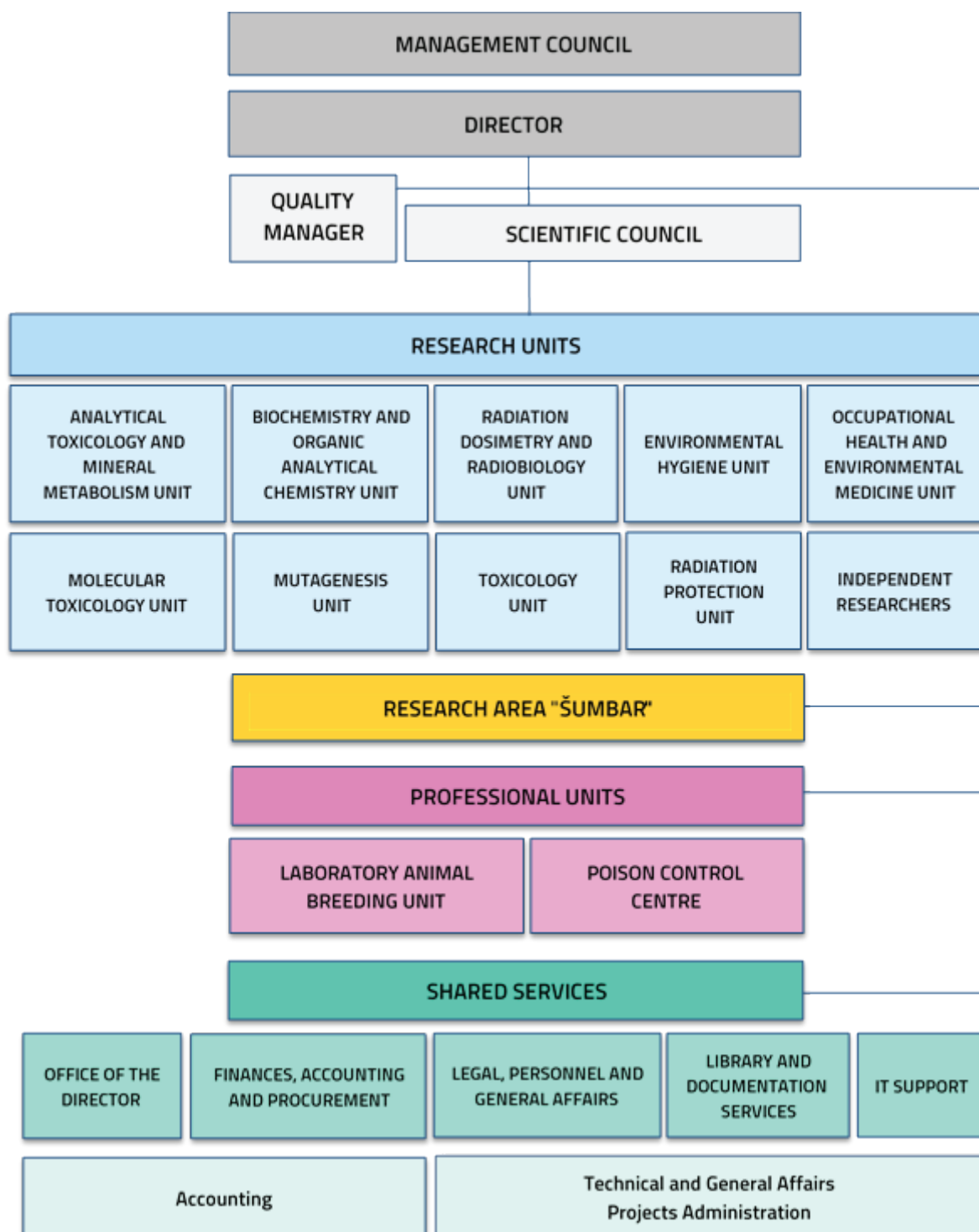
*The mission of the Institute is to become:*

- 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
- a standard and role model of academic distinction and quality.

*The vision of the Institute is to:*

- 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 outcomes of research and development
- educate future leaders in the fields of fundamental and applied sciences.

TOTAL NUMBER OF EMPLOYEES (31 DEC 2019): 157		Number of employees	%
Funding sources	State budget	147	94
	IMROH	4	2
	Croatian Science Foundation	6	4
Sex	Women	115	73
	Men	42	27
Academic titles	PhD	74	47
Teaching titles	Assis Prof (4); Assoc Prof (1); Full Prof (4)	9	6
Specialist titles	Epidemiology (1); Occupational Medicine and Sports (2)	3	2
Scientific work positions	Permanent Scientific Advisor	17	11
	Scientific Advisor	8	5
	Senior Scientific Associate	15	10
	Scientific Associate	16	10
	<b>Total</b>	<b>56</b>	<b>36</b>
Associate work positions	Postdoctoral researcher	15	10
	PhD student, Assistant	15	10
	<b>Total</b>	<b>30</b>	<b>19</b>
Professional work positions	Professional Advisor	3	2
	Senior Professional Associate	1	<1
	Professional Associate	10	6
	<b>Total</b>	<b>14</b>	<b>9</b>
Technicians		<b>28</b>	<b>18</b>
Shared Services		<b>29</b>	<b>18</b>



*The organisational structure of IMROH*

## MANAGEMENT OF THE INSTITUTE

### MANAGEMENT COUNCIL

Prof Nikola Ružinski, PhD, Faculty of Mechanical Engineering and Naval Architecture, University of Zagreb (Chair)

Prof Stipan Jonjić, PhD, School of Medicine, University of Rijeka (Deputy Chair)

Božo Pavičin, Croatian Chamber of Economy

Zdenko Franić, PhD (Representative of the Institute's research staff)

Branka Roić, BEc (Representative of the Institute's employees)

### DIRECTOR

Prof Ana Lucić Vrdoljak, PhD

### DEPUTY DIRECTORS

Irena Brčić Karačonji, PhD

Prof Radovan Fuchs, DVM, PhD (International Affairs)

## SCIENTIFIC COUNCIL

Assoc Prof Branko Petrinc, PhD (Chair)

Davorka Breljak, PhD (Deputy Chair)

## ETHICS COMMITTEE

### CHAIR

Prim Jelena Macan, MD, PhD

### MEMBERS

Prof Radovan Fuchs, DVM, PhD

Maja Peraica, MD, PhD, ERT

Martina Piasek, MD, PhD

Prof Jure Zovko, PhD, Faculty of Philosophy, University of Zadar

Marija Kujundžić Brkulj, BSc (Secretary until 15 Oct 2019)

Jagoda Mandić (from 16 Oct 2019)

## QUALITY MANAGER

Zdenko Franić, PhD

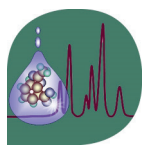
### 14.1. Ethics Committee

All of the provided requests were considered according to the criteria of the Code of Ethics of the Institute for Medical Research and Occupational Health, and applicants were given written opinions which were then officially registered. The number of requests and given opinions was 2.5 times greater in 2019 than in the previous year. In all, 13 meetings and consultations via e-mail were held and ethical principles were considered in 25 claims:

- project proposals submitted by Institute's researchers as leaders or associates on Croatian Science Foundation calls (9 projects)
- proposals for internal projects to be implemented through institutional funding (3 projects)
- research for doctoral or graduation theses of the Institute's and other students (4 projects)
- proposals for international projects with the Institute's researchers as associates (2 projects)
- project proposals from other research institutions (School of Medicine, University of Rijeka, Faculty of Food Technology and Biotechnology, University of Zagreb, Faculty of Veterinary Medicine, University of Zagreb) in cooperation with the Institute (3 projects)
- project proposals from other research institutions (Genos Ltd, Outpatient Clinic Bonifarm, Faculty of Food Technology and Biotechnology, University of Zagreb, Faculty of Economics and Business, University of Zagreb) (4 projects).

## 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	Assist 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, 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	Gordana Marović, PhD	Tel. (01) 4682 650 e-mail: marovic@imi.hr
Toxicology	603	Maja Peraica, PhD, ERT	Tel. (01) 4682 640 e-mail: mperaica@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



## 15.1. Analytical Toxicology and Mineral Metabolism Unit

### EMPLOYEES

#### HEAD

Jasna Jurasović, PhD, permanent scientific advisor

#### RESEARCH STAFF

Martina Piasek, PhD, permanent scientific advisor

Alica Pizent, PhD, permanent scientific advisor

Zorana Kljaković-Gašpić, PhD, scientific advisor

Assist Prof Ivana Vinković Vrček, PhD, scientific advisor

Nataša Brajenović, PhD, senior scientific associate

Irena Brčić Karačonji, PhD, senior scientific associate (Deputy Director)

Maja Lazarus, PhD, senior scientific associate

Anja Katić (Mikolić), PhD, scientific associate

Tatjana Orct, PhD, scientific associate

Blanka Tariba Lovaković, PhD, scientific associate

Ankica Sekovanić, PhD, postdoctoral researcher

Antonija Sulimanec Grgec, PhD, postdoctoral researcher since 17 Dec 2019

Tanja Živković Semren, PhD, postdoctoral researcher since 11 Sep 2019

Rinea Barbir, MSc, PhD student-assistant (HrZZ)

Andreja Jurič, MSc, PhD student-assistant

Nikolina Kalčec, MSc, PhD student-assistant (HrZZ) since 2 Dec 2019

Barbara Pem, MSc, PhD student-assistant

#### TECHNICAL STAFF

Mladen Komesar, senior technician

Vesna Triva, senior technician

Snježana Mataušić, technician

Krešimir Nekić, technician

#### PARTICIPATING RETIRED RESEARCHERS

Maja Blanuša, PhD, permanent scientific advisor

### SCIENTIFIC RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

##### Long-term research activities

*Assessment of exposure and intake of essential and toxic elements in mother-newborn pairs*

In healthy postpartum women from continental ( $n = 197$ ) and coastal Croatia ( $n = 203$ ), the intake of omega-3 fatty acids (eicosapentaenoic acid + docosahexaenoic acid, EPA + DHA), essential elements Na, K, Ca, Mg, Fe, Zn, Cu and Se, toxic metals Hg, Cd and Pb, and the metalloid

As was assessed through seafood consumption. The profile of fatty acids was determined by gas chromatography (GC) in the most commonly consumed fish ( $n = 84$ ) species sardine, European hake, gilthead seabream, and seabass. In addition, multielement analysis was carried out by inductively coupled plasma mass spectrometry (ICP-MS) in wild-caught ( $n = 813$ ) and farmed fish from the eastern Adriatic Sea ( $n = 24$ ) as well as in frozen ( $n = 64$ ) and canned fish ( $n = 37$ ). The results on analytes in fish were related to the data on study participants from the questionnaires and element status in mother and offspring was estimated in relation to seafood intake and predetermined element levels in maternal hair, blood and serum, and umbilical cord blood. It was shown that sardines and anchovies are a valuable food source of Fe, Zn and Cu, and sardines and picarels for Se. The estimated intake through medium size fish meal of 130 g is on average 956 mg EPA + DHA, i.e. about 4 times the dietary reference value (DRV), up to 20 % of the DRVs for measured essential macroelements, about 10 % of the DRVs for microelements, and >60 % of the DRV for Se. In the samples of mother-infant pairs from the continental vs. coastal area higher concentrations of Fe, Zn and Cu (as red meat and cereals are their main dietary sources) and lower Se in maternal serum, lower Hg and Se in maternal hair, and lower Hg and As in maternal and cord blood were determined. In all of the measured biological samples the levels of Hg, As and Se positively correlated with the frequency of fish consumption. Given the average fish consumption per week of 130 g and the content of toxic metals in fish with  $<0.16 \text{ mg Hg kg}^{-1}$  (with the exception of  $>0.42 \text{ mg Hg kg}^{-1}$  in wild red mullet and gilthead seabream) and  $<0.02 \text{ mg kg}^{-1}$  for both Cd and Pb plus the values of tolerable weekly intake (TWI) that were <15 % for methyl-Hg and several hundreds lower for both Cd and Pb, it was concluded that there was no risk of increased toxic metal intake. Regarding As, its main chemical form in marine fish is arsenobetaine, which is non-toxic. The original contribution of this research is evidence that marine fish in Croatia can be recommended as nutritionally highly valuable food for all population groups. Moreover, these results can serve in drawing up national guidelines on fish consumption in women during the reproduction period due to health risks of prenatally exposed offspring, especially by consumption of fish species from the Adriatic Sea for which increased levels of Hg ( $>0.5 \text{ mg kg}^{-1}$  muscle meat) were determined (181).

Inductively coupled plasma mass spectrometry (ICP-MS) method for the determination of essential and toxic elements As, Ca, Cd, Cu, Mg, Mn, Mo, Fe, Hg, Pb, Se and Zn in human hair was developed and validated together with the exploration of different solution efficiency in hair sample washing to remove the external metal contamination as no standard procedure for that purpose has yet been accepted. Hair washing procedures by ethyl acetate, methanol, ethanol, acetone, and detergent, with or without the use of an ultrasonic bath gave satisfactory results, whereas usage of nitric and hydrochloric acid was found unsuitable. The tested validation parameters were within previously defined eligibility criteria. In the analyzed hair samples of healthy postpartum women ( $n = 167$ ) from coastal vs. continental Croatia, concentrations of Hg, Fe, Mn, Se, and Zn were higher and Ca and Mg were lower, which may be related with the differences in intake of fish, dairy products and mineral-vitamin supplements as well as different soil mineral content in two studied areas (188).

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

#### *1. Investigation of interactions between irinotecan and tetrahydrocannabinols on laboratory rodents using integrated biochemical, molecular biology, pathohistological, and analytical methods*

We published results on the effects of tetrahydrocannabinol (THC) on DNA in white blood and brain cells of Wistar rats (34, 312). Effects of rat exposure to irinotecan (IRI), THC, and their combination on haematological and biochemical parameters, cholinesterase activities, markers of oxidative stress, and levels of primary DNA damage were presented at the 4<sup>th</sup> Congress of the Slovenian Society

of Toxicology "Cannabis under scrutiny: their toxicity and medical utility" (337). Extraction and gas chromatography-mass spectrometry (GC-MS) analysis conditions were optimised for determining THC and its metabolite in rat urine. Enhanced urinary THC metabolites excretion was noted in rats administered combined treatment compared to single THC treatment (21, 279). Genotoxic and cytotoxic effects of irinotecan on human hepatocellular carcinoma cell line (HepG2) and the colon adenocarcinoma cell line (Caco-2) (296). The effect of IRI on levels of primary DNA damage were investigated in white blood cells, liver, and brain of rats (301).

## 2. *Nutritive and toxicological properties in organic vs. conventional honeys*

Since the beginning of the project (August 2019), 15 certified organic honey producers from Banovina, Baranja, Istra, island Rab, Ozalj, and Velebit area have been contacted, as well as conventional producers matching the same areas. Element levels, total phenolic content, and antioxidative properties were measured in 63 samples of chestnut, acacia, sage, and winter savory honey. Quantification of antibiotic and chemotherapeutic residuals (sulphonamides, aminoglycosides, tetracyclines and tylosin), 112 pesticides and their metabolites, physicochemical parameters and melissopalynological analysis are underway at our collaborative institutions (Croatian Veterinary Institute, Faculty of Agriculture University of Zagreb).

## 3. *Evaluation of reproductive toxicity of commonly used pesticides followed by chronic low-dose exposure in vivo*

The planned research is a continuation of the project of the Institute for Medical Research and Occupational Health OPENTOX (Organic Environmental Pollutants – Markers and Biomarkers of Toxicity, IP-2014-8366, lead by D. Želježić), supported by the Croatian Science Foundation. The implementation of the project began in December 2019. The aim of the project is to investigate the potential toxic effects of insecticides  $\alpha$ -cypermethrine and imidacloprid and herbicides terbutylazine and tembotrione on reproductive health in *in vivo* conditions (male Wistar strain rats). Analyses of oxidative stress parameters are underway, and a Master's thesis ("Effects of  $\alpha$ -cypermethrine and imidacloprid on oxidative stress parameters in testes and epididymis of male Wistar strain rats") has been applied to the Faculty of Science in Zagreb by A. Jančec (under the supervision of B. Tariba Lovaković).

## Other research activities

Results on the protective role of strong antioxidant strawberry tree (*Arbutus unedo* L.) honey and its main bioactive constituent homogentisic acid against the cyto/genotoxic effects induced by UVB radiation in human peripheral blood lymphocytes *in vitro* were presented at the 12<sup>th</sup> Symposium of the Croatian Radiation Protection Association (131).

Radionuclides and stable elements combined with risk/benefit analysis for consumers of wildlife meat were reported for exotic Barbary sheep (*Ammotragus lervia*) population residing on Mt. Mosor, Croatia (39).

A quantitative profile of free amino acids and elements in urine and levels of oxidative stress parameters in blood were compared between men with testicular cancer ( $n = 99$ ) and control subjects ( $n = 68$ ). The subjects with testicular cancer had significantly higher concentrations of aspartic acid, manganese, and zinc and higher activity of superoxide dismutase and significantly lower concentrations of threonine, serine, histidine, cobalt and glutathione, as well as lower total oxidant status in comparison to control subjects. Additionally, linear discriminant analysis (LDA) performed to examine whether the created amino acid profile discriminated subjects with testicular cancer from control subjects showed a discrimination rate of 86 % when all amino acids were included in the model. A qualitative profile of volatile organic metabolites in urine was created



to detect which species, depending on their functional groups, can be detected in urine of men with testicular cancer. GC-MS analysis resulted in about 200 peaks of volatile organic metabolites detected in urine, and 123 of them were identified and 17 confirmed by standard. After receiving chemotherapy (bleomycin, etoposide and cisplatin), men with cancer had increased concentrations of the majority of amino acids and elements in urine and glutathione in blood plasma in comparison to values measured before chemotherapy. One year after chemotherapy, the results showed that the concentrations of most amino acids and elements were similar to those measured in control subjects, except for threonine, serine and mercury which had significantly higher values, and manganese and platinum, which had significantly lower values than the control subjects (182, 184, 260, 261).

## RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

### National projects (Chapter 16.1.)

- Assessment of daily exposure to metals and maternal individual susceptibility as factors of developmental origins of health and disease (METALORIGINS, HrZZ-IP)
- Interaction of metallic nanoparticles with sulphur-containing biomolecules – implications for nano-bio interface (NanoFaceS, Hrzz-IP)
- Application of Nanobiotechnology for Nutritional Supplementation with Selenium (NutriTENSE, HrZZ-IP)
- Development, validation and application of analytical methods for PBDE determination (DeValApp, HrZZ-UIP)
- Biological monitoring of the effects of volatile aromatic hydrocarbons (BTEX) on the health of the Primorje-Gorski Kotar County population (UNIRI)
- Opportunistic pathogens in the water supply system: a new challenge in water treatment (UNIRI)

### International projects (Chapter 16.2.)

- European Concerted Programme on Radiation Protection Research (CONCERT, Horizon 2020)
- Science-based risk governance of nano-technology (RiskGONE, H2020)
- Safe-by-Design Approach for Development of Nano-Enabled-Delivery Systems to Target the Brain (SENDER, HrZZ-PZS)
- Anti-Microbial Coating Innovations to prevent infectious diseases (AMICI, COST)
- Cancer nanomedicine – from the bench to the bedside (Nano2Clinic, COST)
- The pharmacokinetic profile of silver nanoparticles: the role of biological barriers (Bilateral CRO-AT)
- Multiplex characterization platform for nanobio interfaces (Bilateral CRO-DE)

## PROFESSIONAL SERVICES

Professional analyses were carried out on the request of various institutions, companies, and individuals on metals and metalloids in samples of different origins (by ICP-MS and AAS) and drugs of abuse in hair and urine samples (by GC-MS).

A total of 320 analyses of specific indicators of exposure and effect to toxic metals/metalloids and essential trace element status in the human organism were performed. Most of the analyses were related to determining biological markers of Pb exposure [concentrations of Pb and erythrocyte protoporphyrin (EP) and activity of  $\delta$ -aminolevulinic acid dehydratase (ALAD) in blood] during the assessment of professional exposure in workers at different workplaces ( $n = 116$ ). Concentrations of Hg in urine, blood, and hair (48 analyses) and a wide range of elements (Al, As, Cd, Co, Cr, Cu, I, Li, Mg, Mn, Mo, Ni, Pb, Se, Sn, Tl and Zn) in those biological samples (156 analyses) were also

determined. Based on a contract signed with the Institute of Public Health of Brod-Posavina County, analyses of Pb, Ni, Cr, V, Mn, and Tl in whole blood, serum, urine, and hair samples of 41 subjects, in total 738 analyses (341), were performed. Apart from analyses of human biological samples, Cd was measured in dried tobacco leaves (6 samples) on the manufacturer's request.

Pursuant to the contract with the Pčelarska udruga Petrinja on the characterisation of conventional honey from Banovina (Banski med), levels of 25 elements, total phenolic content, and antioxidative potential were measured in 25 samples of Banski med.

Drugs of abuse from the amphetamine and opiate groups, methadone, and cocaine were determined in 39 hair samples (60 analyses in total). THC-COOH and buprenorphine (5 samples) and opiates (1 sample) were analysed in urine. A total of 60 queries were received regarding the analysis of drugs of abuse via the e-mail address infodroge@imi.hr.

#### *List of intercomparisons*

ORGANISER	TEST	AREA	DATE
Society of Hair Testing, Strasbourg, France	Proficiency Test 2019	Analysis of drugs of abuse in hair	6/2019 and 12/2019 (two times per year, three hair samples)

### ■ PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

#### *I. Brčić Karačonji*

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 Presidency of the Croatian Society of Toxicology.

#### *J. Jurasović*

Member of the Presidency of the Croatian Society of Toxicology.

#### *M. Lazarus*

Secretary of the Croatian Laboratory Animal Science Association (CroLASA); member of the Organising Committee of professional Symposium "Education of professional and technical staff involved in the care of animals used in biomedical research", Zagreb, 18 Oct 2019 and professional workshop "How successfully apply for animal experiment licence", Zagreb, 9 Apr 2019.

#### *M. Piasek*

Member of the international professional associations International Commission on Occupational Health – ICOH and MEDICHEM, also an ICOH scientific committee for occupational health in chemical industry; member of the Presidency (until 13 Nov 2019) and member of the Supervisory Board (since 13 Nov 2019) of the Croatian Society of Toxicology.

#### *I. Vinković Vrček*

Member of the Working Group of the Ministry of Health for Development of the Position of the Republic of Croatia in the New Food Area; member of the Referent Group of the Ministry of Science and Education for Nanotechnology, Advanced Materials, Biotechnology, Advanced Production Processes; member of the Thematic Innovation Council for Health and Quality of Life of the Ministry of Economy, Entrepreneurship and Crafts of the Republic of Croatia; member of the Editorial Board of the journal *Diacovensia*.

### ■ SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

Scientific degree of scientific advisor was gained by *M. Lazarus*.

Scientific degree of permanent scientific advisor was gained by *Z. Kljaković-Gašpić*.



## 15.2. Biochemistry and Organic Analytical Chemistry Unit

### EMPLOYEES

#### HEAD

Snježana Herceg Romanić, PhD, permanent scientific advisor

#### RESEARCH STAFF

Zrinka Kovarik, PhD, permanent scientific advisor

Goran Šinko, PhD, scientific advisor

Anita Bosak, PhD, senior scientific associate

Sanja Fingler Nuskern, PhD, senior scientific associate

Maja Katalinić, PhD, senior scientific associate

Gordana Mendaš Starčević, PhD, senior scientific associate

Sanja Stipičević, PhD, senior scientific associate since 11 Jul 2019

Darija Klinčić, PhD, scientific associate

Marija Dvorščak, PhD, postdoctoral researcher

Nikolina Maček Hrvat, PhD, postdoctoral researcher

Josip Madunić, PhD, postdoctoral researcher since 2 Oct 2019

Nikola Maraković, PhD, postdoctoral researcher

Tamara Zorbaz, PhD, postdoctoral researcher since 20 Feb 2019

Tena Čadež, MSc, PhD student-assistant (HrZZ) since 2 Feb 2019

Karla Jagić, MSc, PhD student-assistant (HrZZ) since 1 Feb 2019

Ana Matošević, MSc, PhD student-assistant

Antonio Zandona, MSc, PhD student-assistant

#### TECHNICAL STAFF

Maja Meštrović, technician

#### PARTICIPATING RETIRED RESEARCHERS

Prof Vlasta Drevenkar, PhD, permanent scientific advisor

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

##### Scientific collaborations

Our collaboration with Dr D. Opsenica from the Institute of Chemistry, Technology and Metallurgy, IHTM, Belgrade, Serbia, continued. A series of quinoline derivatives were synthesized and shown to have an inhibitory potential for human acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) (10).

The results of determination of scoring functions and *in silico* parameters for the interactions of 68 AChE-ligand complexes were published for the purposes of a tool for predicting inhibition potency (78).

In collaboration with colleagues from the Faculty of Science University of Zagreb (principal investigator: Prof S. Tomić), a series of 14 novel heterocyclic  $\beta$ -D-glucosylconjugates and  $\beta$ -D-galactosylconjugates were designed and synthesized, but 4 of them showed an inhibitory effect with benzimidazolium and 1-benzylbenzimidazolium substituents in a 10-50 micromolar range. The

molecular modelling analysis indicated key residues of the BChE active site, which contributed to a higher affinity toward the selected compounds. It was shown that benzimidazole derivatives of pyranosyl sugars represented the structural scaffold in the development of anti-Alzheimer's disease drugs (9).

A part of research on the topic of the diploma thesis by PhD student A. Zandona was published within the results of the project HrZZ-IP-2013-11-9158 (principal investigator Prof B. Šantek) at the Faculty of Food Technology and Biotechnology under supervision of Prof I.K. Svetec (79).

Cooperation with scientific institutions in Serbia, Institute of Physics Belgrade and Faculty of Chemistry, University of Belgrade continued for the purpose of complementary analysis of persistent compounds in environmental samples and application of advanced statistical methods. Within the framework of the collaboration, preliminary data on the application of sophisticated methods such as numerical and statistical modeling, as well as the use of machine learning algorithms in processing the results of persistent compounds in breast milk, have been published (31). This cooperation is linked to the long-term collaboration with the Department of Health Studies of the University of Zadar.

In collaboration with the Environmental Hygiene Unit, a method for the determination of PCBs in atmospheric deposition was developed and evaluated. The method was applied to determine PCBs in monthly samples collected during 2018 and 2019 (156, 252, 253, 331).

The occurrence and distribution of persistent organochlorine compounds in soil collected near a coal-fired power plant and urban soil (16) and in lake sediment cores from the Plitvice Lakes National Park, Croatia (15) were investigated.

In collaboration with the University of Zagreb Faculty of Agriculture, the phytotoxic effects of mesotrione residues on sugar beet (*Beta vulgaris* L.) were determined in two agricultural soils in order to indicate the relevance of soil characterisation in crop rotation practice (108).

Sampling continued within the framework of the MONET project, which has been conducted since 2009 under the auspices of the RECETOX, Regional Center for Environmental Chemistry and Toxicology, Masaryk University, Brno, Czech Republic (272).

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

#### *1. Design, synthesis and evaluation of selective inhibitors of butyrylcholinesterase*

The interactions of human cholinesterases and selected quinolines were analyzed (10).

#### *2. Persistent Organic Pollutants – Environmental Impact Assessment and Stability of Human Genetic Material*

The results of the study of persistent organic pollutants (POPs) in edible fish from different fishing zones of the Croatian Adriatic will be presented in Graduate thesis of Mirna Štrbac "Organochlorine compounds in fish from the Adriatic Sea", University of Rijeka, Department of biotechnology, Drug research and development, 2020. POPs were investigated in farmed tuna and in wild tuna.

#### *3. Investigation of interactions between irinotecan and tetrahydrocannabinols on laboratory rodents using integrated biochemical, molecular biology, pathohistological, and analytical methods*

An analytical procedure consisting of solid phase extraction and final HPLC analysis of irinotecan and its metabolite SN-38 in whole blood of mice was developed.

## **RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES**

### **National projects (Chapter 16.1.)**

- Analysis of Butyrylcholinesterase Interactions with Novel Inhibitors and Reactivators

(AnalyseBChE, HrZZ-IP)

- Activity and guided design of bioactive small molecules (Adesire, HrZZ-IP)
- Development, validation and application of analytical methods for PBDE determination (DeValApp, HrZZ-UIP)
- Molecular Mechanisms Underlying the Toxicity of Antidotes and Potential Drugs (CellToxTargets, HrZZ-UIP)
- Cell response to exposure to chlorinated bispyridinium compounds (HAZU)

#### **International projects (Chapter 16.2.)**

- CNS-active, Orally Bioavailable, Zwitterionic Oximes for Organophosphate (DTRA, USA)
- Effects of selected pesticides on neuronal acetylcholinesterase expression (Bilateral CRO-CN)
- Persistent organochlorine compounds in human milk and their potential effect on the level of primary DNA damage in human cells (Bilateral CRO-RS)
- Multiplex characterization platform for nanobio interfaces (Bilateral CRO-DE)

### **PROFESSIONAL SERVICES**

*Spatial and temporal distribution of pollutants (nitrates, phosphates, pesticides, heavy metals) from agriculture in different agroecological conditions*

Interdisciplinary project of the Hrvatske vode, 2017-2019; Project manager: Prof G. Ondrašek, Faculty of Agriculture, University of Zagreb.

The soil mobility of glyphosate herbicide was evaluated at two contrasting vineyards in terms of soil properties and landscape position by lysimeter and soil column studies (211, 237, 338). Parameters affecting the retention of glyphosate in soil were determined with respect to the physicochemical properties of soils under different climates (327).

### **PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE**

*A. Bosak*

Member of the Executive Board of the Croatian Society of Natural Sciences; a shop steward representing scientific staff at the Independent Trade Union of Science and Higher Education for the branch IMROH.

*S. Fingler Nuskern*

Member of the TO-147 Water Quality at the Croatian Standards Institute.

*S. Herceg Romanić*

Member of the Working Group for monitoring and meeting the requirements of the Second National Plan for the Implementation of the Stockholm Convention on Persistent Organic Pollutants.

*M. Katalinić*

Secretary and member of the Executive Board of the Society and Science Committee of the Croatian Society of Biochemistry and Molecular Biology (HDBMB); secretary and a member of the Organising Committee of the congress of the Croatian Society of Biochemistry and Molecular Biology HDBMB2019 (25-28 Sep 2019, Lovran); chair of the Organisation committee of the FEBS Young Scientists' Forum (1-4 Jul 2020, Lovran); member of the International Committee of the 45<sup>th</sup> Congress of the Federation of European Biochemical Societies – FEBS2020 (4-9 Jul 2020, Ljubljana, Slovenia).

*Z. Kovarik*

President of the the Croatian Society of Natural Sciences; vice-president and member of the Executive Board of HDBMB; member and vice-chair for technological development and inovations,

Chemistry Board, Croatian Agency for Science and Higher Education; member of the Scientific Advisory Board of the Organisation for the Prohibition of Chemical Weapons (SAB OPCW); member of International Advisory Board on Cholinesterases, International Advisory Board on Cholinergic Mechanisms, and NATO Working Group in The Human Factors And Medicine Panel (HFM) "Translating Medical Chemical Defence Research Into Operational Medical Capabilities Against Chemical Warfare Threat Agents"; member of the Editorial Board of *Molecules*; organizer of one-day symposium about OPEN science (19 Feb 2019, Zagreb); member of the International Scientific Committee, 3<sup>rd</sup> International conference on CBRNE Research and Innovation (20-23 May 2019, Nantes, France); member of the Scientific Committee, HDBMB2019 (25-28 Sep 2019, Lovran); member of the Organizing Committee, 45<sup>th</sup> Congress of the Federation of European Biochemical Societies – FEBS2020 (4-9 Jul 2020, Ljubljana, Slovenia).

*G. Mendaš Starčević*

Member of the Working Group for monitoring and meeting the requirements of the Second National Plan for the Implementation of the Stockholm Convention on Persistent Organic Pollutants; member of the Working Group for Codex Alimentarius, Food Contaminants Committee.

*M. Meštrović*

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



## 15.3. Radiation Dosimetry and Radiobiology Unit

### EMPLOYEES

#### HEAD

Ivica Prlić, PhD, professional advisor in science, scientific associate

#### RESEARCH STAFF

Ivan Pavičić, PhD, senior scientific associate

Ana Marija Marjanović Čermak, PhD, scientific associate

Marija Surić Mihić, PhD, scientific associate

Krunoslav Ilić, MSc, PhD student-assistant

Luka Pavelić, MSc, PhD student-assistant

Ana Buinac, MSc, senior professional advisor in science since 7 May 2019 (3 h per week, IMROH-funded)

Tomislav Meštrović, MSc, senior professional associate in science

Branimir Zauner, PhD, professional associate in science since 29 Oct 2019

Mihaela Justić, MSc, professional associate in science until 17 Oct 2019

Jerko Šiško, MSc, professional associate in science

#### TECHNICAL STAFF

Selvije Sefić, BSc, senior technician

Silvija Kobeščak, BSc, technician

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

##### Long-term research activities

##### *Integrated hardware-software system for monitoring microlocation environmental parameters*

The IPPSO project contributes in a very direct way to sustainable development, in particular environmental protection, with the aim of protecting the health and well-being of humans as well as biota. In order for appropriate institutions to make the correct implementation, and in particular health conclusions, they must have as many relevant validated data as possible. This is especially important in case of natural disasters or accidental events, when the amount of credible information on the ground enables rapid decision-making by those responsible for mitigating such complex situations and then directly contributes to the reduction of damage to all species and mortality of humans and animals. The project contributes directly to the economy by creating databases and cartography of the state of the environment and urban areas. The project was designed at IMI, based on the results of years of research in the fields of radiation protection and environmental hygiene (air protection). The Unit's employees are experienced field workers who encounter daily ionizing and non-ionizing radiation in the environment, medicine, industry and life in general. In May 2016, the final report for the IPPSO project (<http://ippso.imi.hr/>) was issued. Considering that project visibility lasts five years after its formal completion, this project is still in progress, and a report was issued during 2019 after the third year of project implementation on 30 Jun 2019 (362). The visibility of all activities done by IMROH as an applicant for the IPPSO project in the field and in new project activities, using equipment (infrastructure) or knowledge acquired through the implementation of the IPPSO project, continues to be systematically presented in every public and written communication.



**In-house scientific projects (Chapter 16.1.A.3.)***1. Thermometry, thermography and sensory evaluation of electromagnetic radiation in medicine (TTSem2)*

Research was completed (WP1) within our investigations regarding thermographical characteristics of the healing process of the brisk bone fracture in adult subjects. A PhD thesis was written on the topic by Damir Halužan, MD, School of Medicine, University of Zagreb. Further research is in progress, with the support of experimental IR thermography methods conducted at the University Hospital Centre Zagreb (WP5).

We also studied the thermographical characteristics of breasts in women who have invasive ductal cancer. This was the subject of another PhD thesis accepted by the School of Medicine, University of Zagreb and written by plastic surgery specialist Marko Mance, MD. Research regarding the thermographical characteristics of the healing process of clavicle bones in children (WP4) is in progress in cooperation with the University Hospital Centre Zagreb and Children's Hospital Zagreb. Preliminary results obtained during 2019 are being processed for the purpose of publication.

The Unit is also preparing for the continuation of clinical research (WP2) regarding the mapping of the temperature symmetry of the skin region, in children and adults in both sexes. The measurements will be performed during examinations at the University Hospital Centre Zagreb, Clinic for Surgery. The aim of this study is to standardise physiological deviations in healthy populations and measure standard deviations for individual anatomic regions. So far, similar measurements have been made, but there are no real studies of age-related differences. The clinical part of the study (WP3) has to do with skin thermometry below substrate immobilization in thoracic fractures. After repeated testing, experiment-ready IMROH thermometers, specially designed by the Institute's partners, are available for contact measuring and storage of information regarding the temperature of the given skin/tissue throughout the time of carrying immobilization on hand. The measurement plan is implemented in patients at the University Hospital Centre Zagreb, Clinic for Surgery, which are in the standard treatment of fractures as soon as the optimal number of thermometers becomes available. In the process of research, a protocol is being prepared for patients' consent to participate in the measurement project settlement.

*2. Development of UV radiation sensors (SUVIndex)*

The Unit, together with its external associates from the companies ALARA Uredaji, Haj-Kom, and clinics of the University Hospital Centre Zagreb, is developing ultraviolet radiation sensors that will, together with a computer processor, enable the continuous individual monitoring of exposure to sunlight by persons working in the open and exposed to UV radiation (agriculture, seafarers, fishermen, etc.), which will be the basis for the design of Occupational Health Protocols on the implementation of preventive protection against excessive exposure to UV radiation. Several pilot prototypes are ready for field measurements that will be launched early in the spring of 2020 in cooperation with the Occupational Health and Environmental Medicine Unit.

**Other research activities**

Within research funded by the Unit, the development of an eye lens dosimeter started. A prototype of an eye lens dosimeter holder was designed and printed using a 3D printer, as the first of its kind in the world to be made and has been validated by the Secondary Standard Dosimetry Laboratories (SSDL) of the Jožef Stefan Institute. Irradiations for type testing were performed using irradiation sources of SSDL of Ruđer Bošković Institute in Zagreb and Jožef Stefan Institute in Ljubljana, Slovenia. The results of type testing for photon energies are promising and the results were presented at the 4<sup>th</sup> European Radiological Protection Research Week in Stockholm, Sweden. The research on the development of the eye lens dosimeter will be the objective of an internal project of the Institute in 2020.



## RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

### National projects (Chapter 16.1.)

- Determination of the radiological status of the working environment in IPNP, INA Group
- Significance of interaction of metal nanoparticles with sulfur biomolecules for nano-bio interface (NanoFaceS, IP-HrZ7)
- Quantum-chemical design, preparation and biological properties of organometallic nucleobase derivatives(OrDeN, IP-HrZ7)

### International projects (Chapter 16.2.)

- European Concerted Programme on Radiation Protection Research (CONCERT, H2020)
- Science-based risk governance of nano-technology (RiskGONE, H2020)
- Safe-by-Design Approach for Development of Nano-Enabled-Delivery Systems to Target the Brain (SENDER, HrZZ-PZS)
- Single layer gamma-ray polarimeter for medical imaging applications and fundamental physics research (SiLGaP, HrZZ-PZS)
- The pharmacokinetic profile of silver nanoparticles: the role of biological barriers (Bilateral CRO-AT)
- Multiplex characterization platform for nanobio interfaces (Bilateral CRO-DE)

## PROFESSIONAL SERVICES

For the needs of INA Group members involved in drafting protocols for the implementation of business activities involving the manipulation of natural radioactive materials (NORM), in particular for residues, the preparation of a plan of activities in the event of an incident involving radiological risks and to determine the need for specialized vocational education and the implementation of safety measures related to ionising radiation and the appearance of residues at INA Group's production sites, a number of studies were contracted, one of which was created for STSI d. o. o. in 2019.

Professional experimental work at the STSI company in Strušac resulted in the development of an internal institute research project whose experimental development part during 2018 was piloted in collaboration with RIT Croatia – Rochester Institute of Technology, Rochester, New York, US and external collaborators ALARA Uredaji and Haj-Kom, stemming from our recent cooperation with Ericsson Nikola Tesla through the ERDF project IPPSO.

A pilot measurement system of the ALARA UAV (Unmanned Aerial Vehicle) was developed to be prepared for field measurements of ionising radiation (and other agents) on large areas of the environment using UAVS. We plan to prepare documentation for the application of this pilot project for international funding and experimental technological development in full experimental form (research/technological development of measuring instrumentation).



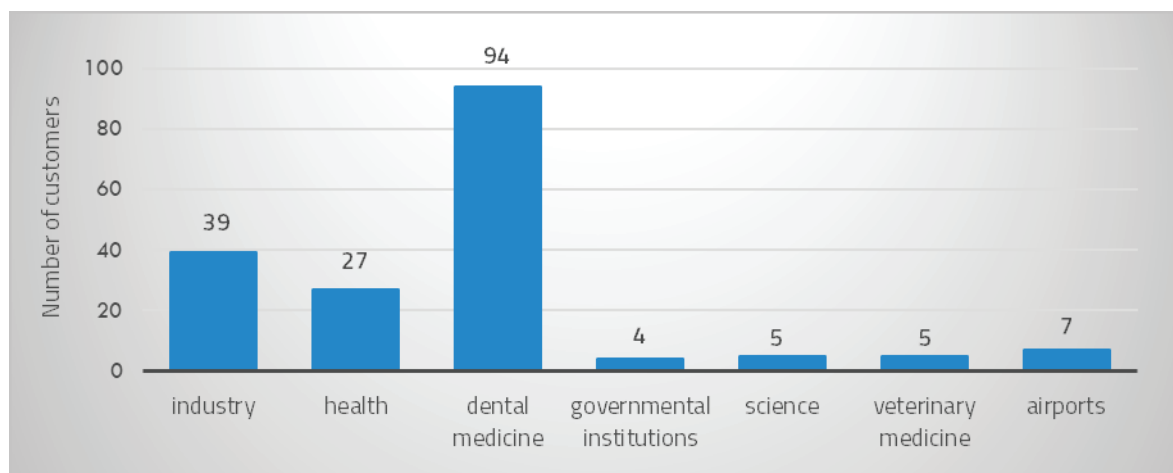
*Unmanned aircraft (UAV; colloquially drone) and the measuring system ALARA UAV-IPPSO*

### Professional risk assessment studies

In total, 11 risk assessment studies were performed focusing on the use of ionising radiation sources in medicine, dental medicine, research, and industry:

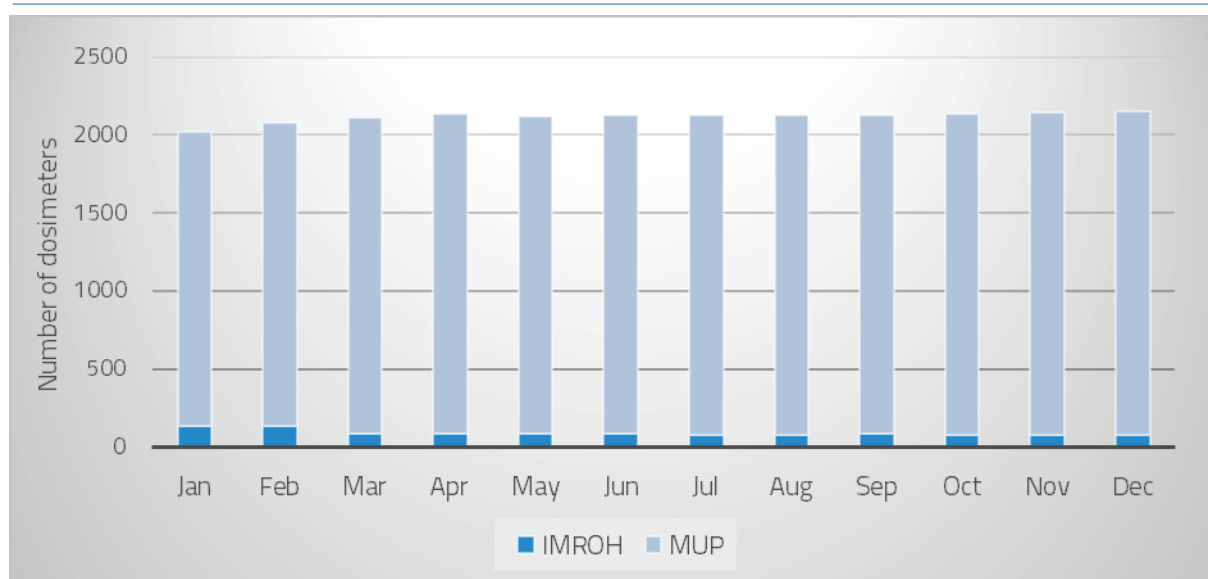
CONTRACTOR	REPORT AUTHOR
Poliklinika Radiochirurgia Zagreb	M. Surić Mihić
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Đuro Đaković kompenzatori d. o. o.	M. Surić Mihić
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Hrvatska brodogradnja Trogir d. o. o.	M. Surić Mihić
Našicecement d. d.	M. Surić Mihić
HERMED Servis medicinske opreme d. o. o.	M. Surić Mihić

During 2019, the Unit conducted the personal dosimetry control and testing of ionizing radiation for 181 contractual users from various fields of activity.



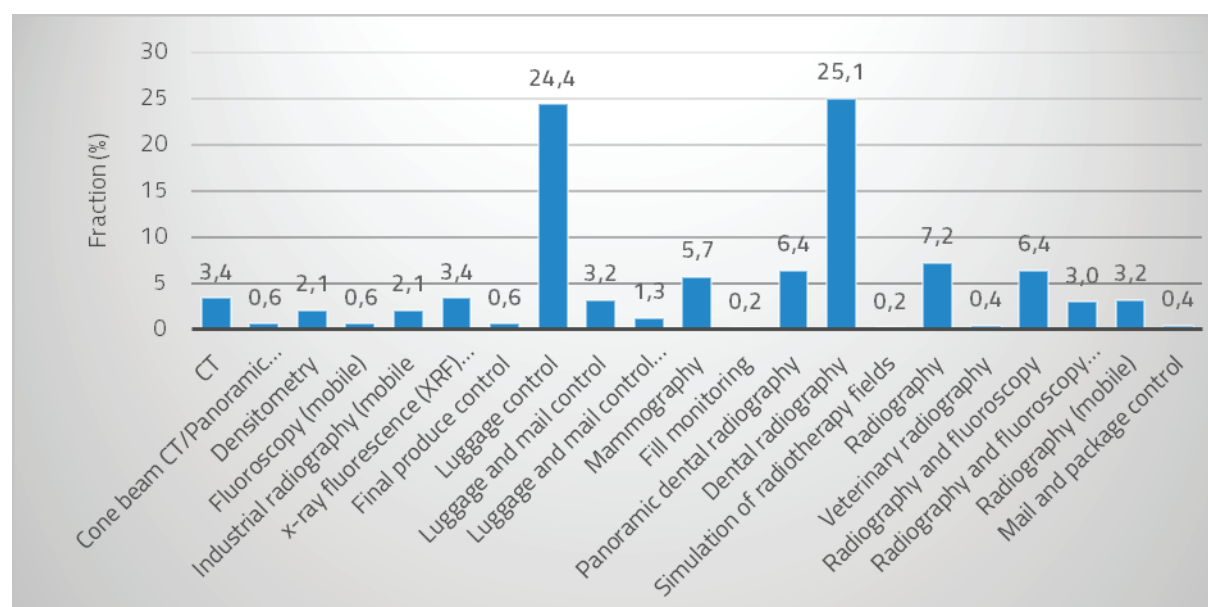
*Number of contracting customers of the Unit by field of work*

During 2019, more than 25,000 dosimetry measurements were made, based on which more than 3,000 dosimetric reports were prepared for contracting users of personal dosimetry monitoring. The unit is working on the preparation of a protocol that will enable the online delivery of dosimetric reports to the users of authorized technical service and thus further modernize the business and relationship with customers.



*Number of tested dosimeters per month*

In 2019, more than 600 field tests were conducted – quality control and radiological protection parameters for about 550 electrical devices that produce ionizing radiation (X-ray devices and linear accelerators) and about 50 radioactive sources used in medicine, industry and scientific institutions. Based on the examination, more than 1,200 expert reports and more than 1,300 expert opinions have been prepared.



*Distribution of tested ionizing radiation electrical devices by their type*

In our laboratory, we conducted testing of the human serum immune response to specific allergens of 7 individuals. Identification of all types of asbestos in solid materials was accompanied according to the International Organization for Standardization (General requirements for the competence of testing and calibration laboratories International Standards Organisation (ISO), Geneva: 1999). We performed eight analysis of solid materials sent from commercial companies to determine the presence and type of asbestos. Analysis of the material was performed by a standardized

method for the stereomicroscopy and polarized microscopy MDHS 77-HSE Document Method for the Determination of Hazardous Substances; series 77 – Asbestos in bulk materials (In: HSG 248 Asbestos: The analysts' guide for sampling, analysis and clearance procedures. Appendix 2: Asbestos in bulk materials: sampling and identification by polarized light microscopy).

#### *List of intercomparisons*

ORGANISER	TEST	AREA	PLACE AND DATE
EURADOS	Extremity & Eye lens dosimeter intercomparison IC2019exteye	Personal dosimetry – $H_p(0,07)$ and $H_p(3)$ measurements	Cavendish Nuclear Limited, UK 9 May 2019

#### *List of accredited methods*

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 $\mu$ Sv – 100 mSv and energy range 33 keV – 1.3 MeV
ME-608-002 (In-house method)	Determination of ambient equivalent dose rate; $H^*(10)/t$ data dose range 100 nSv/h – 100 mSv/h and energy range 36 keV – 1.3 MeV

The Unit's quality manager: *T. Meštrović* (until Feb 2019) and *J. Šiško* (from Feb 2019).

## ■ PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

### *T. Meštrović*

Member of the TO-45 Nuclear instrumentation at the Croatian Standards Institute; radiation protection expert since 2018.

### *L. Pavelić*

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

### *I. Pavičić*

Member of the Working Group in charge of drafting the Position of Croatia in the area of protection against electromagnetic fields.

### *I. Prlić*

Appointed member of the Committee in charge of producing a Draft of the Amendments to the Act on Radiological and Nuclear Safety; member of the Working Group formed by the State Office for Standardisation and the Ministry of Health for legal metrology in the field of medical equipment (especially the one producing radiation); member of the Executive Board of the Croatian Biomedical Engineering and Medical Physics Society (CROMBES); member of the Education and Training Committee of European Federation of Organisations for Medical Physics (EFOMP); member of the TO Non-destructive testing, TO-45 Nuclear instrumentation, and TO-62 Electronical equipment in medical practice; head of the section TO-62B Imaging in medicine at the Croatian Standards Institute; member of the Working Group for drafting and applying a Country Frame Programme (CFP) of the Republic of Croatia; member of the International Atomic Energy Agency (IAEA); member of the Working group of the European Commission Environmental Radiation-Effect: International Perspectives – part of the project relating to Croatia; the Croatian representative in the International Organization for Medical Physics and International Union for Physical and Engineering Sciences in Medicine; member of the Ministry of Health's Committee for the revision and evaluation of studies in the field of use of nonionizing radiation sources; member and expert of the European ALARA Network for Naturally Occurring Radioactive Materials (EAN NORM) group; international expert for the International Road Transport Union (IRU) and International Labour Organization (ILO); member of the Management Committee of MELODI (Multidisciplinary European Low Dose Initiative); member of the Management Committee of the international project COST4BUILDING Materials, Transport

and Urban Development COST Action TU1301.

*M. Surić Mihić*

Associate member of the European Radiation Dosimetry Group (EURADOS); member of the Working Groups WG2 and WG3-S2; member of the TO-62 Electrical equipment in medical practice at the Croatian Standards Institute; radiation protection expert since 2018; appointed expert for accreditation scheme Testing laboratories (HRN EN ISO/IEC 17025) for field T18 Ionising radiation since 2019 (Croatian accreditation agency); appointed professional member with the IAEA for field TSA2 – radiation protection of exposed workers within RASIMS system since 2019 (Civil protection directorate of the Republic of Croatia Ministry of the Interior).

*J. Šiško*

Associate member of the European Radiation Dosimetry Group (EURADOS) Working Group WG3-S2; radiation protection expert since 2018.



## 15.4. Environmental Hygiene Unit

### EMPLOYEES

#### HEAD

Assist Prof Gordana Pehnec, PhD, scientific advisor

#### RESEARCH STAFF

Ivan Bešlić, PhD, senior scientific associate

Ranka Godec, PhD, scientific associate

Silva Žužul, PhD, scientific associate

Silvije Davila, PhD, postdoctoral researcher

Ivana Jakovljević, PhD, postdoctoral researcher

Jasmina Rinkovec, PhD, postdoctoral researcher

Iva Šimić, MSc, PhD student-assistant since 23 May 2019

Suzana Sopčić, PhD, professional associate in science

Valentina Gluščić, BSc, professional associate in science

Zdravka Sever Štrukil, BSc, professional associate in science

#### TECHNICAL STAFF

Ana Filipec, statistician, senior technician

Zvonimir Frković, senior technician until 23 Sep 2019

Samuel Ljevar, senior technician

Magdalena Vincetić, MSc, senior technician since 17 Jun 2019

Marija Antolak, technician

Matea Kuzel, technician

Karmenka Leš Gruborović, technician

Martin Mihaljević, technician

Martina Šilović Hujčić, MSc, technician

#### PARTICIPATING RETIRED RESEARCHERS

Krešimir Šega, PhD, permanent scientific advisor

Vladimira Vađić, PhD, permanent scientific advisor

Mirjana Čačković, PhD, senior scientific associate

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

##### Long term research activities

Measurements of metals in the  $PM_{10}$  fraction of particulate matter and total deposited matter by inductively coupled plasma mass spectrometry (ICP-MS) continued at different locations with different pollution sources. Application of the energy dispersive X-ray fluorescence (ED-XRF) method was investigated for preliminary analysis of metal content in filter media before the sampling of airborne particulate matter. The results showed high content of some elements in quartz microfiber filter blanks and high variability between packagings. ED-XRF analysis can be used for preliminary qualitative analysis of Fe, Zn, Ba, Mn, Ni, and Cu. For more accurate quantitative analysis at low



concentration levels further improvements in the calibration of the method are required (148). Several types of filter media for elemental analysis of  $PM_{2.5}$  particulate matter were investigated for method optimization. Influence on limits of detection and pretreatment of filter media were also tested. Results have shown that quartz filter media are least suitable for sampling and analysis of low concentration levels of elements because of high filter blanks. The lowest detection limits were found for membrane nitrocellulose and teflon filters (137). In cooperation with University of Rijeka and Faculty of Science in Sarajevo, BIH, analysis of  $PM_{10}$  particle fraction at several sampling sites in the Sarajevo Canton, BIH were carried out in order to characterise the organic and inorganic atmospheric pollutants. Preliminary results of mass concentrations of  $PM_{10}$  and As, Cd, Ni, and Pb showed high values of particulate matter in winter as well as significant difference in metal concentrations between measuring sites (263).

In addition to the continuous measurement of polycyclic aromatic hydrocarbons (PAHs) in  $PM_{10}$  particle fraction at locations with different pollution sources (traffic, industry, households) (143, 245), the determination of PAHs in the  $PM_1$  particle fraction was continued (130, 153, 219, 300). PAH mass concentrations in  $PM_{2.5}$  particle fraction at one traffic location in Zagreb (245, 246) were investigated as well. In cooperation with University of Rijeka and Faculty of Science in Sarajevo, BIH, carcinogenic activity of PAHs at urban locations in Zagreb and Sarajevo was determined (154, 318). The results showed high PAH mass concentrations in Sarajevo air compared to Zagreb air, and thus significantly higher carcinogenic activity in Sarajevo. Benzo(a)pyrene (BaP) had the highest contribution to the total carcinogenicity regardless of the relatively small contribution to the total PAH mass, which pointed BaP as a good indicator for estimation of the carcinogenicity of PAH mixture (318). Optimisation of new accelerated solvent extraction method was started in order to increase preparation efficiency (220).

Measurements of elemental and organic carbon in  $PM_{2.5}$  particle fraction continued at monitoring sites with different characteristics (urban background, urban traffic and rural background). The influence of maritime traffic and sea spray on carbon pollution was studied for the city of Rijeka (152, 251, 292, 293). Measurements carried out in the coastal area showed that air pollution in this area is not only of local origin, but also from the long-range transport. Comparison of carbon levels in different particle fractions showed that the seasonal distribution of carbon in smaller particles ( $PM_1$ ) followed seasonal distribution in  $PM_{2.5}$  particle fraction.

The development of analytical method for the determination of molecular markers of organic carbon in particulate matter in air has started. Specific carbohydrates which originate from biomass burning and the natural processes during the vegetation of trees and plants will be determined. Measurements of ozone and its precursors nitrogen oxides and carbon monoxide were continued in order to study their trends and relationships (230).

Measurements of anion ( $Cl^-$ ,  $NO_3^-$ ,  $SO_4^{2-}$ ) and cation ( $Na^+$ ,  $NH_4^+$ ,  $K^+$ ,  $Mg^{2+}$ ,  $Ca^{2+}$ ) content in particle fraction as well as measurements of acidic components ( $Cl^-$ ,  $NO_3^-$ ,  $SO_4^{2-}$ ) in total deposited matter continued at different locations (151, 205, 280, 291). Trend of anions in total deposited matter were studied at different locations in Zagreb. In the northern, residential part of the town with moderate traffic nitrate levels showed statistically significant decreasing trend, while chloride and sulphate levels showed decreasing but statistically insignificant trend (213). Nitrate levels in total deposited matter at the measuring station in the centre of Zagreb with dense traffic and at the measuring station on the western, industrial part of the town also show significant decreasing trend, while chloride and sulphate levels in total deposited matter fluctuate without clear trend (214).

Investigation of sensors for air quality monitoring started in 2017 within the project Ecological Map of the City of Zagreb and in cooperation with Andrija Štampar Teaching Institute of Public Health continued in 2019. Results obtained by parallel measurements with sensors (AQMeshPod) and with reference methods at IMROH location during one year were analysed. Statistical analysis showed great discrepancy of sensor measurements compared to reference methods as well as on the importance of calibration of sensors prior measurements at the measuring site (150, 281). Results of interlaboratory comparison of the sensors conducted by the French Central Air

Quality Monitoring Laboratory (LCSQA) for 6 weeks in Lille were analysed. As part of the parallel measurement, 16 participants from seven countries participated with 44 sets of air quality sensors. There are great differences in the accuracy of sensor measurements between different manufacturers as well as large differences in measuring accuracy with the same type of device but with different electrochemical cells. The results also indicate the problem with sensor performances of several manufacturers (206).

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

#### *1. Levels of platinum group elements (PGE) near roads*

In previous investigations at IMROH the method for determination of Pt, Pd, and Rh in  $PM_{10}$  particulate matter was developed as a part of doctoral dissertation. The first measurements of Pt, Pd, and Rh in particulate matter samples collected at three locations with different traffic load showed that at all three measurement sites, the PGE concentration followed the sequence  $Pd > Pt > Rh$ , and that there are statistically significant differences between locations with high traffic and those with moderate traffic. The measured concentrations were compared with the published results of similar studies in the world (65). The sampling of particulate matter continued at three locations in Zagreb in differently polluted parts of the city, as well as collecting vegetation samples (grass, plantain) and also soil samples at two different depths (0–5 cm and 5–10 cm) were collected twice a year (at the beginning of vegetation and at the end of vegetation). In cooperation with the Faculty of Agriculture, University of Zagreb, basic agrochemical analyses [soil reaction (pH), conductivity (EC), organic matter (OM), hydrolytic acidity of soil (HA), a cation exchange capacity of the soil (CEC), the determination of the exchangeable ions of  $Na^+$ ,  $K^+$ ,  $Ca^{2+}$  and  $Mg^{2+}$ , the content of  $H_2O$  and carbonates, the total nitrogen, sulphur and plants accessible phosphorus and potassium (PAL and KAL)] were done for the collected samples. Similar studies in the world to date regarding PGE determination in soil and vegetation have shown that PGE concentrations are highest along roads and at high traffic intensities. There was also a trend of decreasing concentration with increasing soil depth (33). The study will provide the first information on Pt, Pd and Rh levels in the environment (vegetation, soil) in Croatia and the five year trend of PGE concentrations in particulate matter will be determined.

#### *2. Organic content of $PM_1$ particle fraction*

Collection of 24-hour  $PM_1$  fractions of particulate matter continued during the year at IMROH location and the location in the centre of Zagreb. Organic and elemental carbon and polycyclic aromatic hydrocarbons were analysed in the collected samples. The results are systematized and statistically processed. Measurements of  $PM_1$  organic content in winter period showed the high value of the OC/EC ratio which suggests a large amount of secondary organic carbon (SOC). The low values of PAHs with a small number of rings (fluoranthene and pyrene) and high PAHs concentrations with a higher number of aromatic rings [benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(j)fluoranthene, benzo(ghi)perylene and indene(1,2,3-c,d)pyrene] indicate the traffic as the dominant source of PAHs in  $PM_1$  fraction of particle matter at this location. The first results were presented as oral presentations and posters at one international and two national conferences with international participation (130, 143, 219, 245, 251).

### **RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES**

#### **National projects (Chapter 16.1.)**

- Biochemical responses of oligotrophic Adriatic surface ecosystems to atmospheric deposition inputs (BiREADI, HrZZ-IP)



**International projects (Chapter 16.2.)**

- Project of extension and modernisation of the national network for continuous air quality monitoring (AIRQ, ERDF)
- Enhancing the Inventory of Aerosol Source Profiles Characterized by Nuclear Analytic Techniques in Support of Air Quality Management (IAEA)

**PROFESSIONAL SERVICES**

The monitoring of air pollution continued in Zagreb at 6 measuring stations of the local measuring network. At Zagreb stations, the Environmental Hygiene Unit measured different pollutants in the air: sulphur dioxide, black carbon, PM<sub>10</sub> particle fraction, metals: As, Cd, Ni, Pb, Mn, Fe, Cu, and Zn, and PAHs in PM<sub>10</sub> particle fraction, PM<sub>2.5</sub> particle fraction, nitrogen dioxide, ozone, carbon monoxide, benzene, total deposited matter, and metals: As, Cd, Ni, Pb, and Mn in the total deposited matter.

Pursuant to contracts with the Ministry of Environment and Energy and Meteorological and Hydrological Service of Croatia and the Air Protection Act (OG 130/11, 47/14, 61/17, 118/18, 127/19), the Environmental Hygiene Unit as a reference laboratory performs the sampling of particulate matter (PM<sub>10</sub> and PM<sub>2.5</sub>) 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 (PM<sub>10</sub> and PM<sub>2.5</sub>) in the air. In 2018, air pollutants were measured at the monitoring sites Zagreb-1, Zagreb-3, Sisak-1, Slavonski Brod-1, Slavonski Brod-2, Plitvice Lakes National Park, Ksaverska cesta, Velika Gorica, Kutina, and Rijeka-2. Cooperation with the Ministry of Environment and Energy in the air quality data processing continued.

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 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 Waste Water Treatment Plant in Zagreb was continued. The monitoring of levels of hydrogen sulphide, ammonium, and total mercaptans and meteorological parameters was carried out at five measuring stations.

In line with the contract with the Meteorological and Hydrological Service of Croatia, metals in total deposited matter were analysed at one monitoring station located on the military training polygon of Slunj.

In the vicinity of the Jakuševac waste site, the levels of PM<sub>10</sub> and mercaptans are continuously measured. During different seasons, levels of Pb, As, Ni, Cd, and PAHs in PM<sub>10</sub> fraction were also measured.

Measurements of particle fraction PM<sub>10</sub> and polycyclic aromatic hydrocarbons in PM<sub>10</sub> fraction were carried out at a measuring site within Zagreb International Airport.

Measurements of PM<sub>10</sub> particle fraction were carried out at one location near an asphalt facility in Žminj.

Measurements of total deposited matter were carried out at two locations at "Brezovi Rebar" sand excavation near Karlovac.

*List of intercomparisons*

ORGANISER	TEST	AREA	DATE
LGC	LGC-AIR PT Workplace Air, Ambient Air and Stack Emissions, Round 30 (AR030); 16-Diesel Fume	Determination of mass concentration of elemental carbon in particles	Jan/Feb 2019
ACTRIS	Interlaboratory comparison exercise for TC and EC measurements (ref: OCEC-2019-1)	Determination of mass concentration of total and elemental carbon in particles	Feb/Mar 2019
INERIS	Analytic interlaboratory comparisons organized for laboratories involved in regulatory emissions control	Determination of mass concentration of benzo(a)anthracene, benzo(k)fluoranthene, benzo(b)fluoranthene, benzo(a)pyrene, dibenz(a,h)anthracene, benzo(ghi)perylene, fluoranthene and indeno(1,2,3-cd)pyrene in particles at filter	May/Jun 2019
Lab Service Analytica S.r.l., Italia	InterCinD2019SE (Summer2019) QA/QC study	Determination of polycyclic aromatic hydrocarbons in air: benzo(a)anthracene, benzo(b)fluoranthene, benzo(j)fluoranthene, benzo(k)fluoranthene – expressed as benzo(b+j+k)fluoranthene; dibenz(a,h)anthracene, indeno(1,2,3-cd)pyrene, benzo(a)pyrene, chrysene, benzo(ghi)perylene	Sep/Oct 2019

*List of accredited methods*

METHOD	TYPE OF TEST, RANGE
HRN EN 14625:2012 (EN 14625:2012)	Determination of the concentration of ozone 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 PM <sub>10</sub> 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
HRN EN 14211:2012 (EN 14211:2012)	Determination of the concentration of nitrogen oxide in the ambient air
HRN EN 12341:2014 (EN 12341:2014)	Determination of mass concentration of PM <sub>10</sub> and PM <sub>2.5</sub> particle fraction
HRN EN 14212:2012 (EN 14212:2012), HRN EN 14212:2012/Ispr. 1:2014 (EN 14212:2012/AC:2014)	Determination of the concentration of sulphur dioxide 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, 2018-06-03	Determination of thallium in atmospheric deposition

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 Environment and Energy of the Republic of Croatia; member of the Commission for Reference Laboratory Work Monitoring at the Ministry of Environment and Energy 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 "Air Protection '19" conference Scientific Committee.

### *S. Davila*

Member of the Croatian Air Pollution Prevention Association's Presidency; member of the "Air Protection '19" conference Organizing Committee.

### *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 the "Air Protection '19" conference Organizing Committee.

### *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 Environment and Energy of the Republic of Croatia; member of the Commission for Air Quality Improvement Monitoring in the area of Slavonski Brod; president of the "Air Protection '19" conference Organizing Committee.

### *J. Rinkovec*

Member of the "Air Protection '19" conference Organizing Committee.

### *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; member of the "Air Protection '19" conference Scientific Committee.

## SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

The scientific degree of scientific associate was gained by *I. Jakovljević* and *J. Rinkovec*.



## 15.5. Occupational Health and Environmental Medicine Unit

### EMPLOYEES

#### HEAD

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

#### RESEARCH STAFF

Prof Selma Cvijetić Avdagić, MD, PhD, permanent scientific advisor  
Jasminka Bobić, PhD, permanent scientific advisor until 13 Oct 2019  
Veda Maria Varnai, MD, PhD, permanent scientific advisor  
Assist Prof Adrijana Bjelajac, PhD, scientific associate  
Željka Babić, PhD, postdoctoral researcher  
Jelena Kovačić, PhD, postdoctoral researcher  
Zrinka Franić, MD, PhD student-assistant  
Rajka Turk, MSc, professional advisor in science

#### TECHNICAL STAFF

Marija Kujundžić Brkulj, BSc, senior technician  
Marija Lieberth, administrator, senior technician until 20 Feb 2019  
Rajka Luzar, nurse, senior technician  
Franka Šakić, BSc, senior technician (90 % of working hours and 10 % in the Institute's company)  
Monika Vuletić, MSc, senior technician since 1 Jun 2019  
Jagoda Mandić, nurse, technician since 3 Apr 2019

#### PARTICIPATING RETIRED RESEARCHERS

Božica Kanceljak-Macan, MD, PhD, permanent scientific advisor  
Assist Prof Biserka Ross, PhD, scientific advisor

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

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

1. *Interaction of constitutional and occupational risk factors on the incidence of occupational contact dermatitis in hairdressing apprentices during vocational training (SkinWork)*

In the period between April and June 2019, 406 hairdressing apprentices were included in the second follow-up of the prospective cohort study and evaluated according to the protocol. The study was performed in 25 schools from 25 towns in Croatia (Zagreb, Krapina, Čakovec, Varaždin, Oroslavje, Ivanić Grad, Opatija, Split, Makarska, Omiš, Sinj, Imotski, Garešnica, Slavonski Brod, Osijek, Beli Manastir, Đakovo, Vinkovci, Županja, Samobor, Velika Gorica, Sisak, Đurđevac, Vukovar, and Našice). Moreover, in 32 hairdressing apprentices who reported skin symptoms that were present for at least 3 months, patch testing with European baseline series and additional hairdresser series was performed. Initial results showed high prevalence of self-reported atopy symptoms (45 %), and moderate prevalence of self-reported and clinically observed skin symptoms (12 % and 18 %,

respectively) on the hands/wrists of hairdressing apprentices at the beginning of their vocational education. Filaggrin gene mutations were not indicated as a risk factor, as such a mutation was found in only one apprentice (268).

## 2. *Contact hand dermatitis in dentists and medical doctors: prevalence and risk factors*

The recruiting of subjects and data collection were finished in 2019. Examination is performed in 185 subjects divided in 5 groups (37 subjects in each group): medical doctors-surgeons and non-surgeons, dentists (surgeons and non-surgeons), and control subjects occupationally not exposed to skin irritants/allergens. Methods included an questionnaire, skin examination, skin prick and patch test, and measurement of skin pH and transepidermal water loss. The highest prevalence of hand eczema was found in both groups of dentists, and medical doctors-surgeons, ranging from 37.8 to 56.8 %. This result suggests that these groups of healthcare workers are at high risk for development of occupational hand eczema. The completion of doctoral and graduate theses performed within this project is planned for 2020.

## 3. *Determination of body composition and chronic stress by bioimpedance method*

In approximately 400 subjects, body composition and functioning of the autonomic nervous system were assessed using bioimpedance. In order to validate the bioimpedance device, in about half of the subjects body composition measurements were made with another devices. Cortisol saliva samples were taken in about 70 subjects. Nutritional and sleeping habits were assessed in students. The preliminary results showed a significant association of obesity with increased sympathetic nervous system activity (increased LF/HF ratio and decreased heart rate biovariability), as well as the low values of the HPA index, which estimates the daily rhythm of cortisol secretion (339).

## 4. *Relationship between chronic inflammation and osteopenia in patients on chronic hemodialysis*

The project has started, which assesses the impact of chronic inflammation on sarcopenia, bone remodeling, and bone density in hemodialysis patients. About 70 participants are planned. Results have been published on the prevalence of osteoporosis and calcium intake in people living in nursing homes (13).

## 5. *Preventing child poisonings by educational intervention aimed at parents of preschool children*

The project finished in February 2019. Data from the pilot phase of the project (spring 2018) was published (4), the most important findings are that around 80 % of parents of preschool children keep the products which can cause poisoning in children out the reach of children, but not in locked compartments, and that around one third of parents sometimes keep the products in non-original packaging which could easily lead to poisoning. Data collected in the main phase of the project (second half of 2018 and beginning of 2019) from 527 parents of children attending kindergartens in the city of Zagreb was statistically analysed. The most important result was that parents who underwent intervention started keeping the Poison Control Centre number by the telephone or in the list of important numbers: 1 % of parents in the intervention group reported this habit in the baseline questionnaire and 65 % in the follow-up questionnaire after the intervention, which was significantly larger increase than that noted in the control group (3 % vs. 12 %). The results remained significant also in the more complex statistical model which included personal characteristics of parents (sex, employment status, number of children, education level). Publishing of these results in a scientific journal is currently in progress.

# RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

## National projects (Chapter 16.1.)

- Assessment of daily exposure to metals and maternal individual susceptibility as factors of developmental origins of health and disease (METALORIGINS, HrZZ-IP)
- Well-being of different family generations in contemporary work designs (UNIZg)

**International projects (Chapter 16.2.)**

- European Concerted Programme on Radiation Protection Research (CONCERT, H2020)
- Identification of Member State guidance and support materials linked to exposure to dangerous substances at work places from Croatia and Slovenia (EU OSHA)
- Network on the Coordination and Harmonisation of European Occupational Cohorts (OMEGA-NET, COST)
- Diagnosis, Monitoring and Prevention of Exposure-Related Noncommunicable Diseases (DiMoPEX, COST)
- Genomics of MusculoSkeletal traits Translational Network (GEMSTONE, COST)

**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 course for 6 residents in occupational and sport medicine over one month was conducted in the field of "Occupational diseases, work-related diseases, and occupational toxicology". A training in "Clinical Toxicology" of one week duration was conducted for one resident. J. Macan was appointed as main supervisor by the Croatian Ministry of Health for 7 residents in occupational and sports medicine.

For hairdressers, teachers in vocational schools in the sectors for health and social services, and personal and other services, lectures were delivered in the field of health and safety at work. Additional lecture about actual epidemiological investigations performed in this field within the Unit for Occupational and Environmental Health was delivered.

In collaboration with Poison Control Centre and Unit for Analytical Toxicology and Mineral Metabolism metal concentration measurement in biological samples for residences in Slavonski Brod was carried out. This was followed by the health risk assessment of determined metal levels (341).

**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.

*A. Bjelajac*

Member of the Committee for evaluation of programs for propaedeutics in psychotherapy of the Association of Psychotherapy Societies of Croatia; member of the founding committee for the preparation of the foundation of Croatian Chamber of Psychotherapists; member of the Ethics Committee of the Croatian society of gestalt and integrative psychotherapists.

*J. Bobić*

Member of the committee for acknowledgement of clinical psychologists at the Croatian Psychological Chamber.

*Zr. Franić*

Member of the Croatian Society of Toxicology; member of the Croatian Medical Chamber.

*J. Kovačić*

External expert of the Agency for Medicinal Products and Medical Devices of Croatia.

*J. Macan*

Member of the Croatian Academy of Medical Sciences, Collegium for Public Health; member of the Croatian Society of Occupational Health 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 Working group for climate changes at the Ministry of Health, Republic of Croatia; court expert witness in occupational medicine; member of the Croatian Medical Chamber.

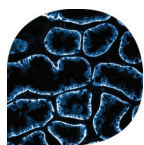
*R. Turk*

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 Committee for the development of Ordinance on the conditions for distribution and sale of pesticides of the Ministry of Agriculture.

*V. M. Varnai*

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





## 15.6. Molecular Toxicology Unit

### EMPLOYEES

#### HEAD

Davorka Breljak, PhD, scientific advisor

#### RESEARCH STAFF

Marija Ljubojević, PhD, senior scientific associate

Ivana Vrhovac Madunić, PhD, scientific associate

Dean Karaica, PhD, postdoctoral researcher

#### TECHNICAL STAFF

Ljiljana Babić, technician

#### PARTICIPATING RETIRED RESEARCHERS

Ivan Sabolić, PhD, MD, permanent scientific advisor

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

During 2019, our scientific collaborations continued and a new collaborative studies was established at institutional, national, and international levels. In the frame of collaborative research with Analytical Toxicology and Mineral Metabolism Unit of IMROH, two original scientific articles were published in journals indexed in the *Web of Science* (WoS) bibliographic database (7, 56). Within the frame of collaborative studies with the Veterinary Faculty of the University of Zagreb (Croatia), one review scientific article was published in the WoS-indexed journals (54), whereas some results were presented at The 10<sup>th</sup> Meeting of the Young Generation of Veterinary Anatomists, YGVA 2019, and published in the Abstract Book (317). Furthermore, one original scientific article was published in the WoS-indexed journal (17) within the frame of new collaborative studies that have been established with the Croatian Institute for Biodiversity – CIB (Zagreb, Croatia) and Biota (Grubišno Polje, Croatia). Also, one diploma thesis was defended (183) in co-operation with the Faculty of Pharmacy and Biochemistry of University of Zagreb (Croatia).

#### RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

##### National projects (Chapter 16.1.)

- Aging-related expression of membrane transporters in rat (AGEMETAR, HrZZ-IP)
- Adverse effects of single and combined mycotoxins produced by *Aspergilli* (MycotoxA, HrZZ-IP)
- Molecular mechanisms underlying the toxicity of antidotes and potential drugs (CellToxTargets, HrZZ-UIP)

##### International projects (Chapter 16.2)

- Correlated Multimodal Imaging (COMULIS, COST)
- European Network of Multidisciplinary Research and Translation of Autophagy (TransAutophagy, COST)
- Assessment of Toxicological Safety of Foodborne Toxins (SafeFood, Bilateral CRO-SI)



## ● PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

*D. Karaica*

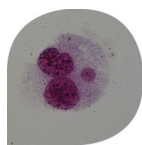
Management Committee member for COST Action CA17121 COMULIS; member of Board for Inclusiveness Target Countries (ITC) grants for COST Action COMULIS.

*M. Ljubojević*

Management Committee member for COST Action CA15138 TransAutophagy.

*I. Vrhovac Madunić*

Member of the Commission for Science and Society of the Croatian Society of Biochemistry and Molecular Biology (HDBMB); Management Committee member for COST Action CA17121 COMULIS; Coordinator of Board for Inclusiveness Target Countries (ITC) grants for COST Action COMULIS.



## 15.7. Mutagenesis Unit

### EMPLOYEES

#### HEAD

Nevenka Kopjar, PhD, permanent scientific advisor

#### RESEARCH STAFF

Vilena Kašuba, PhD, permanent scientific advisor

Prof Davor Želježić, PhD, ERT, permanent scientific advisor

Mirta Milić, PhD, senior scientific associate

Goran Gajski, PhD, scientific associate

Marko Gerić, PhD, scientific associate

Vedran Mužinić, MSc, PhD student-assistant (HrZZ)

#### TECHNICAL STAFF

Maja Nikolić, senior technician

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

##### *In vitro* studies

In the past year, research focused on *in vitro* investigations of the toxicological profile of various physical and chemical agents (biotoxins, copper complexes, cytostatics, natural products, probiotics, waste waters, etc.) for their cyto/genotoxic effects has been continued. The obtained results indicating either their harmful or beneficial effects were published in a series of scientific papers, proceedings, and conference abstracts (27, 77, 94, 164, 210, 270, 271, 290, 294, 295, 296, 304). The aneugenic potential of low concentrations of pesticides chlorpyrifos, imidacloprid, alpha-cypermethrin, terbutilazine, and glyphosate was investigated on human peripheral blood lymphocyte model using cytokinesis-blocked micronucleus assay coupled with fluorescence *in situ* hybridization (FISH) with directly labeled pancentromeric probes for chromosomes 9, 18, X, and Y. Obtained results suggest treatment-related defects in chromosome segregation, and aneuploidy induction for chromosomes 18, 9, X and Y, increasing the risk of malign transformation (50, 236, 273). Cyto-/genoprotective and antioxidant effects of strawberry tree honey and its constituent homogentisic acid on UVB-induced damage were investigated on a human lymphocyte model. The observed effects are the result of several mechanisms, the most important of which are free radicals scavenging, as well as changed activities of antioxidant enzymes and glutathione levels (131). *In vitro* testing of dandelion (*Taraxacum officinale* L.) and rosemary (*Rosmarinus officinalis* L.) extracts on the squamous cell carcinoma cell line CAL27 indicated that both possessed genoprotective properties, suggesting their possible use as effective herbal remedies (297).

##### Human biomonitoring studies

Studies were continued on different human populations to determine the sensitivity and specificity of molecular-biology methods applicable in biomonitoring (96) and the importance of new biomarkers in the early detection of disease (313). The cytogenetic status of subjects with thyroid disease (43), genome sensitivity in patients with papillary carcinoma (284), and the influence of periodontitis on genome changes in gingival epithelial cells of patients (82) were investigated.

We continued with assessments of different occupational hazards and cytogenetic risks associated with exposure to physical and chemical hazards at the workplace (28, 81, 139), risks of exposure to asbestos (168), investigated genotoxic effects of toothpaste ingredients (80), and estimated levels of DNA damage in buccal cells after exposure to antiseptic mouthwash (118). The impact of dietary preferences on levels of DNA damage was investigated as well (286, 287). The buccal micronucleus assay cytome assay provided preliminary data on the impact of radiological diagnostics on genome stability in children (138). The results of all biomonitoring studies indicate the high sensitivity and specificity of the methods used and their great importance in human biomonitoring, regardless of the routes of exposure or entry of genotoxic agents into the body. Furthermore, the role of the comet assay, the standard micronucleus assay and novel version of the buccal micronucleus cytome assay as additional biomarkers in assessing the health status of subjects with various diseases was confirmed.

### Research on animal models

Using the alkaline comet assay, the adverse effects of 28-day oral exposure of male Wistar rats to low doses (0.0007, 0.0013, and 0.7 mg kg<sup>-1</sup> *b. w.* per day) of the herbicide tembotrione were studied. The tested doses correspond to the acceptable operator exposure level (AOEL), residential exposure level (REL), and 1000×AOEL values. All three doses produced statistically significant deviations in the levels of DNA damage in the kidney cells according to the control group of rats. Doses of AOEL and 1000×AOEL caused significantly higher levels of DNA damage in liver parenchymal cells, while significant increases of DNA damage in non-parenchymal liver cells were observed only at the dose corresponding to the AOEL. In the same animals, the activity of the enzyme glutathione peroxidase was also measured, which at the tested doses of tembotrione did not significantly deviate from the control values (97). Using the alkaline comet assay, we investigated the temporal dynamics of the occurrence and elimination of DNA damage inflicted by cytostatic irinotecan in leukocytes, liver, and brain cells of male Wistar rats. The highest level of DNA damage in liver and brain cells was measured on the fourth day and in leukocytes on the eighth day after treatment. The observed pattern of DNA damage is a consequence of both the induction and repair of lesions, whose mechanisms cause additional breaks in the DNA molecule that can be detected using the comet assay. Brain cells are most sensitive to irinotecan activity (301). The effects of the anesthetic isoflurane and  $\gamma$ -radiation (2 Gy dose) were investigated using a comet assay on Swiss albino mouse model. Six hours after exposure, the leukocytes and kidney cells of mice demonstrated synergistic effects of the tested agents on the level of DNA damage. Twenty-four hours later, higher levels of damage were observed in kidney cells than in leukocytes, probably due to the metabolism of the tested anesthetic. The results obtained indicate that the potential adverse effects of anesthetics during medical procedures using ionizing radiation should be anticipated (124).

## RESEARCH Project FUNDED BY EXTERNAL SOURCES

### National projects (Chapter 16.1.)

- Aging-related expression of membrane transporters in rat (AGEMETAR, HrZZ-IP)
- Adverse effects of single and combined mycotoxins produced by *Aspergilli* (MycotoxA, HrZZ-IP)
- Interaction of metallic nanoparticles with sulphur-containing biomolecules – implications for nanobio interface (NanoFaceS, HrZZ-IP)
- Genotoxic and Oxidative Status of Imatinib Mesylate in Non-Target Human Cells (HAZU)

### International projects (Chapter 16.2)

- European Concerted Programme on Radiation Protection Research (CONCERT, H2020)
- A sustainable future for the Danube river basin as a challenge for the interdisciplinary humanities (Danube: Future)
- The comet assay as a human biomonitoring tool (hCOMET, COST)

- Personalized nutrition in aging society: Redox Control of major age-related diseases (NutRedOx, COST)
- "Good biomarker practice" to increase the number of clinically validated biomarkers (CliniMARK COST)
- Occupational exposure to cytotoxic agents in veterinary hospitals and clinics (CytoVet, IPL, PT)
- El proyecto general es evaluación del riesgo genotóxico por exposición a contaminantes ambientales (University of Tlaxcala, MX)
- Assessment of toxicological safety of foodborne toxins (SafeFood, Bilateral CRO-SI)
- Acetylcholinesterase Inhibitors as Potential Anti-Alzheimer Drugs: Prooxidative and Cytogenotoxic Properties (SafeAChE, Bilateral CRO-RS)
- Persistent organochlorine compounds in human milk and their potential effect on the level of primary DNA damage in human cells (Bilateral CRO-RS)
- Distribution of antibiotic resistance genes in waste water treatment plants and receiving environments of China and Croatia (Bilateral CRO-CN)

## PROFESSIONAL SERVICES

The Mutagenesis Unit performs five different analyses: analysis of chromosomal aberrations; analysis of sister chromatid exchanges (SCE); micronucleus assay; comet test; cell viability assay.

The professional services provided by the Mutagenesis Unit included collaboration with occupational health specialists and occupational medicine clinics involved in medical examinations of workers occupationally exposed to physical mutagens (ionising and non-ionising radiation) and/or chemical mutagens (cytotoxic drugs and other genotoxic agents). During 2019, two analyses of chromosomal aberrations and one of micronucleus assay were performed for the purpose of health surveillance of occupationally exposed medical workers.

## PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

*G. Gajski*

Member of the Supervisory Board of the Croatian Association for Cancer Research (HDIR); member of the Editorial board of *Medicine* (Wolters Kluwer Health, Inc.); Guest Editor of Special Issue: Comet Assay (ICAW 2019) of *Toxicology Letters* (Elsevier); Scientific committee of 13<sup>th</sup> International ICAW Workshop, Russia; member of the Working Group on Biotechnology of the Applied Genomics Committee of the Croatian Academy of Sciences and Arts (HAZU).

*N. Kopjar*

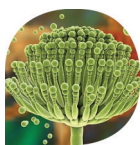
Member of the Presidency of the Croatian Society of Toxicology.

*M. Milić*

Member of the Court of Honor (until 13 Nov 2019) and a member of the Presidency of the Croatian Society of Toxicology (since 13 Nov 2019); member of the Presidency of the Croatian Society of Toxicology; member of the Scientific Committee of the 10<sup>th</sup> International Congress of the Turkish Society of Toxicology (16 – 19 Oct 2019, Antalya, Turkey).

*D. Želježić*

Member of the Editorial board of *BioMed Research International*; vice-president and a member of the Presidency of the Croatian Society of Toxicology (till 13 Nov 2019); expert in biological methods of testing in the Member State Committee of the European Chemicals Agency (ECHA); expert in genotoxicity of the Working Group for Food Enzymes of the Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) – European Food Safety Authority (EFSA).



## 15.8. Toxicology Unit

### EMPLOYEES

#### HEAD

Maja Peraica, MD, PhD, ERT, permanent scientific advisor

#### RESEARCH STAFF

Prof Radovan Fuchs, DVM, PhD, permanent scientific advisor (Deputy Director, International Affairs)

Prof Ana Lucić Vrdoljak, PhD, permanent scientific advisor (Director)

Ivana Novak Jovanović, PhD, senior scientific associate

Dubravka Rašić, PhD, scientific associate

Suzana Žunec, PhD, scientific associate

#### TECHNICAL STAFF

Jasna Mileković, senior technician

Lea Stančin, technician

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

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

1. *Investigation of interactions between irinotecan and tetrahydrocannabinol on laboratory rodents by integrating biochemical, molecular biology, pathohistological and analytical methods*

Due to growing public interest for the antitumor potential of delta-9-tetrahydrocannabinol (THC) and its possible role as an agent for alleviating side-effects of chemotherapy, some oncology patients often take unregistered cannabis preparations that may contain up to 90 % THC. Taking into account the fact that the metabolic pathways of one of the most commonly used cytostatics for the treatment of advanced colon cancer, irinotecan (IRI) and THC in the body overlap, we conducted a pilot study on healthy male Wistar rats in order to investigate how high THC concentrations affect the toxicity of IRI. Effects rats exposure to IRI (100 mg kg<sup>-1</sup>, single dose, *i. p.*) and THC (7 mg kg<sup>-1</sup>, consecutively for 24 hours, 3 days, and 7 days, *p. o.*) and their combination on haematological and biochemical parameters. Cholinesterase activity, markers of oxidative stress, and primary DNA damage were presented at the 4<sup>th</sup> Meeting of the Slovenian Toxicological Society "Cannabis under scrutiny: their toxicity and medical utility". Overall, the results indicated a significant synergistic enhancement of IRI toxicity caused by the concomitant administration of THC (337).

The mechanism of antitumor activity of IRI is based on binding to topoisomerase I-DNA complex causing double-strand DNA breakage and cell death. Considering the well-established sensitivity of the alkaline comet assay for detection of DNA damage in single cells, we have expanded the IRI toxicity study to elucidate (I) dynamics of DNA instability in liver, leukocyte, and brain cells of rats that were administered single IRI dose of 100 mg kg<sup>-1</sup> and (II) differences between levels of DNA damage produced in the studied cell types. The results were evaluated at the first, fourth, and eighth day after exposure to IRI. Appropriate control groups were studied in parallel. To establish the overall toxic effects of IRI, we also estimated changes in total body, liver, and brain weights of experimental animals. Treatment with IRI reduced the total body weight of rats at all time points and also affected liver and brain weights compared to controls. The highest level of primary DNA damage

was determined on the fourth day after treatment in liver and brain cells and on the eighth day in leukocytes (301). The cytotoxic and genotoxic effects of IRI and the ability to induce free radicals depending on the concentration and time of exposure were examined in greater detail *in vitro* on two types of cell lines. The results showed that IRI toxicity increased depending on its concentration in the liver cell line, whereas no concentration dependence was demonstrated in colon cells. Also, the cytotoxic effect of IRI was shown to be related to the induction of free radicals. The genotoxic effect of IRI was observed on both treated cell lines with the prolongation of incubation time (296).

Although THC is known today to be anti-emetic, anticonvulsant, anti-inflammatory and analgesic, existing knowledge about this cannabinoid is controversial in many aspects. For example, the acute effects of THC are known to be associated with cognitive impairment (reaction time, motor coordination and attention, learning perception). THC has been found to reduce the synthesis of the neurotransmitter acetylcholine in the hippocampus, suggesting its negative effects on cognitive processes. On the other hand, based on the high lipophilicity and coupled tricyclic structure of THC, some authors have suggested that THC can bind to the enzyme acetylcholinesterase (AChE). Inhibition of this enzyme by THC may result in the improvement of neurological deficits. Computational modeling of THC-AChE interactions showed that THC binds to the allosteric peripheral anion site (PAS) of AChE, which has a link to the aetiology of Alzheimer's disease (AD) as a concomitant prevention of AChE-promoted A $\beta$ E protein aggregation. The related enzyme butyrylcholinesterase (BChE) is also present in neurite plaques characteristic of AD and could be another target for THC inhibition. Therefore, we tested *in vitro* the ability of THC to inhibit human recombinant AChE and BChE isolated from human plasma. THC caused inhibition of AChE and BChE in the micromolar range with some selectivity for BChE indicating that, in addition to affecting the endocannabinoid system, THC may also affect other neural systems, including central cholinergic neurotransmission crucial for cognitive function (262). The fact that the increase in the use of illegal highly concentrated THC preparations for consumers may mean an even greater likelihood of adverse and unpredictable reactions motivated us to evaluate the toxicity of THC *in vivo* on the Wistar rat model. In blood and brain samples of rats acutely exposed to a dose of THC comparable to those found in illicit preparations (7 mg kg<sup>-1</sup>), we determined the proportion and dynamics of primary DNA damage, the level of oxidative stress, and cholinesterase activity. The results of the alkaline comet assay showed higher levels of DNA damage in brain cells relative to leukocytes, posing a threat to neurons in terms of genome viability and stability, while ineffective DNA repair could lead to their progressive loss. High levels of DNA damage in the brain were accompanied by an increased concentration of lipid peroxidation products and glutathione and a decrease in the activity of the antioxidant enzyme superoxide dismutase. Acute exposure to high doses of THC did not affect cholinesterase activities in the plasma and brain of rats (34, 312).

Furthermore, we developed an analytical method for the determination of the mass concentration of THC and its metabolites [11-hydroxy-delta-9-tetrahydrocannabinol (THC-OH) and 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (THC-COOH)] in the urine of rats treated only with THC and treated simultaneously with THC and irinotecan. For this purpose, hydrolysis and solid phase extraction conditions of the investigated analytes were optimised and a gas chromatography-mass spectrometry (GC-MS) method was developed to determine all three analytes in rat urine. Enhanced urinary THC-COOH excretion was noted in rats administered combined treatment compared to single THC treatment (21, 279).

Three lectures were held at a partner institution at the University Center of Varaždin, University of the North, presenting the results published so far and presenting a plan for further experiments on an experimental model of mice that will be injected with tumor cells (CT26WT line) for induction of intestinal tumors aimed at investigating the impact of THC and IRI on tumor biology and pathophysiology. The lectures were given for the teachers and students of the undergraduate and university graduate studies of Nursing and undergraduate professional study of Physiotherapy of the University of the North.

2. *Investigation of electrochemical and antioxidant properties of polyphenols and their complexes with essential metals*

## RESEARCH Project FUNDED BY EXTERNAL SOURCES

### National projects (Chapter 16.1.)

- Aging-related expression of membrane transporters in rat (AGEMETAR, HrZZ-IP)
- Analysis of Butyrylcholinesterase Interactions with Novel Inhibitors and Reactivators (AnalyseBChE, HrZZ-IP)
- Adverse effects of single and combined mycotoxins produced by Aspergilli (MycotoxA, HrZZ-IP)
- Exploring the antioxidative potential of benzazole scaffold in the design of novel antitumor agents (AntioxPot, HrZZ-IP)

### International projects (Chapter 16.2.)

- European Concerted Programme on Radiation Protection Research (CONCERT, H2020)
- CNS-active, Orally Bioavailable, Zwitterionic Oxime Antidote to Organophosphates (DTRA, USA)

## 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 and the Institute for Medical Research and Occupational Health at the Ministry of Environment and Energy of the Republic of Croatia.

### M. Peraica

President and member of the Croatian Society of Toxicology's Presidency; member of the Medical Academy of Croatian Physicians Association.

### D. Rašić

Secretary and member of the Croatian Society of Toxicology's Presidency.

### S. Žunec

Member of the Court of Honor of the Croatian Society of Toxicology (since 13 Nov 2019).

## SCIENTIFIC, TEACHING AND ACADEMIC ADVANCEMENT OF EMPLOYEES

The scientific degree of scientific advisor was gained by *I. Novak Jovanović*.





## 15.9. Radiation Protection Unit

### EMPLOYEES

#### HEAD

Gordana Marović, PhD, permanent scientific advisor until 31 Dec 2019

#### RESEARCH STAFF

Zdenko Franić, PhD, permanent scientific advisor since 23 May 2019

Assist Prof Dinko Babić, PhD, scientific advisor

Gina Branica, PhD, senior scientific associate

Assoc Prof Branko Petrinec, PhD, senior scientific associate

Tomislav Bituh, PhD, scientific associate

Davor Rašeta, PhD, postdoctoral researcher since 22 Jul 2019

Božena Skoko, PhD, postdoctoral researcher since 10 Sep 2019

Iva Franulović, BSc, professional associate in science (replacement: Helena Jauk, MSc, until 19 Sep 2019)

Milica Kovačić, BSc, professional associate in science

#### TECHNICAL STAFF

Mak Avdić, senior technician

Jasminka Senčar, senior technician

Ljerka Petroci, technician

### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

The study of radioactive contamination of the environment with natural and fission radionuclides (6, 18, 20, 44, 58, 59, 95) continued, with particular attention being paid to risk analysis (58, 76).

The results of long-term post-Chernobyl studies of concentrations of  $^{134}\text{Cs}$  and  $^{137}\text{Cs}$  in multifloral and chestnut honey sampled in northwestern Croatia were analysed. Concentrations of radiocesium activity in honey correlate well with fallout, indicating that fallout is the primary source of radioactive contamination of honey. The results of the research have shown that the consumption of honey in Croatia is not a critical route for the intake of radioactive cesium from the environment (18, 20).

The results of long-term post-Chernobyl studies of the concentrations of  $^{134}\text{Cs}$  and  $^{137}\text{Cs}$  in chicken eggs and chicken meat in northwestern Croatia were analysed. Concentrations of radiocesium activity correlated well with fallout, indicating that fallout was the primary source of radioactive contamination. The results of the study showed that the consumption of chicken meat and eggs is also not a critical route of intake of radioactive cesium from the environment (95).

Data on elevated concentrations of  $^{106}\text{Ru}$  activity measured in 2017 in the air in Croatia were also investigated. These data were compared with test results (1,100 atmospheric data and 200 atmospheric deposition data) conducted in other European countries. It was concluded that a huge atmospheric release of radioactive  $^{106}\text{Ru}$  occurred in Eurasia in 2017, which must have been caused by a significant, but not yet reported, nuclear accident (44).

Between 2013 and 2015, concentrations of radon activity at more than 1000 randomly selected locations in Istria were investigated. Due to the geological structure of the Istrian peninsula, which is mainly composed of limestone, characterized by karst topography on its surface, it is expected that there are areas with elevated radon levels in the soil, as well as within buildings, with particularly high risk for objects with children (homes, kindergartens, schools). The average value of indoor radon in



homes was 102 Bq m<sup>-3</sup>, while the average radon concentrations in kindergartens and schools were twice as high as in households. In accordance with the obtained results, areas with elevated radon levels indoors as well as radon levels in the soil were identified and radon maps were prepared using different geostatistical approaches (59).

A radiological risk analysis of coal ash for terrestrial wildlife was conducted. Specifically, the ashes generated by the combustion of coal and slag in landfills have an increased content of radionuclides from the uranium series. Using the ERICA computer model, dose rates in the environment and the risk of resulting radiobiological effects on wild fauna were estimated. The estimated dose rates for reference animals and lichens and flycatchers were above the rate of the screening dose rate for most organisms and averaged 13 times the estimated dose rate of the baseline radiation. The results of the study indicated the need to further gather experimental data related to radiological risk assessments to mitigate the conservatism of the ERICA model that overestimates environmental dose rates (76).

Particular attention was paid to the issue of field radioactivity measurement methods in order to achieve better and faster efficiency in obtaining data in the event of adverse events, nuclear/radiological accidents, where the crucial role of mobile radiological measuring laboratories is demonstrated.

Radiochemical and measurement methods for monitoring radioactivity in various media are still being developed. By monitoring new knowledge in the field of radiation science and radiation protection, as well as in metrology and sampling, procedures are standardized and methods harmonized 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 efficiency in obtaining relevant data (58).

## RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

### International projects (Chapter 16.2.)

- Science-based Risk Governance of Nano-technology (RiskGONE, H2020)
- Ensuring Radiation Safety (INTERREG CRO-SI)

## PROFESSIONAL SERVICES

### List of international intercomparisons

ORGANISER	TEST	AREA	DATE
IAEA	IAEA-TEL-2019-04	Determination of radioactivity in water, soil, and surface contamination	May 2019 – Oct 2019
IAEA	IAEA-RML-2019-01	Determination of tritium, strontium and caesium isotopes in sea water	Aug 2019 – in progress
IAEA	IAEA-NAEL-2019	Determination of radionuclides in shrimps	Aug 2019 – in progress

### List of accredited methods

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

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

## PROFESSIONAL ACTIVITIES OF THE EMPLOYEES OUTSIDE THE INSTITUTE

### *T. Bituh*

Technical evaluator of projects Support to the development of competence centers – CEKOM; Partner (Deputy Representative of the Republic of Croatia) on the IAEA project RER7014 Improving environmental monitoring and assessment for radiation protection in the region.

### *Z. Franić*

Member of Management board of the Croatian Radiation Protection Association; member of the TO-45 (Nuclear Instrumentation) of the Croatian Standards Institute; member of the European Commission Board of Governors of Joint Research Centre JRC EC (until November 2019); member of the Programme Committee HORIZON 2020 for SC5 (Climate Activities, Environment, Resource Efficiency and Raw Materials); member of Ethics Committee in the Dental Polyclinic Zagreb; Chairperson of "Zrinska gora" NGO; Lead auditor of Croatian Accreditation Agency for accreditation schemes HRN EN ISO/IEC 17025:2017 (General requirements for the competence of testing and calibration laboratories) and HRN EN ISO 14065 (Greenhouse gases – Requirements for greenhouse gas validation and verification bodies for use in accreditation or other forms of recognition).

### *G. Marović*

Member of the Supervisory Board of the Croatian Radiation Protection Association; member of the Management Board of the Croatian Nuclear Society; member of the Public Committee of the Croatian Nuclear Society; member of the Scientific Committee of 12<sup>th</sup> Symposium of the Croatian Radiation Protection Association (10-12 Apr 2019, Varaždin).

### *B. Petrinec*

President of the Firefighters Community of the Town of Ivanić-Grad; member of the Governing Council of the Firefighters Community of the Town of Ivanić-Grad; vice-president of the City Council of the Town of Ivanić-Grad; member of the Presidency of the Firefighters Community of the Zagreb County; quality manager for the Firefighters Community of the Town of Ivanić-Grad; firefighter judge; Senior firefighting officer 1<sup>st</sup> class; firefighter with special authorisations and responsibilities; head of IMROH's defence preparation; member of the TO-45 (Nuclear Instrumentation) of the Croatian Standards Institute; member of the Editorial Board of the journal *Fire and Fire management*.

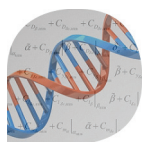
### *D. Rašeta*

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

### *J. Senčar*

Member of the Management Board of the Croatian Radiation Protection Association; member of the Organising Scientific Committee of 12<sup>th</sup> Symposium of the Croatian Radiation Protection Association (10-12 Apr 2019, Varaždin).

## 15.10. Independent researchers



### 15.10.1. Independent researcher

**Aleksandra Fučić, PhD**  
permanent scientific advisor

#### RESEARCH

##### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

A book entitled "Medical Genetics" (ISBN 987-5-98811-4) has prepared for publication in collaboration with Dr A. Aghajanyan, Peoples' Friendship University of Russia in Moscow. The book will be published by Practical Medicine and used by medical colleges of the Russian Federation. Editors: Aghajanyan, Fucic, Chovrebova, Lasan.

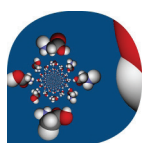
##### RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

###### National projects (Chapter 16.1.)

- The role of oestrogen and androgen receptor activation in the stroma of oral cancer and their impact on the survival of patients (ACTIVESTROMORALCANCER, HrZZ- IP)

###### International projects (Chapter 16.2.)

- Scientific Centre of Excellence for Reproductive and Regenerative Medicine: Reproductive and Regenerative Medicine – Exploring New Platforms and Potentials (CERRM, EFRR)
- European Human Biomonitoring Initiative (HBM4EU, H2020)



### 15.10.2. Independent researcher

**Jasmina Sabolović, PhD**  
scientific advisor (since 11 Jun 2019)

#### RESEARCHER

Jelena Pejić, MSc, PhD student-assistant (HrZZ)

#### RESEARCH

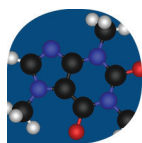
##### RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

###### National project (Chapter 16.1.)

1. Combined molecular modelling and experimental studies of physiologically and stereochemically important copper(II) amino acid complexes (CopperAminoAcidates, HrZZ-IP)

#### SCIENTIFIC, TEACHING, AND ACADEMIC ADVANCEMENT OF EMPLOYEES

The scientific degree of scientific advisor was gained by *J. Sabolović*.



### 15.10.3. Independent researcher

Ante Miličević, PhD  
scientific advisor

#### RESEARCH

#### RESEARCH ACTIVITIES WITH INSTITUTIONAL FINANCING

##### In-house scientific project (Chapter 16.1.A.3.)

1. *Investigation of electrochemical properties and antioxidant activity of polyphenolic compounds and their complexes with essential elements*

In 2019 we compared semi-empirical (PM6) with density functional theory (DFT) calculations, on the set of 20 flavonoids for which we measured first oxidation potentials,  $E_{p1}$ , at pH 3 and pH 7, used for making models for the estimation of  $E_{p1}$  values (46, 47). PM6 method yielded significantly better results than much demanding DFT calculations. In the third paper (45), on the set of 14 flavonoids, we showed that by averaging of the antioxidant activities (AA) measured by four different methods the correlation of AA with  $E_p$  is better ( $r^2 = 0.960$ ) than separate correlations ( $r^2 = 0.561 - 0.848$ ) using AA values measured by one method. On paper about benzimidazole derivatives (51), we identified electroactive groups of eight analyzed molecules using theoretical PM6 calculations.

#### RESEARCH PROJECTS FUNDED BY EXTERNAL SOURCES

##### National project (Chapter 16.1.)

- Interaction of metallic nanoparticles with sulphur-containing biomolecules – implications for nano-bio interface (NanoFaceS, HrZZ-IP)

#### PROFESSIONAL ACTIVITIES OUTSIDE THE INSTITUTE

##### A. Miličević

The chief shop steward at the Independent Trade Union of Science and Higher Education for the branch IMROH.

## 16. PROJECTS

## 16.1. NATIONAL PROJECTS



## 16.1.A. RESEARCH PROJECTS LED BY IMROH RESEARCHERS

## 16.1.A.1. Croatian Science Foundation

## Research projects (5 projects)



LEADER	PROJECT	DURATION
Davorka Breljak, IMROH	Aging-related expression of membrane transporters in rat (AGEMETAR, IP-2013-11-1481)	1 Oct 2014– 31 Mar 2019

IMROH ASSOCIATES: G. Gajski, M. Gerić, J. Jurasović, D. Karaica, M. Ljubojević, V. Micek, I. Novak Jovanović, T. Orct, M. Peraica, D. Rašić, I. Sabolić, I. Vrhovac Madunić  
EXTERNAL ASSOCIATES: L. Nanić and I. Rubelj (Ruđer Bošković Institute, Zagreb)

## SUMMARY

In accordance with the working project plan, various tissues/organs were collected from males/females following 21-mo H<sub>2</sub>O (control) and EtOH treatment in the rat experimental model. For the immunofluorescence analysis, organs were fixed by perfusion *in vivo*, whereas for monitoring of the renal/hepatic endocytosis, animals were perfused with FITC-dextran *in vivo*. Furthermore, total cell membranes/cytosolic fractions/RNA/DNA were isolated from the renal/hepatic tissues. Within the project framework, two group seminars and one presentation were held at IMROH, showing the results of the performed scientific research. Also, we published one original scientific article in a WoS-indexed journal (40). Furthermore, results were disseminated through the poster/oral presentation at international scientific meeting 1<sup>st</sup> Science & Wine World Congress (325) and international scientific workshop "Mouse genetics; models for human diseases" ICGEB Course. Other results will be published within the scientific articles under preparation. Following the submission of the final project report, AGEMETAR was rated by the final grade B having good progress and achieving most of the project objectives. Also, it was highlighted that reasons for the some project discrepancies were objective. Even though the project AGEMETAR was formally finished, we continue to work in order to finish all the planned activities that could not be finished in the given project period. In organs/tissues of all experimental groups following the 21-mo EtOH treatment, various parameters were measured in urine, blood serum, kidneys, liver, and brain using various techniques such as DNA/RNA isolation, reverse transcription, RT-PCR (end-point/quantitative), SDS-PAGE/western analysis, immunocytochemistry/fluorescence microscopy, ELISA, comet assay, ICP-MS, HPLC and telomere's length determination. Upon completion of the AGEMETAR project, several work meetings were additionally held at IMROH in order to prepare data for further dissemination of results in relevant scientific publications.

LEADER	PROJECT	DURATION
<b>Zrinka Kovarik, IMROH</b>	<b>Analysis of Butyrylcholinesterase Interactions with Novel Inhibitors and Reactivators (AnalyseBChE, IP-2018-01-7683)</b>	<b>1 Oct 2018– 30 Sep 2022</b>

IMROH ASSOCIATES: A. Bosak, N. Maček Hrvat, G. Šinko, M. Katalinić, S. Žunec, A. Matošević  
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 at San Diego, La Jolla, USA)

#### SUMMARY

This project is aimed at studying of the mechanisms of interaction of butyrylcholinesterase (BChE) with known and novel compounds using a comprehensive analysis of findings and results of a past project funded by the Croatian Science Foundation (CHOLINESTERASE, HrZZ-IP-2013-11-4307) (37). The biochemical mechanism of enzymatic interactions is studied at the molecular level by *in silico*, *in vitro*, and *ex vivo* methods in line with the defined four project objectives: (a) Identification of the structural characteristics of new BChE ligands, (b) Determination of related reaction rate constants, (c) Conversion of BChE from stoichiometric to a catalytic OP bioscavenger, and (d) Development of new BChE therapeutics and purposeful scientific activities. Already in the first year of the project, our findings have made it possible to identify reversible BChE inhibitors from a series of newly synthesized 4-aminoquinolines (10) and oxazole benzylamine derivatives (111) as potential candidates for the treatment of neurodegenerative diseases. Then, a series of pyridinium triazole oximes was investigated as reactivators of BChE phosphorylated by nerve agents – tabun, VX, sarin, and cyclosarin (38, 103, 123). Efficient reactivators of BChE inhibited by cyclosarin and sarin were identified among the high-affinity phenyltetrahydroisoquinoline aldioximes (103). From the reactivation study on a series of chlorinated pyridinium compounds dichlorinated bispyridinium oxime with a propyl linkage stood out (89). Its BChE reactivation potency was showed to be promising when compared to the standard oximes used in medical practice (HI-6 and 2-PAM), especially in case of sarin and tabun. This finding could be used in the pseudo-catalytic scavenging of the most nerve agents due to its cumulative capacity to reactivate both BChE and related acetylcholinesterase, a key enzyme for in neurotransmission.

LEADER	PROJECT	DURATION
<b>Martina Piasek, IMROH</b>	<b>Assessment of Daily Exposure to Metals and Maternal Individual Susceptibility as Factors of Developmental Origins of Health and Disease (METALORIGINS, IP-2016-06-1998)</b>	<b>1 Jun 2017– 31 May 2021</b>

IMROH ASSOCIATES: J. Jurasović (Deputy Leader), T. Orct, A. Pizent, M. Lazarus, I. Brčić Karačonji, N. Brajenović, A. Katić, B. Tariba Lovaković, A. Sekovanić, A. Sulimanec Grgec, T. Živković Semren, Z. Kljaković-Gašpić, J. Kovačić, A. Jurić  
EXTERNAL ASSOCIATES: D. Pašalić, S. Stasenکو, K. Branović Čakanić, L. Škratić, I. Miškulin

#### SUMMARY

The project evaluates the health effects of the daily exposure and intake of essential and major toxic elements in vulnerable population groups – pregnant women that, in addition to individual susceptibility of the expectant mother, may have an impact on foetal epigenetic regulation and act as the factors of developmental origins of health and disease in adulthood (according to the concept of developmental origins of health and disease, DOHaD). A cross-sectional epidemiological study is carried out by the methods of human biological monitoring in mother-newborn pairs connected to previously collected compatible data and biological samples from >200 participants.

We completed the recruitment of in total 156 participants, healthy non-smoking and cigarette smoking postpartum women, which included collection of the data on study participants by questionnaire and biological samples from mother-newborn pairs closely before or after vaginal term birth in maternity wards of the collaborating clinical hospitals. All biological samples, maternal urine and blood, umbilical cord blood and whole placentas, were prepared for the planned analyses and stored according to the project protocols.

Part of the planned element analysis in biological samples collected before and during the current project was conducted. Concentrations of Hg were determined (by ICP-MS method) in the samples of maternal blood and hair, placenta, and umbilical cord blood in association with the consumption of seafood in mother-infant pairs after normal delivery at a maternity hospital in coastal Croatia ( $n = 96$ , mean age of participants 29 years). Concentrations of Hg in all of the measured samples were proportional to seafood intake and expectedly higher in maternal hair (about 220 times) and cord blood (about 1.6 times) than in maternal blood.

The high correlation coefficient of Hg concentrations ( $>0.80$ ) in all measured samples proves that in the studies on mother-infant pairs, non-invasively collected samples of the placenta and umbilical cord blood are valuable biological samples, and their Hg concentration can serve as reliable biomarkers of exposure to highly toxic Hg due to maternal seafood consumption, mainly fish. Therefore, invasive sampling of maternal blood can be avoided and hair sample collection may not be necessary (which participants may refuse to give or the sample is unsuitable for analysis due to insufficient length or chemical treatment of the hair) (244).

The following results have been obtained to date: the antioxidant protection indicators by determining the activities of antioxidant enzyme superoxide dismutase (SOD) and glutathione peroxidase (GPx) in maternal and cord blood plasma and the levels of metallothionein (MT) in maternal and cord blood serum samples of non-smoking and smoking postpartum women as well as the mass concentrations of cotinine in urine as a biomarker of exposure to tobacco smoke.

The preliminary results on candidate miRNAs in the samples of maternal blood plasma from non-smokers ( $n = 13$ ) and smokers ( $n = 13$ ) pointed to aberrant expression of miR-21 and miR-146a related to tobacco smoke exposure, whereas miR-1537 and miR-190b were not expressed or with threshold cycle (Ct) value  $>35$  in 95 % and 50 % of analysed samples (274). We further optimized the protocol for circulating miRNA analysis (by Qiagen miRNA assays) and tested the preamplification step to increase the sensitivity of quantitative polymerase chain reaction (qPCR) analysis and the number of detectable extracellular miRNAs in 19 paired maternal and umbilical cord blood plasma samples. By using the  $\Delta\Delta C_t$  method of relative quantification, we analysed fold change for miRNA expression in the samples from healthy smoking ( $n = 10$ ) and non-smoking ( $n = 9$ ) postpartum women collected immediately after delivery. Preamplification facilitated the detection of all assayed candidate miRNAs and yielded a mean Ct improvement of  $6.7 \pm 1.1$  ( $p < 0.01$ ) compared with Ct values derived from the direct qPCR method. Values of  $\Delta C_t$  between the compared methods were highly correlated ( $r > 0.9$ ) for miR-16, miR-21 and miR-146a, and their Ct values previously determined by direct qPCR were less than 35. Our results confirm that preamplification is a useful and reliable procedure to facilitate detection of the expression of circulating miRNA in blood plasma. Determined fold changes for miR-1537 and miR-190b in cord blood plasma of 3.5 and 1.6 showed their upregulation related to tobacco smoke exposure (221).

Among our internal dissemination activities, continuous mutual consultations and exchange of experiences within the project consortium carried on with the presentations for methods and new procedures to be used during the study and on the of the first results on the project during three internal seminars. The information on the project's website and the entries on the research data in the project database sheets are regularly updated.

LEADER	PROJECT	DURATION
<b>Jasmina Sabolović, IMROH</b>	<b>Combined molecular modelling and experimental studies of physiologically and stereochemically important copper(II) amino acid complexes (CopperAminoAcidates, IP-2014-09-3500)</b>	<b>1 Sep 2015– 28 Feb 2020</b>

IMROH ASSOCIATE: J. Pejić

EXTERNAL ASSOCIATES: D. Vušak (Faculty of Science, University of Zagreb), M. Ramek (Technische Universität Graz, Graz, Austria), G. Szalontai (NMR laboratórium, Pannon Egyetem, Veszprém, Hungary)

#### SUMMARY

According to the work plan of the project, the experimental and computational research of copper(II) complexes with amino acids has been performed. In collaboration with M. Ramek, A-M. Kelterer, M. Marković, and I. Mutapčić (Technische Universität Graz, Graz, Austria), theoretical results of conformational analyses of the physiological bis(L-asparaginato)copper(II)  $[\text{Cu}(\text{L-Asn})_2]$  and (L-histidinato)(L-asparaginato)copper(II)  $[\text{Cu}(\text{L-His})(\text{L-Asn})]$  complexes obtained by the density functional theory (DFT) method in vacuum and aqueous solution were published (60). The structural properties and energy landscapes were explored. The conformational analyses in the gas phase and implicitly modeled water medium, and magnetic parameters of electron paramagnetic resonance spectra were attained. The apical Cu(II) coordination and hydrogen bonding were analysed. The predicted lower-energy structures enabled the confirmation and, for apical bonding, also the refinement of structural proposals from the literature. Available experimental results were indecisive regarding the amido-group binding in the Cu(II) equatorial plane in solutions, but the examination of the relative stability of  $\text{Cu}(\text{L-Asn})_2$  conformers in 30 binding modes confirmed the glycine-like mode as the most stable one. Previously reported experimental results for  $\text{Cu}(\text{L-His})(\text{L-Asn})$  were interpreted for L-His to have a tridentate histamine-like mode. However, our prediction is that the aqueous conformers with L-His in the glycinato mode also have low energies, which does not contradict the tridentate L-His binding.



The predicted magnetic parameters of conformers with an apical oxygen atom (intramolecular or from a water molecule) can reproduce the experimental data (60, 326). An extent of conformational flexibility and abundance of L-His-containing ternary copper(II) amino acid complexes under physiological conditions may be related (60). The DFT conformational analyses of several other physiological copper(II) amino acid complexes are under progress.

In collaboration with the scientists of the Department of Chemistry at the Faculty of Natural Sciences and Mathematics in Zagreb, D. Vušak and D. Matković-Čalogović, and G. Szalontai of the Pannonian University (Veszprém, Hungary), we worked on exploring different approaches in syntheses and preparations of new crystal forms of the copper(II) complexes with leucine, the X-ray crystal structure refinement (222), and solid-state and solution NMR characterization. Besides, the theoretical conformational analyses were performed using DFT and a molecular mechanics force field to rationalize why a specific conformer/stereoisomer had crystallized.

LEADER	PROJECT	DURATION
<b>Ivana Vinković Vrček, IMROH</b>	<b>Interaction of metallic nanoparticles with sulphur-containing biomolecules – implications for nano-bio interface (NanoFaceS, IP-2016-06-2436)</b>	<b>15 Mar 2017– 14 Mar 2021</b>

IMROH ASSOCIATES: M. Milić, G. Šinko, I. Pavičić, A. Miličević

EXTERNAL ASSOCIATES: I. Capjak, S. Šupraha Gopreta, M. Milić, B. Vuković, V. Šerić, W. Goessler, D. Horak, E. Omanović-Miklićanin

#### SUMMARY

The main objective of the proposed project is to provide new information on the nature of the “nano-bio” interface between metallic theranostic nanomaterials and sulphur-containing biomolecules (S-biomolecules), which play an important and complex functional role in living systems. The model of this project consists of: i) a set of silver, gold and iron oxide nanoparticles with different physicochemical properties (size, surface charge and chemical composition) and (ii) five important S-biomolecules: cysteine, glutathione, metallothionein, albumin, and insulin. The project is a multimethodological and multidisciplinary approach that will provide new insights into the nature of specific biological interactions of NPs with S-biomolecules, thus significantly contributing to the knowledge of the nanomedical field.

During 2019, the following was investigated: 1) interactions of AgNP and SPION with cysteine (CYS) and glutathione (GSH) in various biological media (related to WP3 and WP6), 2) interactions of AgNP and SPION with albumin (ALB), glycosylated transferrin (gTRF) and non-glycosylated transferrin (ngTRF) and in different biological media (related to WP3 and WP6), 3) dissolution processes of AgNP and SPION in the presence of S-biomolecules in different biological media (related to WP4), and 4) biological effects of AgNP- and to human cells *in vitro*. One PhD thesis was drafted and submitted for evaluation. All members of the research team actively participated in the dissemination activities.

#### Installation research projects (2 projects)



LEADER	PROJECT	DURATION
<b>Maja Katalinić, IMROH</b>	<b>Molecular mechanisms underlying the toxicity of antidotes and potential drugs (CellToxTargets, UIP-2017-05-7260)</b>	<b>1 Mar 2018– 28 Feb 2023</b>

IMROH ASSOCIATES: A. Zandona, I. Vrhovac Madunić, J. Madunić (since 2 Oct 2019)

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

#### SUMMARY

During 2019 we continued with the research of cell effects of antidotes against organophosphorus compounds (OP) according to the project's work plan. The main goal this year was to uncover the trigger mechanism leading to the unwanted effects and define possible structural features/moieties of tested compounds triggering certain effects. We tested the time- and dose-dependent effect of selected compounds (based on results from previous year) on the set of selected cells and determined potential cell targets (223). Results indicated that the tested 3-hydroxy-2-pyridinium, pyridinium and quinuclidinium compounds activated specific enzymes, caspases, which govern the process of regulated cell death known as apoptosis (335). On the other hand, the tested imidazolium compounds changed the cell membrane integrity and by that, cell death by necrosis (258). We analysed these results in terms of structure-activity relationship and compared them to the structures of known actions from available databases (229). We tested the cytotoxic effect of several new sets of compounds investigated as treatment in OP poisoning (227, 308, 336).

The second topic from this project focused on the investigation of neuropathy target esterase-related enzyme (NRE). During 2019, we followed changes in NRE mRNA and protein level in the muscle cells exposed to different stimuli (changes in nutrients/oxygen level, differentiation stimulators hormones, cytokines). Based on the obtained results we gained insight into the potential physiological role of NRE and set the course for the future research (302, 303). Along with that, we isolated the NRE mRNA sequence from the muscle tissue, prepared cDNA and cloned it into a vector. A plasmid was sent to analysis and our sequence confirmed.

The importance of this research was presented at scientific conferences as well as in the form of popular and professional lectures (171).

LEADER	PROJECT	DURATION
<b>Darija Klinčić, IMROH</b>	<b>Development, validation and application of analytical methods for PBDE determination (DeValApp, UIP-2017-05-6713)</b>	<b>1 Oct 2018–30 Sep 2023</b>

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

#### SUMMARY

The first activities of the project involved the purchase of the planned equipment and chemicals, and furthermore, the sensitivity and selectivity of gas chromatographic determination of polybrominated diphenyl ethers (PBDEs) with electron capture detectors, mass spectrometers and coupled tandem mass spectrometry systems were determined. Microwave assisted extraction (MAE) using various combinations of organic solvents was used to extract selected PBDE congeners from house dust samples. After selecting the most suitable solvent, the other parameters for MAE (solvent volume, extraction temperature and extraction time) were optimized by a mathematical modeling procedure in collaboration with T. Safner (Faculty of Agronomy, Zagreb). We started the optimization of extract purification by solid phase extraction and/or shaking with concentrated sulfuric acid. A review paper was published (98) summarizing the literature data on the levels and distribution of PBDEs in samples from humans and the environment reported in the last five years. The project theme was presented in popular scientific lectures by participating in teaching within the course "Hygiene and Preventive Medicine" for the students of the Nursing School Vrapče, Zagreb.

### 16.1.A.2. Croatian Academy of Science and Art Foundation (2 projects)



LEADER	PROJECT	DURATION
<b>Goran Gajski, IMROH</b>	<b>Genotoxic and Oxidative Status of Imatinib Mesylate in Non-Target Human Cells</b>	<b>2018–2019</b>

IMROH ASSOCIATE: M. Gerić  
EXTERNAL ASSOCIATE: A-M. Domijan

#### SUMMARY

The aim of the project is to investigate the genotoxic effect of imatinib mesylate (IM), a selective tyrosine kinase inhibitor used in cancer therapy, at concentrations relevant to environmental, occupational, and therapeutic exposure and oxidative stress mechanisms in normal human cells in *in vitro* conditions. At higher concentrations, IM exposure produced oxidative stress that affected non-target cells (23, 191, 217).

LEADER	PROJECT	DURATION
<b>Antonio Zandona, IMROH</b>	<b>Cell response to exposure to chlorinated bispyridinium compounds</b>	<b>2018–2019</b>

IMROH ASSOCIATES: M. Katalinić, Z. Kovarik, T. Zorbaz

#### SUMMARY

The activity of one group of oximes (chlorinated bispyridinium) was measured on cell level, since their efficacy as antidotes in organophosphorus poisoning in previous *in vitro* studies. The aim was to determine which molecular mechanism: internal (mitochondrial pathway) or external signal pathway (receptor pathway) would lead to cell death (apoptosis) and which part of the structure is responsible for this signal. In order to determine the mechanism of death, the cell membrane integrity and the caspase-8 and caspase-9 activity were monitored. In addition, since apoptosis is an active process, the ATP ratio in cells was quantified over time and at certain oxime concentrations. The theme and importance of this project as well as the project results will be presented at upcoming congresses and workshops.

## 16.1.A.3. In-house scientific projects (16 projects)



LEADER	PROJECT
<b>Ž. Babić</b>	<b>Preventing child poisonings by educational intervention aimed at parents of preschool children</b>
IMROH ASSOCIATES: R. Turk, J. Macan, A. Bjelajac, V. M. Varnai, Lj. Prester, S. Cvijetić Avdagić, Zr. Franić, J. Kovačić, M. Kujundžić Brkulj, M. Deranja (until 7 Nov 2018), F. Šakić	
<b>A. Bosak</b>	<b>Design, synthesis and evaluation of selective inhibitors of butyrylcholinesterase</b>
IMROH ASSOCIATES: M. Katalinić, G. Šinko, Z. Kovarik, A. Miličević, A. Zandona EXTERNAL ASSOCIATES: I. Primožić and A. Ramić (Faculty of Science, University of Zagreb)	
<b>S. Cvijetić Avdagić</b>	<b>Determination of body composition and chronic stress by bioimpedance method</b>
IMROH ASSOCIATES: A. Bjelajac, J. Macan, Ž. Babić, J. Jurasović, Zr. Franić, T. Orct, R. Luzar, F. Šakić EXTERNAL ASSOCIATES: I. Colić Barić, I. Keser (Faculty of Food Technology and Biotechnology, University of Zagreb), J. Ilich Ernst (Florida State University, Tallahassee, USA)	
<b>S. Cvijetić Avdagić</b>	<b>Relationship between chronic inflammation and osteopenia in patients on chronic hemodialysis</b>
IMROH ASSOCIATES: J. Macan, V. M. Varnai, R. Luzar, J. Mandić EXTERNAL ASSOCIATES: K. Altabas i P. Kovačević (KBC Sestre Milosrdnice, Zagreb), I. Keser (Faculty of Food Technology and Biotechnology, University of Zagreb), J. Ilich Ernst (Florida State University, Tallahassee, USA)	
<b>R. Godec</b>	<b>Organic content of PM<sub>1</sub> particle fraction</b>
IMROH ASSOCIATES: G. Pehnek, I. Bešlić, I. Jakovljević, Z. Sever Štrukil, I. Šimić	
<b>S. Herceg Romanić</b>	<b>Persistent organic pollutants – environmental impact assessment and stability of human genetic material</b>
IMROH ASSOCIATES: G. Mendaš Starčević, S. Fingler Nuskern, S. Stipičević, D. Klinčić, M. Dvorščak, D. Želježić, V. Mužinić EXTERNAL ASSOCIATES: B. Mustač (Department of Ecology, Agronomy and Aquaculture, University of Zadar), G. Vuković and A. Stojić (Institute of Physics, University of Belgrade, Serbia)	
<b>M. Lazarus</b>	<b>Nutritive and toxicological properties in organic vs. conventional honeys</b>
IMROH ASSOCIATES: Z. Franić, A. Jurić, T. Orct, A. Sekovanić, B. Tariba Lovaković EXTERNAL ASSOCIATES: N. Bilandžić i M. Denžić Lugomer (Croatian Veterinary Institute), D. Bubalo (Faculty of Agriculture, University of Zagreb)	
<b>A. Lucić Vrdoljak</b>	<b>Investigation of interactions between irinotecan and tetrahydcannabinols on laboratory rodents using integrated biochemical, molecular biology, pathohystologic and analytical methods</b>
IMROH ASSOCIATES: Ž. Babić, N. Brajenović, I. Brčić Karačonji, M. Dvorščak, R. Fuchs, A. Jurić, N. Kopjar, G. Mendaš Starčević, V. Micek, A. Katić, I. Novak Jovanović, Lj. Prester, S. Žunec PARTNER: University North, Koprivnica	
<b>J. Macan</b>	<b>Interaction of constitutional and occupational risk factors on the incidence of occupational contact dermatitis in hairdressing apprentices during vocational training</b>
IMROH ASSOCIATES: S. Cvijetić Avdagić, V. M. Varnai, J. Bobić, Zr. Franić, Ž. Babić, J. Kovačić, A. Bjelajac, M. Deranja, M. Kujundžić Brkulj, F. Šakić, M. Milić	
<b>J. Macan</b>	<b>Contact hand dermatitis in dentists and medical doctors: prevalence and risk factors</b>
IMROH ASSOCIATES: A. Bjelajac, Ž. Babić, Zr. Franić, F. Šakić EXTERNAL ASSOCIATES: L. Lugović Mihić and I. Japundžić (School of Dental Medicine, University of Zagreb)	

<b>A. Miličević</b>	<b>Investigation of electrochemical properties and antioxidant activity of polyphenolic compounds and their complexes with essential elements</b>
IMROH ASSOCIATES: I. Novak Jovanović, I. Pavičić EXTERNAL ASSOCIATES: N. Bregović (Faculty of Science, Zagreb), G. I. Miletić (Ruđer Bošković Institute, Zagreb)	
<b>B. Petrincec</b>	<b>Radiological characterization of Kopački rit</b>
IMROH ASSOCIATES: D. Babić, T. Meštrović, M. Šošćarić PARTNERS: Physics Department of J. J. Strossmayer University, Osijek	
<b>I. Prlić</b>	<b>Development of UV radiation sensors (SUVIndex)</b>
IMROH ASSOCIATES: J. Macan, Lj. Orešić (till 15 Sep 2017), M. Surić Mihić, L. Pavelić (since 1 Jun 2017) PARTNERS: Haj-Kom (M. Hajdinjak), ALARA Uređaji (Z. Cerovac), KBC Zagreb, ACI Marina Vodice	
<b>I. Prlić</b>	<b>Thermometry, thermography and sensory evaluation of electromagnetic radiation in medicine</b>
IMROH ASSOCIATES: M. Surić Mihić, I. Bešlić, Lj. Orešić (until 15 Sep 2017), L. Pavelić (since 1 Jun 2017), J. Šiško, M. Justić, S. Kobeščak PARTNERS: KBC Zagreb (A. Antabak, head of the clinical part of the research and associates at KBC Zagreb, Zagreb Children's Disease Clinic), General Hospital Karlovac, Haj-Kom (M. Hajdinjak), ALARA Uređaji (Z. Cerovac)	
<b>J. Rinkovec</b>	<b>Levels of platinum group elements (PGE) near roads</b>
IMROH ASSOCIATES: G. Pehnec, S. Žužul, I. Bešlić, S. Davila EXTERNAL ASSOCIATE: Ž. Zgorelec (Faculty of Agriculture, University of Zagreb)	
<b>B. Tariba Lovaković</b>	<b>Evaluation of reproductive toxicity of commonly used pesticides followed by chronic low-dose exposure <i>in vivo</i></b>
IMROH ASSOCIATES: A. Pizent, Z. Kljaković-Gašpić, A. Sekovanić, T. Orct, V. Kašuba	

## 16.1.B. COLLABORATION ON RESEARCH PROJECTS OUTSIDE THE INSTITUTE



## 16.1.B.1. Croatian Science Foundation (6 projects)

LEADER	PROJECT	DURATION
<b>Sanja Frka Milosavljević, Ruđer Bošković Institute, Zagreb</b>	<b>Biochemical REsponses of oligotrophic Adriatic surface ecosystems to atmospheric Deposition Inputs (BiREADI, IP-2018-01-3109)</b>	<b>29 Oct 2018 – 28 Oct 2022</b>

IMROH ASSOCIATES: I. Bešlić, R. Godec, S. Žužul, I. Šimić, G. Pehnec (consultant)

## SUMMARY

The annual meeting of the project was held on 28 Oct 2019 at the Ruđer Bošković Institute. Activities completed during the first year of the project were presented. All activities were carried out according to the schedule and all planned goals have been achieved. The aim of the project is 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. In the first phase of the project, 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. Associates from IMROH from February to July 2019 carried out sampling of airborne particulate matter, total deposition, and wet deposition at location Martinska near Šibenik. Chemical analysis of particulate matter content as well as the content of total deposited matter and wet deposition were performed.

LEADER	PROJECT	DURATION
<b>Marijana Hranjec, Faculty of Chemical Engineering and Technology of the University of Zagreb</b>	<b>Exploring the antioxidative potential of benzazole scaffold in the design of novel antitumor agents (AntioxPot Number, IP-2018-01-4379)</b>	<b>1 Nov 2018– 31 Oct 2022</b>

IMROH ASSOCIATE: I. Novak Jovanović

## SUMMARY

The electrochemical behaviour of potential antitumor benzimidazole derivatives [benzo(b)thieno(2,3-b)pyrido(1,2-a)benzimidazoles and benzimidazo(1,2-a)quinolines] bearing one or two piperazine substituents was studied in detail at a glassy carbon electrode (GCE) using cyclic and square-wave voltammetry in a wide range of pH values and potential scan rates. The mechanisms of electrochemical oxidation and reduction of studied compounds were proposed (51). The assignment of electroactive sites in molecules of interest was confirmed by theoretically calculated differences of Net atomic charges between the cation (or anion) and neutral molecule, using the PM6 method. The electrochemical oxidation of four different amino-substituted benzamide derivatives (with a variable number of methoxy and hydroxy substituents) was studied for a wide range of solution conditions, using cyclic and square-wave voltammetry.

Amino-substituted benzamide derivatives are very attractive compounds due to their capacity to act as powerful antioxidants by scavenging free radicals. Knowledge on electrochemical oxidation mechanisms will provide a better understanding of the free radical scavenging activity of the antioxidants studied here. A paper describing the findings of this research is in preparation.

LEADER	PROJECT	DURATION
<b>Tomica Hrenar, Faculty of Science, Zagreb</b>	<b>Activity and <i>in silico</i> guided design of bioactive small molecules (Adesire, IP-2016-06-3775)</b>	<b>1 Mar 2017– 28 Mar 2021</b>

IMROH ASSOCIATE: A. Bosak

## SUMMARY

The inhibitory potential of a series of carbamate derivatives of cinchonine and cinchonine against human cholinesterases and their selectivity for human AChE and BChE was determined (242). The fluorinated derivatives of *Cinchona* alkaloids were synthesised, their inhibitory potential against human cholinesterases were evaluated, and a certain structural characteristics of fluorinated quinoline derivatives responsible for the demonstrated inhibition and selectivity were determined (321).

LEADER	PROJECT	DURATION
<b>Maja Šegvić Klarić,</b> Faculty of Pharmacy and Biochemistry, Zagreb	<b>Adverse effects of single and combined mycotoxins produced by <i>Aspergilli</i> (MycotoxA, IP-09-2014-5982)</b>	<b>8 Feb 2016– 7 Feb 2020</b>

IMROH ASSOCIATES: D. Breljak, D. Karaica, N. Kopjar, M. Peraica, D. Rašić, D. Želježić

#### SUMMARY

The production of aflatoxins by *Aspergilli* (section Flavi) isolated from the air in different environments and their cytotoxic, genotoxic and proinflammatory properties *in vitro* were assessed on A549 and THP-1 cell lines. Aflatoxin caused higher levels of DNA damage than the extracts tested (30).

The study of the continuous treatment of experimental animals with nephrotoxic mycotoxins ochratoxin A (OTA) and citrinin (CTN) on oxidative stress was finished (63). In rats orally treated with OTA (0.125 and 0.250 mg kg<sup>-1</sup>) for 21 days alone or together with CTN (2 mg kg<sup>-1</sup>) protein carbonyls were measured in kidney and liver, as was the activity of the enzyme glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT) and glutathione concentration (GSH) in kidney, liver and plasma, and malondialdehyde (MDA) concentration in kidney, liver, plasma and urine. Apart from CAT, which was not affected by treatments in kidney and liver, the other parameters of oxidative stress were modified, but not equally in all organs. The analysis of the same parameters in biological material of animals treated with OTA+CTN and resveratrol (RSV; 20 mg kg<sup>-1</sup>) revealed that RSV could not fully protect animals from mycotoxin-induced oxidative stress.

The genotoxic effect of OTA and CTN on liver and kidney cells of male Wistar rats and the possible protective effect of RSV were also investigated. Results of alkaline comet assay showed increased primary DNA damage. Results of the comet assay with hOGG1 enzyme showed a significant increase in oxidative damage due to mycotoxin treatment. The level of damage was higher in kidney cells, and for OTA. Generally, RSV did not significantly reduce the level of primary damage but showed limited ability to diminish oxidative damage. It was concluded that oxidative stress does not represent the primary mechanism of genotoxic action of tested mycotoxins (64).

We have performed data analysis of individual and combined effects of mycotoxins (OTA and CTN) as well of antioxidant RSV on protein expression (western analysis) and cell localization (immunocytochemical analysis) of various membrane transporters for organic anions (Oats), including Oat1, Oat2, Oat3 and Oat5 *in vivo*. Furthermore, we have performed data analysis of protein expression/cell localization of various membrane proteins for cations Oct (including Oct1 and Oct2), glucose co-transporters Sglt (including Sglt1 and Sglt2), aquaporins AQP (including AQP1 and AQP2), membrane pump Na/K-ATPase and cytoskeletal protein beta-actin in rat kidneys following the mycotoxin/RSV treatment. In the frame of scientific manuscript, results will be published in a relevant scientific journal.

The acute effect of sterigmatocystin administered *p. o.* to male rats was investigated. The target organs of STC toxicity are liver and kidney, and the mechanism of its toxicity is not known. In our study test, animals were treated with a single STC dose of 10, 20, and 40 mg kg<sup>-1</sup>, which corresponded to 1/16 LD, 1/8 LD and 1/4 LD, respectively, while the controls received the vehicle (corn oil). In their plasma, kidney and liver the activity of antioxidative enzymes CAT, GPx and SOD was measured, while the concentration of heat shock proteins (Hsp 70 and Hsp 27) was measured only in kidney and liver. Activity of CAT was unchanged in plasma, kidney, and liver of STC-treated animals. Activity of GPx was significantly lower in liver treated with 20 and 40 mg kg<sup>-1</sup> and the activity of SOD was significantly higher in kidney of animals treated with 10 and 40 mg kg<sup>-1</sup>. STC treatment with the lowest dose (10 mg kg<sup>-1</sup>) increased significantly Hsp 70 in liver, but returned to control values after the highest dose (40 mg kg<sup>-1</sup>). STC did not cause changes in Hsp 27 in either organ. It could be concluded that STC increases oxidative stress in target organs (275). Additionally, the level of primary DNA damage was measured in the liver and kidney cells by comet assay. A single dose of sterigmatocystin led to a significant increase in primary DNA damage detected by the alkaline comet assay and oxidative DNA damage detected by hOGG1-modified comet assay. The obtained results suggest that liver cells were more susceptible to the genotoxic effect of the tested compound than the kidney cells (109).



LEADER	PROJECT	DURATION
<b>Tomislav Vinković, Faculty of Agriculture, Osijek</b>	<b>Application of Nanobiotechnology for Nutritional Supplementation with Selenium (NutriINTENSE, IP-2018-01-8119)</b>	<b>21 Jan 2019– 31 Dec 2022</b>

IMROH ASSOCIATE: A. M. Marjanović Čermak

#### SUMMARY

Selenium (Se) is an essential trace element with an important role in metabolism and many other vital functions. Due to its protective activity in immune response and cancer, it is widely used as a diet supplement. As plants are the main dietary source of Se for humans and animals, different strategies such as biofortification and plant-based extracts are used to develop Se dietary supplements. Selenium bioavailability varies depending on several factors including the chemical form of Se, other dietary components, physiological status and selenium status of the organism. The major obstacles in achieving optimal Se intake are highly variable Se content in different food types and narrow safety margin of supplemental Se forms. Nanotechnology enables the application of selenium nanoparticles (SeNPs), due to their enhanced antioxidant activities and lower toxicity as compared to other Se forms. The NutriINTENSE project aims to investigate the efficacy and safety of innovative SeNPs-based nutraceuticals and functional food using nanobiotechnological tools. This will be achieved by following the development of two innovative classes of Se-nutraceuticals: functional SeNPs biofortified vegetables (FBVegs) and Se-nanoceuticals (SeNCes) using food waste extracts for biogenic synthesis of SeNPs. Both types of Se-nutraceuticals will be subjected to in vitro and/or in vivo testings to investigate their biocompatibility, safety, pharmacokinetic properties and pharmacological activity compared to selenite and chemically synthesized SeNPs. In addition, the possible synergistic action of biogenic SeNPs and specific bioactive compounds found in NutriINTENSE plants and extracts will be evaluated. Results obtained within NutriINTENSE will be of great interest for consumers, agricultural producers, and the food industry as the final beneficiaries of the project. It should be highlighted that NutriINTENSE is a green project aimed at increasing the implementation of healthy and environment-friendly products.

LEADER	PROJECT	DURATION
<b>Valerije Vrčec, Faculty of Pharmacy and Biochemistry, Zagreb</b>	<b>Quantum-chemical design, preparation and biological properties of organometallic nucleobase derivatives (OrDeN, IP-2016-06-1137)</b>	<b>1 Mar 2017– 28 Feb 2021</b>

IMROH ASSOCIATE: A. M. Marjanović Čermak

#### SUMMARY

Organometal nucleobase derivatives (OrDeNs) are a new generation of conjugates in which metallocenes are linked to the underlying superstructural elements of inheritance. Due to its electrophoretic and bioactive properties, OrDeN's use in (bio)analytical and medical chemistry and penetrate into the field of therapy, molecular diagnostics and nanotechnology. The main purpose of this project is to design and synthesize new biologically active organometallic nucleobase derivatives (OrDeNs) for which quantum-chemical calculations suggest the desirable electrochemical and biological properties. With the assistance of quantum-chemical accounts, the reaction conditions for efficient preparation of OrDeN will be defined, with a high percentage of utilization and a high degree of regioselectivity. Electroactive and biological properties of newly prepared compounds will be determined, which will be compared with the results of the obtained quantum-chemical calculations. Analogously published results that OrDeNs may be in the group of apoptosis inducer and tumor cell growth inhibitors will be subjected to biological testing on several different tumor cell lines within this project.

LEADER	PROJECT	DURATION
<b>Vanja Vučičević Boras, School of Dental Medicine, Zagreb</b>	<b>The role of oestrogen and androgen receptor activation in the stroma of oral cancer and their impact on the survival of patients (ACTIVESTROMORALCANCER, IP-2014-09-6985)</b>	<b>1 Oct 2015– 30 Sep 2019</b>

IMROH ASSOCIATE: A. Fučić

#### SUMMARY

Oral cancer was studied on tissue samples from 101 patients without metastasis and 95 patients with metastases by immunohistochemistry to determine androgen receptor (AR) and Ki-67 levels in neoplastic epithelium and stroma. More than 20% of AR-positive cytoplasmic epithelial staining was significantly associated with nuclear level of AR in epithelium and increased level of AR in stroma. In patients with metastatic disease, Ki-67 was significantly higher than in patients who did not have metastatic disease. Using a detailed questionnaire on social status, education, exposure to living and occupational environment, family and lifestyle, patients with head and neck cancer (HNC) (103 cases, 76.7 % male) were compared with control subjects (244 subjects, 73 % male). The results of this study showed that smoking and low education were important risk factors for HNC regardless of gender. Family HNC and breast cancer were significant predictors of HNC risk.



### 16.1.B.2. University projects

#### University of Zagreb



LEADER	PROJECT	DURATION
<b>Jasminka Despot Lučanin, Croatian Studies, Zagreb</b>	<b>Well-being of different family generations in contemporary work designs</b>	<b>2018–2019</b>

IMROH ASSOCIATE: A. Bjelajac

#### SUMMARY

The main objective of this project is to examine different indicators of well-being of three family generations in contemporary work designs in Croatia. The relationship between contemporary forms of parenting and some aspects of parental behavior and their well-being, the well-being of their children and of grandparents has been examined. The results of the research are presented at two international (208, 282) and two national meetings (207, 226).

#### University of Rijeka



LEADER	PROJECT	DURATION
<b>Aleksandar Bulog, Faculty of Medicine, Rijeka</b>	<b>Biological monitoring of the effects of volatile aromatic hydrocarbons (BTEX) on the health of the Primorje-Gorski Kotar County population</b>	<b>2019–2021</b>

IMROH ASSOCIATE: I. Brčić Karačonji

#### SUMMARY

The project includes the determination of the mass concentration of volatile aromatic hydrocarbons of benzene, toluene, ethylbenzene, and isomers of xylene (BTEX) in the urine of subjects in the industrial area, which we will compare with those of the control areas (209). The results obtained in the urine of the subjects will be correlated with the concentrations of the same pollutants in the ambient air. All data obtained from participants will be compared with the immune, epidemiological and respiratory data on the health status of the subjects.

LEADER	PROJECT	DURATION
<b>Ivana Gobin, Faculty of Medicine, Rijeka</b>	<b>Opportunistic pathogens in the water supply system: A new challenge in water treatment</b>	<b>2019–2021</b>

IMROH ASSOCIATE: I. Brčić Karačonji

#### SUMMARY

The aim of the project is to investigate the antimicrobial potential of natural substances (essential oils and hydrolates), active metabolites of bacteria of the genus *Bacillus* and selected synthesized photodynamically active compounds against resistant bacteria that colonize part of the water distribution system.

## 16.1.C. PROFESSIONAL PROJECTS

PROJECT	CONTRACTOR	LEADER
<b>Service provider: Environmental Hygiene Unit</b>		
Monitoring air pollution in the City of Zagreb (from 1963)	City of Zagreb, City Office for Energy, Environmental Protection and Sustainable Development	V. Vadić (1963–2014), G. Pehnec (from 2015)
Monitoring of the Total Effects of CPS Molve on the Ecosystem (from 1998)	INA-Naftaplin and Institute for Public Health of the Koprivnica-Križevci County	V. Vadić (1998–2014), G. Pehnec (from 2015)
Monitoring Air Quality at the CWWTP Construction Site in Zagreb (from 2003)	Zagreb Wastewater Ltd.	V. Vadić (2003–2014), G. Pehnec (from 2015)
Monitoring Air Pollution at National Network Stations for the Purpose of Continued Air Quality Monitoring (from 2015)	Ministry of Environment and Energy 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 Environment and Energy and Meteorological and Hydrological Service of Croatia	I. Bešlić
Monitoring Air Pollution at a Station at Military Training Polygon in Slunj (from 2009)	Meteorological and Hydrological Service of Croatia	V. Vadić (2009–2014), G. Pehnec (from 2015)
<b>Service provider: Radiation Dosimetry and Radiobiology Unit</b>		
Determination of the radiological status of the working environment in IPNP	INA Group	I. Prlić
Preparation of documentation for the approval of the Republic of Croatia Ministry of the Interior on the building permit for the construction of the space of the linear accelerator and associated services in the new building of the General Hospital Zadar (clinic) activity with sources of ionizing radiation	General Hospital Zadar Capital ing	I. Prlić
<b>Service provider: Radiation Protection Unit</b>		
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	G. Marović
Results of Monitoring of Environmental Radioactivity in Vicinity of Plomin Coal-Fired Power Plant, IMI-P-383	HEP proizvodnja Thermal power plant Plomin I, Plomin	G. Marović
Results of Radioactivity Measurements at Gas Field Molve, IMI-P-384	Koprivnica-Križevci County, Koprivnica	G. Marović
Development of field methods for environmental radioactivity monitoring in Republic of Croatia (PZ-12-18)	Civil protection directorate of the Republic of Croatia Ministry of the Interior	B. Petrinec



## 16.2. INTERNATIONAL PROJECTS

### 16.2.A. SCIENTIFIC RESEARCH PROJECTS

#### 16.2.A.1. European Union programs EUROPEAN REGIONAL DEVELOPMENT FUND

##### Operational Program Competitiveness and Cohesion (3 projects)



Operativni program  
KONKURENTNOST  
I KOHEZIJA

INSTITUTION (Leader)	PROJECT	DURATION
<b>IMROH, Zagreb (R. Fuchs)</b>	<b>Research and Educational Centre of Environmental Health and Radiation Protection – Reconstruction and Expansion of the IMROH</b>	<b>2017–2021</b>

IMROH ASSOCIATES: A. Lucić Vrdoljak, Z. Franić, S. Stankić, B. Roić, S. Barbarić, M. Herman

#### SUMMARY

The grant of 232,602,280.72 HRK is intended for the implementation of the project over 52 months, during which the Institute will be expanded with a new building of 6,785.15 m<sup>2</sup>, while our existing building of 2,067.41 m<sup>2</sup> will be renovated. The Institute will also acquire a significant amount of modern research and IT equipment, which together with the aforementioned construction makes this project one of the central development project crucial not only for Croatia but also for the wider region. The Centre itself is conceptualised as an administrative and organisation unit within the Institute and will function as its part, whereas its operation will rely on the Institute's researchers and professionals. The project will dramatically improve the Institute's infrastructure, which includes both the aspect of fundamental research and that of applied research in the fields of occupational medicine, environmental health, radiation and related disciplines, as well as those aimed at lifewide education and class within certain postgraduate study programmes. The project also plans the introduction of a "mini technology park" within which modular laboratories would enable the Institute's researchers to cooperate with guest researchers and conduct specific, in some cases market-oriented, research.

INSTITUTION (Leader)	PROJECT	DURATION
<b>School of Medicine, Zagreb (D. Ježek)</b>	<b>Scientific Center of Excellence for Reproductive and Regenerative Medicine (CERRM, KK.01.1.1.01.0008)</b>	<b>2014–2019</b>

IMROH ASSOCIATE: A. Fučić

#### SUMMARY

Fifty newborns of both sexes, whose mothers were not professionally exposed to any known carcinogen or drug, were analysed. All mothers completed a questionnaire on lifestyle, diet, and residence. Multivariate analyzes for the dependent variables were made using generalized linear/nonlinear regression analyzes with the construction of all-effects models. The results show that there are significantly higher levels of estradiol and the ratio of estradiol to testosterone in newborns of mothers from the agricultural area than in those born to mothers with urban residence. Similarly, a higher estradiol ratio and estradiol to testosterone ratio were measured in the infants of mothers who drank coffee, milk, ate fish more than once a week, and smoked. Testosterone was significantly higher in infants of mothers with an agricultural residence. The incidence of genome damage was significantly higher in the infants of mothers who dyed during pregnancy, drank alcohol, and used disinfectants. IL6 levels were higher in infants of mothers with agricultural residence, but also in those living less than 100 m from the motorway.

INSTITUTION (Leader)	PROJECT	DURATION
<b>Meteorological and Hydrological Service of Croatia (C. Kosanović)</b>	<b>AIRQ – Project of extension and modernisation of the national network for continuous air quality monitoring (KK.06.2.1.02.0001.)</b>	<b>2017–2021</b>

IMROH ASSOCIATES: G. Pehnek (leader), R. Godec, I. Bešlić, S. Žužul, S. Stankić, B. Roić, S. Barbarić, M. Herman

#### SUMMARY

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. This entails developing integrated strategies and projects which enable the evaluation, planning and implementation of adequate procedures for controlling air quality by means of measuring relevant parameters. In the end, the project thus aims to improve the monitoring programme for short-lived climate forcers and introduce climate-sensitive measures against air pollution. Lead beneficiary is Croatian meteorological and Hydrological Service (DHMZ) and the partner institution is IMROH. The project will receive a grant in the amount of 125,123,500.00 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 of full functionality; developed and functional model for the assessment of ground level concentrations of pollutants; additional equipment of DHMZ and IMI 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 calibration laboratory for calibration of air quality measures and related measurement sizes. Through this project, the Environmental Hygiene Unit acquires equipment for the purpose of air quality monitoring at measuring stations of the State Network in the part related to sampling and physical and chemical analysis of PM<sub>10</sub> and PM<sub>2.5</sub> particle fractions and equivalence testing of non-reference methods for the determination of PM<sub>10</sub> and PM<sub>2.5</sub> mass concentrations, in accordance with legal obligations. In 2018 public procurement procedures were carried out, for procurement of the IMROH chemical laboratory equipment and for an off-road vehicle. In 2019 the vehicle and all chemical laboratory equipment, laboratory furniture, and accessories were delivered. All equipment was put in operation. Trainings and method developments are in progress.

### Operational Program INTERREG V-A Slovenia-Croatia



INSTITUTION (Leader)	PROJECT	DURATION
<b>Jožef Stefan Institute, Ljubljana, Slovenia</b>	<b>ENsuring RAdiation Safety (ENRAS)</b>	<b>2018–2020</b>

IMROH ASSOCIATES: B. Petrinec (leader), T. Meštrović, T. Bituh, D. Babić, Z. Franić, M. Kovačić, M. Avdić  
 PARTNERS: Slovenian Fire Association, Croatian Fire Association, Civil protection directorate of the Republic of Croatia Ministry of the Interior, Slovenian Nuclear Safety Administration, Administration of the Republic of Slovenia for Protection and Rescue

#### SUMMARY

The ENRAS project will help develop cross-border services in the field of ensuring safety (civil protection) in cases of nuclear or radiological accidents. The shared challenge within the project is meant to enable harmonised and safe joint interventions in cases of such accidents. The main goal is to strengthen cross-border cooperation among subjects participating in the area of protection for the purpose of more effective rescue and intervention, increasing training and skills, and establishing the first system for joint interventions in cross-border areas.

## EUROPEAN RESEARCH AND INNOVATION PROGRAMME



## HORIZON 2020 (3 projects)

INSTITUTION (Leader)	PROJECT	DURATION
<b>Bundesamt für Strahlenschutz, Salzgitter, Germany (T. Jung)</b>	<b>European Concerted Programme on Radiation Protection Research (CONCERT, 662287 COFOUND EJP-Topic: NFRP-2014-2015), within the framework of Euroatom Horizon 2020</b>	<b>2015–2020</b>

IMROH ASSOCIATES: I. Prlić (leader for Croatia and POM Contact point, Program Manager, member of the project consortium management), I. Brčić Karačonji, A. Lucić Vrdoljak, R. Fuchs, D. Željezić, J. Macan, M. Surić Mihić

Consortium: 36 national PoM Institutions from 23 EU Member States and Norway and Switzerland

## SUMMARY

The CONCERT, European Joint Programme for the Integration of Radiation Protection Research under Horizon 2020 operates as an umbrella structure for the research initiatives jointly launched by the radiation protection research platforms MELODI (for low dose risk research), ALLIANCE (for radioecology), NERIS (for nuclear emergency preparedness), and EURADOS (for dosimetry). CONCERT as a co-funded action (70 % EC and 30 % national funding) is aimed at integrating national and European research programmes. Next to research, education and training activities closely linked to research will be carried out by CONCERT to build and maintain the high level of competence in radiation sciences and radiation protection in Europe. In addition, CONCERT will make the best use of the available research infrastructure in Europe, mainly by enhancing the visibility of infrastructures and facilitating access to them. CONCERT has the mission to further reduce uncertainties in the assessment and management of radiation risks to the environment and to humans by targeted science. To achieve this, CONCERT will initiate an open exchange of knowledge and information between science, regulation, and society.

The aim of CONCERT is to set in motion the convergence of three focusing forces: the scientific community, national agencies and research institutions, and EURATOM policies in order to achieve new breakthroughs in radiation protection research. CONCERT strives for a better integration of the radiation protection scientific community at EU level, leading to a better coordination of research efforts and the provision of more consolidated and robust science-based policy recommendations to decision makers in this area. In the long-term, these efforts will translate into additional or improved practical measures in view of the effective protection of people and the environment.

CONCERT is an open project within two transnational tenders for research projects have been launched (in spring 2016 with fund of 10,000,000 € and in spring 2017 with a fund of 7,000,000 €). In total, 9 funding projects were selected for these international tenders. All project results achieved so far can be found on the project's web site (<http://www.concert-h2020.eu/en/Publications>).

INSTITUTION (Leader)	PROJECT	DURATION
<b>German Environmental Agency (M. Gehring-Kolossa)</b>	<b>European Human Biomonitoring Initiative (HBM4EU, Grant Agreement No 733032)</b>	<b>2017–2021</b>

IMROH ASSOCIATE: A. Fučić

Consortium: 24 EU Member States and Norway, Iceland, Israel, Switzerland, European Environment Agency and European Commission

## SUMMARY

Within the project, an analysis of the genome damage of persons with occupational chromium exposure has been completed, a review article on occupational exposure to phthalates is in print, and a review article on the topic of occupational exposure to pesticides is under preparation.

INSTITUTION (Leader)	PROJECT	DURATION
Norwegian Institute for Air Research, Kjeller, Norway (M. Dusinska)	Science-Based Risk Governance of Nanotechnology (RiskGONE, Gran Agreement No 814425)	2019–2023
IMROH ASSOCIATES: I. Vinković Vrček (leader), I. Pavičić, Z. Franić, B. Pem Consortium: 15 EU Member States and USA, and Iran		
<b>SUMMARY</b>		
During the first 12-month period, IMROH was involved in the kick-off meeting, M6 meeting held in Cyprus, Face-to-face meeting of the WP4 held in Luxembourg and teleconference meetings related to the WP2, WP4, WP5, and WP7.		
IMI participated in:		
<ul style="list-style-type: none"> <li>the Round Robin from the Malta Initiative analysing 4 different nanoparticles by means of dynamic light scattering (DLS) (within WP4)</li> <li>the analysis and discussion on dispersion protocols, and standard operational procedures (SOPs) on the particle size determination and effective density to be used within WP4 and WP5</li> <li>the SOPs review and preparation for Round Robin within Task 5.1 "Evaluation and adaptation of <i>in vitro</i> safety testing OECD TGs to enable engineered nanomaterials (ENMs) risk governance"</li> <li>the analysis on nano-related Adverse Outcome Pathways (AOPs).</li> </ul>		

## EUROPEAN SOCIAL FUND

### Operational Programme Efficient Human Resources

#### Croatian Science Foundation – Scientific Cooperation Programme (2 projects)



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 PARTNER: University of Melbourne, Victoria, Australia		
<b>SUMMARY</b>		
<p>Nanotechnology provides innovative and effective therapeutic and diagnostic tools and tools. However, treatment of neurodegenerative disorders is still a major challenge due to the existence of a blood-brain barrier (BBB) that impedes effective drug delivery to the brain. Multifunctional nanoparticles (NPs) represent a new and improved platform for greater efficacy, bioavailability and targeted drug delivery via BBB. The main objective of the proposed project is to develop a multifunctional nanosystem that will enable drug delivery to the brain (BRaiND) for the effective and safe treatment of brain abnormalities associated with aging and degeneration. Specific activities will be carried out:</p> <ul style="list-style-type: none"> <li>design, preparation, and characterization of BRaiND</li> <li>assessment of the stability and fate of BRaiND in biological media</li> <li>mechanical and quantitative assessment of the interaction of BRaiND with BBB</li> <li>profiling the efficacy and safety of BRaiND with a combined <i>in vitro</i> and <i>in vivo</i> approach.</li> </ul> <p>BRaiND will be based on selenium or gold nanoparticles, stabilized by polyethylene glycol and functionalized proteins that target brain receptors. Such multifunctional system will be coupled with model neuroactive drugs to demonstrate the effectiveness, quality and safety of the BRaiND system. Careful <i>in vitro</i> and <i>in vivo</i> studies will be conducted including the stability and interactions of BRaiND in various biological media, BBB permeability, targeting efficacy at specific brain sites, neuroprotective activity, and evaluation of the safety of their administration. The project work plan is based on validated and standardized methodologies as well as innovative experimental techniques. Given the major challenges of translational research into neurodegenerative diseases, SENDER's strategy is based on the Safe-by-Design approach, enabled by nanotechnology tools that analyze and manipulate biological processes at the nanoscale, where diseases originate and thrive. The project activities in the first quarter focused on:</p> <ul style="list-style-type: none"> <li>organizing and getting to know the research team</li> <li>implementation of the selection process and recruitment of candidates for the post of doctoral candidate</li> <li>organize and carry out procurement of the instrument provided for in the project financial plan</li> <li>preparatory phase of strategy development for the preparation of defined drug-conjugated AuNPs and SeNP-BraiNDs.</li> </ul>		

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 ASSOCIATES: L. Pavelić, M. Surić Mihić  
PARTNER: University of Sydney, New South Wales, Australia

#### SUMMARY

Gamma-ray polarization information is valuable in many areas of contemporary physics research. An example in fundamental sector is the phenomenon of quantum entanglement, which may be investigated by analyzing relative polarizations of three gammas originating from ortho-positronium decay. In applications, an important case is the biomedical imaging with Positron Emission Tomography (PET), where it has been shown by simulated model studies, that the polarization information, which is not exploited in existing PET systems, has the potential to improve the image quality. The polarization of a gamma photon can be determined from its Compton scattering, where it produces a recoil electron and a scattered photon. For reconstruction of Compton events, one needs position and energy-sensitive detectors, usually encompassing two layers, for detection of the electron and the scattered photon, respectively. However, in many applications where detectors are highly granular and contain many channels, such as PET, a system based on two-layer readout would be costly. In this project we will construct a new modular detector system for gamma polarization measurements, based on single-layer Compton scattering detectors. The module will contain an array of scintillators, read-out by silicon photomultipliers. Compared to two-layer detectors, the single-layer concept offers a possibility to construct more cost-efficient, compact and versatile devices. We will assemble a sixteen-module system, which will be used in two applications: first, to evaluate experimentally for the first time the feasibility of using the information about gamma-ray polarization in PET, as an important step towards the next generation of more efficient medical imaging devices, and second, to analyze the azimuthal correlations of three gammas from ortho-positronium decay in order to investigate entanglement as a fundamental concept of quantum physics.

## DANUBE REGION STRATEGY



LEADER	PROJECT	DURATION
Institut für Soziale Ökologie, Alpen-Adria-Universität Klagenfurt, Austria (V. Winiwarter)	A sustainable future for the Danube river basin as a challenge for the interdisciplinary humanities (Danube: Future)	2013–2020

IMROH ASSOCIATE: G. Gajski

#### SUMMARY

Danube: Future aims at developing interdisciplinary research and education in the Danube River Basin (DRB) simultaneously as a basis for the solution of pressing environmental issues and a sustainable future of the region. Danube: Future is a multi-year program that consists of three modules: core, capacity building, and sustainability related research with a long-term socio-ecological component. Danube: Future is a unique combination of regional, national, and supra-national initiatives in interdisciplinary sustainability research with training and capacity building. It contributes to the sustainable development of the DRB with a particular focus on the contribution of humanities (149).



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


INSTITUTION (Leader)	PROJECT	DURATION
<b>University Medical Center Hamburg – Eppendorf, Germany (L. T. Budnik)</b>	<b>Diagnosis, Monitoring and Prevention of Exposure-Related Noncommunicable Diseases (DiMoPEX, CA15129)</b>	<b>2016–2019</b>

IMROH ASSOCIATES: J. Macan (Management Committee member), Ž. Babić, Zr. Franić, J. Kovačić, R. Turk, V. M. Varnai

**SUMMARY**

DiMoPEX presents the opportunity for interdisciplinary collaboration between scientists in the field of chronic non-communicable diseases caused by environmental factors. Furthermore, the project is dedicated to increasing the interest of young scientists for this research field, especially for the different aspects of exposition to environmental factors. During 2019, associates of the Occupational and Environmental Medicine Unit took part in a course with the topic on risk assessment and communication.

INSTITUTION (Leader)	PROJECT	DURATION
<b>Institute of Basic Medical Sciences, University of Oslo, Norway (A. Collins)</b>	<b>The comet assay as a human biomonitoring tool (hCOMET, CA 15132)</b>	<b>2016–2020</b>

IMROH ASSOCIATES: G. Gajski (member of the Management Committee), M. Milić (member of the Management Committee, member of Core Group, WG1 leader, responsible for the website of the network)

**SUMMARY**

Many human biomonitoring studies have used the comet assay to measure DNA damage. In most cases, the assay is applied to peripheral blood mononuclear cells. Results from relatively small individual studies are often inconsistent and it is advantageous to carry out a pooled analysis of the combined data from all available studies. hCOMET will be a network comprising researchers who are active in human biomonitoring with this assay. Results supplied by these researchers will be compiled as a single database representing a large number of individual DNA damage measurements. The pooled analysis will allow us to determine which factors affect DNA damage, and to what extent. In addition, hCOMET will address the issue of interlaboratory reproducibility of the assay by devising standard protocols so that in future comparison of results from different studies will be facilitated (3, 12, 24, 25, 48, 69).

INSTITUTION (Leader)	PROJECT	DURATION
<b>Zuyd University of Applied Sciences, Heerlen, Netherlands (F. Crijns)</b>	<b>Anti-Microbial Coating Innovations to prevent infectious diseases (AMICI, CA15114)</b>	<b>2016–2020</b>

IMROH ASSOCIATE: I. Vinković Vrček (Management Committee replacement member)

**SUMMARY**

A workshop for young researchers was held on 7 Mar 2019 in Riga, Latvia. At this workshop, PhD student K. Ilic presented the results obtained during his short term scientific mission (STSM) stay in the group of prof A. Kahru in Tallinn, Estonia. At the same workshop, I. Vinković Vrček gave a lecture entitled "Obstacles and opportunities on development for antimicrobial coatings as a scientist".

INSTITUTION (Leader)	PROJECT	RAZDOBLJE
<b>School of Biochemistry &amp; Immunology, Trinity Biomedical Sciences Institute, Dublin, Ireland (J. Murray)</b>	<b>European Network of Multidisciplinary Research and Translation of Autophagy knowledge (TransAutophagy, CA 15138)</b>	<b>2016–2022</b>

IMROH ASSOCIATE: M. Ljubojević

#### SUMMARY

M. Ljubojević participated in the work meeting that took place 23–25 Apr 2019 (Sofia, Bulgaria), where she was elected member of the Management Committee. A wide range of activities and planned operation actions related to the actions will enhance the knowledge and link the studies of sex and age differences conducted in the Molecular Toxicology Unit with those of autophagocytosis processes conducted in EU countries.

INSTITUTION (Leader)	PROJECT	DURATION
<b>Universite Dijon Bourgogne, Dijon, France (M. Cherkaoui Malki)</b>	<b>Personalized nutrition in aging society: redox control of major age-related diseases (NutRedOx, CA16112)</b>	<b>2017–2021</b>

IMROH ASSOCIATE: M. Gerić (Management Committee member)

#### SUMMARY

The importance of a healthy ageing process becomes apparent when considering that (a) the Generation 50+ (G50+) already has a share in population of around one third across Europe, with obvious regional variations, (b) this share is likely to increase further in the future, and (c) vitality at older age is not only an important measure of quality of life but also key to participation and productivity. The theme “nutrition and ageing” has many different aspects and poses numerous challenges, which provide a fertile ground for many research themes and networks. Among them, the NutRedOx network will focus on the impact of redox active compounds in food on healthy ageing, chemoprevention and redox control in the context of major age-related diseases. The main aim of the NutRedOx network is the gathering of experts from across Europe, including other Mediterranean countries, and from different disciplines that are involved in the study of biological redox active food components and are relevant to the ageing organism, its health, function and vulnerability to disease. Together, these experts will form a major and sustainable EU-wide cluster in form of the “NutRedOx Centre of Excellence” able to address the topic from different perspectives, with the long-term aim to provide a scientific basis for (improved) nutritional and lifestyle habits, to train the next generation of multidisciplinary researches in this field, to raise awareness of such habits among the wider population, and also to engage with Industry to develop age-adequate foods and medicines (304).

INSTITUTION (Leader)	PROJECT	DURATION
<b>Erasmus Universitair Medisch Centrum Rotterdam, Rotterdam, the Netherlands (T. M. Luider)</b>	<b>“Good biomarker practice” to increase the number of clinically validated biomarkers (CliniMARK, CA16113)</b>	<b>2017–2021</b>

IMROH ASSOCIATE: G. Gajski (Management Committee member)

#### SUMMARY

Thousands of circulating proteins have been shown to be hallmarks of emerging disease, response to treatment, or a patients’ prognosis. The identification of these small molecule biomarkers holds a great promise for significant improvement of personalized medicine based on simple blood tests. For instance, diagnosis and prognosis with biomarkers [e.g. carcinoembryonic antigen (CEA)] has significantly improved patient survival and decreased healthcare costs in colorectal cancer patients. Unfortunately, despite significant investments to increase the number of biomarker studies, only ~150 out of thousands of identified biomarkers have currently been implemented in clinical practice. This is mainly caused by the time-consuming process of reliably detecting biomarkers, the irreproducibility of studies that determine a biomarkers’ clinical value, and by a mismatch in studies that are performed by academia and what is required for regulatory and market approval. To increase the number of clinically validated biomarkers, rather than further increasing the number of biomarker discovery studies, CliniMARK will improve the quality and reproducibility of studies and establish a coherent biomarker development pipeline from discovery to market introduction.

INSTITUTION (Leader)	PROJECT	DURATION
<b>National Institute of Occupational Health, Oslo, Norway (I. Sivesind Mehlum)</b>	<b>Network on the coordination and harmonisation of european occupational cohorts (OMEGA-NET, CA16216)</b>	<b>2017–2021</b>

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

#### SUMMARY

The main aim is to establish a network to optimize the usage of cohort from the working and general population in Europe. The aims of the OMEGA-NET projects are promotion of collaboration between existing cohort researches, gathering the information on employment and occupational exposure, coordination and harmonization researches on exposure assessment in working population, and the promotion of integrative strategies for the researches of workers health in Europe. The promotion of evidence-based preventive strategies directed to health at work are expected. Associates of this Unit are involved in working groups focused on prevention of occupational skin diseases and mental disorders related to work. Institute was a host of the Working groups and Management Committee meeting held in Zagreb in October 2019. J. Macan presented at the meeting a lecture about the research performed in the Unit.

INSTITUTION (Leader)	PROJECT	DURATION
<b>University of Lodz, Poland (B. Klajnert-Maculewicz)</b>	<b>Cancer Nanomedicine – from the bench to the bedside (Nano2Clinic, CA17140)</b>	<b>2018–2022</b>

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

#### SUMMARY

PhD student R. Barbir was awarded a scholarship for a short-term research residency at the Instituto de Ciencia de Materiales de Aragon in Zaragoza, Spain. Under the mentorship of prof. J. Martinez de la Fuente, R. Barbir conducted physicochemical studies of the interaction of silver nanoparticles with model proteins. The research residency plan is in line with the workplan of the NanoFaceS project and will form part of Barbir's doctoral thesis. The stay was held from 18 Feb to 14 Apr 2019.

PhD student B. Pem was awarded a fellowship for a short-term research residency at the University of the West of England in Bristol, UK (18 Feb–14 Apr 2019). Under the mentorship of prof A. Adanatzki, she developed computer models to describe and predict the behavior of nanoparticles coated with functional molecules. The developed models will be used to test the interactions of functionalized nanoparticles with biological systems, as part of the NanoFaceS project.

WP2 leader I. Vinković Vrček and R. Barbir attended the first Nano2Clinic Spring School, held in Trieste, Italy (8–11 Apr 2019). During the school, many interesting and instructive lectures were held in all areas of nanomedicine. I. Vinković Vrček had a lecture entitled "Safe-by-design approach to foster clinical translation of nano-enabled medical products", in which she invited members of the scientific community to reflect on material safety and move away from the usual focus on efficiency. R. Barbir presented the poster "Biocompatibility evaluation of selenium nanoparticles as promoting delivery nanosystems". Dr A. Selmani presented a poster "Stability of selenium nanoparticles as a novel anticancer delivery vehicle in relevant biological media" in collaboration with I. Vinković Vrček.

PhD student R. R. Jiménez from Instituto de Ciencia de Materiales de Aragón, Zaragoza, Spain, visited the IMROH in STSM (Short Term Scientific Mission) of the COST Action Program Nano2Clinic (14 Sep–14 Oct 2019). His STSM project focused on understanding the mechanism of action of nanomedicine preparations and improving their biocompatibility and safety. At the Institute, he taught the Safe-by-Design approach to the development of nanosystems for targeted drug delivery for antitumor therapy. The NanoFaceS group also benefited greatly from his experience in the synthesis of nanopharmaceuticals. The study visit resulted in an exchange of knowledge and a deepening of knowledge about specific aspects of the medical application of nanomaterials and the use of more effective and safer preparations.

The First COST Action Conference CA17140 Nano2Clinic (Cancer Nanomedicine: From the Bench to the Bedside) was held on 15–17 Oct 2019 in Riga, Latvia. The conference brought together leading European and world experts in the field of nanomedicine to present the latest developments in the development of nanomaterials for cancer therapy. I. Vinković Vrček, as a leader of Task Force 2 of COST Action, moderated one of the lecture groups. B. Pem had a short lecture "Effect of particle shape and size on interactions of gold nanoparticles with proteins of different glycosylation status".

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

IMROH ASSOCIATES: D. Karaica, I. Vrhovac Madunić

#### SUMMARY

The first meeting of the Steering Committee was held 12 Oct 2018 in Bruxelles (Belgium), where the heads of working groups as well leaders of ITC (Inclusiveness Target Countries) and STSM (Short-term scientific missions) committees were appointed/selected. I. Vrhovac Madunić was elected as ITC Board Manager, while D. Karaica was elected as ITC Board member. Also, the proposed action plan was approved and the location of the next coming COST action meeting in Porto (Portugal) was agreed.

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

IMROH ASSOCIATE: S. Cvijetić Avdagić

#### SUMMARY

The project brings together a wide range of researchers active in musculoskeletal biology and focuses primarily on pharmacogenetics. The goal is to translate new discoveries in the field of musculoskeletal genetics into meaningful clinical applications. One of the working groups is focused on population-based research on epigenetic factors in the etiology of bone diseases.

## OTHER EUROPEAN PROJECTS

### European Agency for Safety and Health at Work



INSTITUTION (Leader)	PROJECT	DURATION
<b>National Public Health Institute, Budapest, Hungary (F. Kudász)</b>	<b>Good practice case study on dangerous substances</b>	<b>2017–2019</b>

IMROH ASSOCIATES: J. Macan, Ž. Babić, Zr. Franić, F. Šakić, M. Deranja

#### SUMMARY

In collaboration with the Hungarian National Public Health Institute, a project financed by the European Occupational Safety and Health Agency (EU OSHA) was implemented. Information about the available guidelines and other materials in Croatian and Slovenian supporting the prevention of exposure to dangerous substances at the workplace were collected. The list of websites with available material was published on the website of the EU OSHA (<https://osha.europa.eu/>).

### Polytechnic Institute of Lisbon, Portugal



INSTITUTION (Leader)	PROJECT	DURATION
<b>Lisbon School of Health Technology, Polytechnic Institute of Lisbon, Lisbon, Portugal (S. Viegas)</b>	<b>Occupational exposure to cytotoxic agents in veterinary hospitals and clinics (CytoVet)</b>	<b>2017–2019</b>

IMROH ASSOCIATE: G. Gajski

#### SUMMARY

CytoVet project will provide experimental data that could enable the prediction of adverse effects and risk assessment for exposed workers in veterinary hospitals and clinics. The project will answer whether exposure to cytotoxic agents might pose a risk to human health in occupational settings (309).

### 16.2.A.2. United Nations Environment Programme (UNEP) International Atomic Energy Agency (IAEA)



INSTITUTION (Leader)	PROJECT	DURATION
Department of Nuclear Sciences and Applications, IAEA Laboratories Seibersdorf, Austria (R. Padilla Alvarez)	Enhancing the Inventory of Aerosol Source Profiles Characterized by Nuclear Analytic Techniques in Support of Air Quality Management (RER/7/011)	2017–2019

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

#### SUMMARY

The project was initially planned for a period of two years and was subsequently extended to 2019. The reason is the completion of the planned activities related to the procurement of equipment and supplies as well as the evaluation of the results obtained. At the 'TC Final Coordination Meeting, EVT (1901605), held from 25 to 29 Nov 2019 in Lisbon, Portugal, representatives of participating countries presented the scopes of the sample collection and performed analysis. Representatives from 19 participating countries attended the meeting. The framework program and planned activities for the next RER 7012 project were agreed, which would be a continuation of the RER7011 project. It was decided to ensure the purchase of more reference particulate matter samplers and MABl aethelometers for the determination of black carbon. It was also decided to continue the sampling campaign started during the last RER project with sampling dynamics every third day. Sampling will be carried out on Teflon filters, and the distribution of the filters has been taken over by IMROH associates, as it was in a previous project. It was decided that during the project the following will be organized: one workshop for working with large databases in Cyprus, one coordination meeting to evaluate the results of the last project in Vienna and a final coordination meeting to be organized in Moldova. At the meeting associates were informed about the status of the scientific paper submitted for review, which includes the results and data analysis of the previous project.

For the new project IMROH has requested 28-element multi-element reference material whose concentrations are at least three times higher than the X-ray fluorescence (XRF) detection limit. One-element certified reference materials for XRF have been ordered for IMROH as well as certified reference materials for elemental carbon (EC) and organic carbon (OC) analysis.

### 16.2.A.3. Government Ministry projects

#### Ministry of Environmental Protection of Mexico Federal Attorney for Environmental Protection (PROFEPA)



INSTITUTION (Leader)	PROJECT	DURATION
Autonomous University of Tlaxcala, Autonomous National University of Mexico, Meksiko (R. Valencia)	The general project of evaluation of the genotoxic risk from exposure to environmental pollutants	2016–2020

IMROH ASSOCIATE: M. Milić

#### SUMMARY

Within the project, studies on the toxicity of aflatoxins and mycotoxins (2) and DNA damage in agricultural workers were continued (332).

**US Department of Defense  
US Defense Threat Reduction Agency (DTRA)**



INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (Z. Kovarik)	CNS-active, Orally Bioavailable, Zwitterionic Oximes for Organophosphate	2019–2022

IMROH ASSOCIATES: S. Žunec, V. Micek  
PARTNERS: P. Taylor and Z. Radić (University of California at San Diego, La Jolla, SAD), K. Barry Sharpless (The Scripps Institute of Science) and others.

#### SUMMARY

Our research is focused on the detailed pharmacokinetics and pharmacodynamics of zwitterionic aldoximes designed in collaboration with Nobel laureate K. Barry Sharpless. These aldoximes promptly cross the blood-brain barrier and therefore could act as centrally-active antidotes in nerve agent poisonings (83).

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



INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (G. Gajski) National Institute of Biology, Ljubljana, Slovenia (B. Žegura)	Assessment of Toxicological Safety of Foodborne Toxins (SafeFood, Bilateral project CRO-SI)	2018–2019

IMROH ASSOCIATES: M. Gerić, I. Vrhovac Madunić, J. Madunić

#### SUMMARY

The aim of the project is to evaluate the toxic effect of toxins present in food in *in vitro* conditions on primary human peripheral blood lymphocytes used as sensitive indicators of individual exposure and human liver cancer cells (HepG2) that contain enzymes involved in the metabolism of toxinates.  $\beta$ -methylamino-L-alanine (BMAA) possesses clastogenic potential for human blood cells therefore further studies are needed to evaluate its chronic effects (26, 288).

INSTITUTION (Leader)	PROJECT	DURATION
IMROH, Zagreb (I. Vinković Vrček) Institute of Pharmaceutical Sciences, University of Graz, Austria (E. Roblegg)	The pharmacokinetic profile of silver nanoparticles: the role of biological barriers (NanoPasS, Bilateral project CRO-AT)	2018–2019

IMROH ASSOCIATES: A. M. Marjanović Čermak, I. Pavičić, K. Ilić

#### SUMMARY

Collaborator of the NanoFaceS project K. Ilić visited the Leibniz Institute for Photonic Technology (Leibniz-IPHT) in Jena, Germany from 1 to 26 Jul 2019. Under the guidance of prof W. Frizsche, he worked on the study of protein adsorption to the surface of nanoparticles by the localized surface plasmon resonance (LSPR) method, continuing and developing previous experiments as part of the Croatian-German collaboration. PhD students S. Hartl and C. Tetyczka, from the Department of Pharmaceutical Technology and Biopharmaceuticals of the University of Graz, visited IMROH from 18 to 22 Feb 2019. During the visit they conducted cellular experiments to determine the toxic effect of silver and selenium nanoparticles. Members of the NanoFaceS Group (I. Vinković Vrček, I. Pavičić, and K. Ilić) participated at the 10<sup>th</sup> BioNanoMed Conference, held in Graz, Austria (15–17 Apr 2019). I. Vinković Vrček held a lecture entitled "Sex-related *in vivo* Response to Metallic Nanoparticles", while I. Pavičić and K. Ilić presented two posters: "Biocompatibility assessment of selenium nanoparticles as novel biocidal nanomaterial" and "Interaction of silver nanoparticles with biological barriers". The 12<sup>th</sup> International Particle Toxicology Conference was held from 11 to 13 Sep 2019 in Salzburg, Austria.



The mission of the conference was to bring together toxicologists from all over the world to discuss issues of safety, application, and research approaches to particle toxicology. Collaborator of the project R. Barbir participated with a poster theme "Sex-related *in vivo* response to silver nanoparticles after subacute oral exposure". She presented the latest results of animal experiments on the effect of sex differences on the organism's response to subcutaneous exposure to silver nanoparticles. PhD student E. Galić also presented his research on the genotoxicity of silver and selenium nanoparticles with a poster: "Genotoxicity of silver and selenium nanoparticles on human epithelial cells". The research was carried out in collaboration with the NanoFaceS Group with the research groups of the Universities of Osijek and Graz. Work on the project resulted in the preparation of 2 scientific publications, which were prepared for submission to scientific journals.

INSTITUTION (Leader)	PROJECT	DURATION
<b>IMROH, Zagreb (I. Vinković Vrček)</b> <b>Leibniz Institute of Photonic Technology (IPHT), Jena, Germany (W. Fritzsche)</b>	<b>Multiplex characterization platform for nanobio interfaces (Bilateral project CRO-DE)</b>	<b>2018–2019</b>

IMROH ASSOCIATES: R. Barbir, G. Šinko, B. Pem, K. Ilić

#### SUMMARY

During the two-year period, all planned experiments were completed, and the preparation of the first joint publication is under way. In addition, new forms of collaboration have been opened – in the field of application of a multiplex characterization platform for the detection of nanoplastics in biological samples.

PhD student B. Pem visited the Leibniz Institute for Photonic Technology in Jena, Germany (11 Nov–7 Dec 2019). She studied the localised surface plasmon resonance (LSPR) technique and performed fibrinogen binding experiments on the surface of gold nanoparticles, which builds directly on the previous work of the NanoFaceS Group PhD students. Also, during the stay, preliminary measurements of protein interactions with nanoparticles were performed using the surface-enhanced Raman spectroscopy (SERS) technique. Ms Pem will be able to apply her newly acquired knowledge to the continuation of the experiment upon her return to Zagreb. On 2 Nov 2019 at the Fraunhofer Institute of Immunology and Cellular Therapy in Leipzig, Germany, The Mitteldeutschland DNA gathering was held, bringing together experts in the field of DNA research and nanoparticle application in the development of sensors and diagnostic devices. The event was organized in collaboration with the Leibniz Institute for Photonic Technology in Jena and the University of Potsdam. PhD student B. Pem had an oral presentation of the NanoFaceS project: "Interaction of metallic nanoparticles with biomolecules: the implications for nano-bio interface". The NanoFaceS Group hosted a young scientist from the Leibniz Institute of Photonic Technology in Jena, Germany E. Podlesnaia (9–16 Dec 2019). Ms Podlesnaia is developing methods for the synthesis of anisotropic gold nanoparticles and intends to extend her field of work to other types of nanomaterials. The aim of her visit was to observe and learn the methods of synthesis of silver and selenium nanoparticles of different sizes and shapes. The NanoFaces team also benefited greatly from her knowledge and experience. This visit resulted in the strengthening of Croatian-German cooperation through a bilateral project, and the exchange of knowledge was to the benefit of both partner institutions.

INSTITUTION (Leader)	PROJECT	DURATION
<b>IMROH, Zagreb (Z. Kovarik)</b> <b>Research Center for Eco-environmental Sciences, Chinese Academy of Sciences, Beijing, China (Q. Xie)</b>	<b>Effects of selected pesticides on neuronal acetylcholinesterase expression (Bilateral project CRO-CN)</b>	<b>2019–2021</b>

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

#### SUMMARY

The aim of this project is to study the effects of pesticides on acetylcholinesterase (AChE) activity and expression to explain the mechanism of AChE regulation at cellular level. So far, we have selected several organophosphate pesticides for testing, described the reversible inhibition of AChE, and identified key interactions in the enzyme's active site by molecular modelling (334).



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 project CRO-RS)	2019–2021

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

#### SUMMARY

The application of advanced statistical methods to evaluate exposure of the general population to persistent organochlorine compounds is studied. Future research will include examining the application of statistical machine learning methods (artificial neural networks, support vector methods, and decision trees) to R and Week programs with respect to factors affecting levels of organochlorine compounds in breast milk.

INSTITUTION (Leader)	PROJECT	DURATION
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 project CRO-RS)	2019–2021

IMROH ASSOCIATES: M. Gerić, M. Milić

#### SUMMARY

SafeAChE will evaluate the prooxidative 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
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 project CRO-CN)	2019–2021

IMROH ASSOCIATES: G. Gajski

#### SUMMARY

The project goal is to evaluate the types and concentrations of typical new organic pollutants in 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. Furthermore, the project will clarify the coupling relationship between new organic pollutants and antibiotic resistance genes, and assess ecological risks.

### 16.2.B. PROFESSIONAL PROJECTS

PROJECT	CONTRACTOR	LEADER
<b>Service provider: Radiation Dosimetry and Radiobiology Unit</b>		
EAN NORM; European ALARA Network for Naturally Occurring Radioactive Materials	Project Coordinator IAF	I. Prlić
Contract no. TREN/H4/51/2005 of the European Commission (EC) (since 2005)	Radioökologie GmbH, Dresden, Germany	I. Prlić
HRPE Development of a training curriculum for radiation protection experts in Croatia	SCK·CEN Academy for Nuclear Science and Technology, Belgium	M. Surić Mihić (IMROH) and T. Clarijs (SCK·CEN Belgium)

## 17. PROFESSIONAL UNITS



### 17.1. Laboratory Animal Breeding Unit

#### EMPLOYEES

##### HEAD

Vedran Micek, DVM, professional associate

##### ASSOCIATE

Mirjana Mataušić Pišl, DVM, PhD, scientific associate until 31 Dec 2019

##### TECHNICAL STAFF

Kata Šmaguc, technician

#### 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. In the context of projects contracted with the Croatian Science Foundation, scheduled *in vivo* experiments were performed for two projects: "Aging-related expression of membrane transporters in rat" (AGEMETAR, IP-11-2013-1481, IMROH) and "Dietary lipids, sex and age in pathogenesis of metabolic syndrome" (DietMetSyn, IP-2016-06-3163, Faculty of Veterinary Medicine, University of Zagreb).



## 17.2. Poison Control Centre

### EMPLOYEES

#### HEAD

Rajka Turk, MSc, professional advisor in science

#### ASSOCIATES

Researchers of the Occupational and Environmental Health Unit (Chapter 15.5.)

### PROFESSIONAL WORK

The information service of the PCC received 2401 calls from health institutions and professionals in Croatia regarding acute poisoning incidents. Following requests from the industry, 97 toxicological evaluations were prepared as well as 4 reports 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, 37 evaluations for the purpose of biocidal products authorization according to the Biocidal products Act and Regulation (EU) No. 528/2012 concerning the placement on the market and use of biocidal products. Collaboration with the Agency for Medicinal Products and Medical Devices of Croatia in monitoring of drug poisonings (pharmacovigilance) continued. Further work on the revision of the National Action Plan for sustainable use of pesticides as well as accompanying ordinances was continued with the Ministry of Agriculture. Collaboration with the Ministry of Work and Pension System 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. Further work on the compilation of new Guidelines for the use of Antidotes in emergency medicine was initiated, in collaboration with the Croatian Institute for Emergency Medicine and Croatian Institute for Public Health Department for Toxicology.

Annual reports of the PCC continued to be published in the journal *Archives of Industrial Hygiene and Toxicology* in English and Croatian (177). A professional paper on occupational poisonings recorded at the PCC in 2018 was also published (117). Publication of short communications for the general public on recent poisoning incidents and their prevention was continued through the Institute's website (180).

The PCC continued to participate in the prospective epidemiological study entitled "Study on Viperidae Family Snakebites in Central and Eastern European Countries (CEE-VIPER)" (leader: M. Brvar, MD, PhD, Slovenian Poison control centre, Ljubljana, Slovenia) with data about incidence and characteristics the European viper envenomations for which the PCC was consulted in 2019.

The PCC also started to participate in the epidemiological study on poisonings by refillable electronic cigarettes entitled "PRECISE Project: Potential Risks from Electronic Cigarettes & their technical Specifications in Europe" (leader: A. Vardavas, MD, PhD, Medical School, University of Crete, Heraklion, Greece). Results of the pilot phase of the PCC project "Preventing child poisonings by educational intervention aimed at parents of preschool children" were presented at the 39<sup>th</sup> International Congress of the European Association of Poisons Centres and Clinical Toxicologists (Naples, Italy) (264).

Evaluation of the proposal for harmonised classification and labelling at EU level of 4-vinylcyclohexene diepoxide, prepared for the European Chemicals Agency (ECHA), as the Committee for Risk Assessment's rapporteur (361).

## 18. RESEARCH AREA "ŠUMBAR"

### ● HEAD

Josip Tončić, MSc, DVM, professional associate in science

### ● PROFESSIONAL WORK

The Research Area "Šumbar" is located east of the city of Karlovac (GPS coordinates: 45.5297, 15.6322) with a zone of 2,153 ha mainly covered by an English oak (*Quercus robur*) and hornbeam (*Carpinus betulus*) forest. "Šumbar" is a unique ecosystem in which the activities of safeguarding, control, and improvement of the habitat's stability are undertaken. Within the scope of these activities, a very important activity is the environmental study of water, soil, air, and biological material, which is related to natural and anthropogenic environmental pollution and the main goal is to preserve a healthy habitat.

A background ionising radiation monitoring RS 131 HP Ionization Chamber: Reuter Stokes type was performed continuously. The entire measuring system is connected to the telecommunication system, which allows real-time online data monitoring. Measurements were performed with mobile ALARA devices at various microlocations. All collected data were later processed, evaluated, and correlated in the Radiation Dosimetry and Radiobiology Unit. Part of the proposed activities in the scope of the Horizon 2020 EUROATOM (Integrating Radiation Protection Research in the European Union) call ref: NFRP-07-2015 programme was also carried out at "Šumbar".

Measurements with HORIBA APNA-360 (Ambient NO<sub>x</sub> Monitor), HORIBA APOA-360 (Ambient O<sub>3</sub> Monitor) and Sven Leckel Sequential Sampler SEQ47/50, which measure NO, NO<sub>2</sub>, NO<sub>x</sub>, O<sub>3</sub> and PM<sub>2.5</sub> were continued within the scope of the programme of monitoring air pollution and quality.

## 19. COMPANY OWNED BY THE INSTITUTE

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

### **DIRECTOR**

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

### **ASSOCIATE**

Franka Šakić, senior technician (90 % of working hours at the Institute, 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 2019 providing services in the domain of occupational and sports medicine, and internal medicine. The outpatient clinic provided a total of 441 medical services for 322 customers. An occupational medicine specialist delivered 10 judicial-medical expertises for the Administrative Court in Zagreb, Municipal Courts in Rijeka, Bjelovar, Velika Gorica, Commercial Court in Zagreb, and Municipal Civil Court in Zagreb). J. Macan was appointed as main supervisor by the Croatian Ministry of Health for 7 residents in occupational and sports medicine. The Psychotherapy Office led by A. Bjelajac, PhD, psychologist and psychotherapist, continued working within the company. Twelve clinical psychological examinations were performed on the request of the occupational medicine specialist. The company operated positively in 2019.

## 20. PUBLISHING

The Institute is the publisher of the scientific journal *Arhiv za higijenu rada i toksikologiju* – *Archives of Industrial Hygiene and Toxicology*, print: ISSN 0004-1254, online: ISSN 1848-6312.

<b>HONORARY EDITOR</b> <b>Prof Dr Marko Šarić, F.C.A.</b>	<b>THE OFFICIAL JOURNAL OF</b> Croatian Medical Association – Croatian Society on Occupational Health Croatian Society of Toxicology Slovenian Society of Toxicology Croatian Radiation Protection Association Croatian Air Pollution Prevention Association
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### 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. The *Archives* is issued four times a year.



The *Archives* is indexed in SCI-Expanded, Medline/PubMed, Scopus, and many other databases. The Impact Factor (IF) for 2019 was 1.436, which is the highest IF value since the journal was listed in *InCites Journal Citation Reports* (Clarivate Analytics). The 5-year IF was 1.606, which is the highest value ever achieved in the journal's history. The *Archives* is currently ranked within the third Quartile (Q3) in the Public, Environmental & Occupational Health and the fourth Quartile (Q4) in the Toxicology area, based on the previous year's achievements. The *Archives* ranks fifth on the list of all Croatian journals by IF value (regardless of the area of publication).

*IF values of the Archives since its listing in InCites Journal Citation Reports (Clarivate Analytics)*

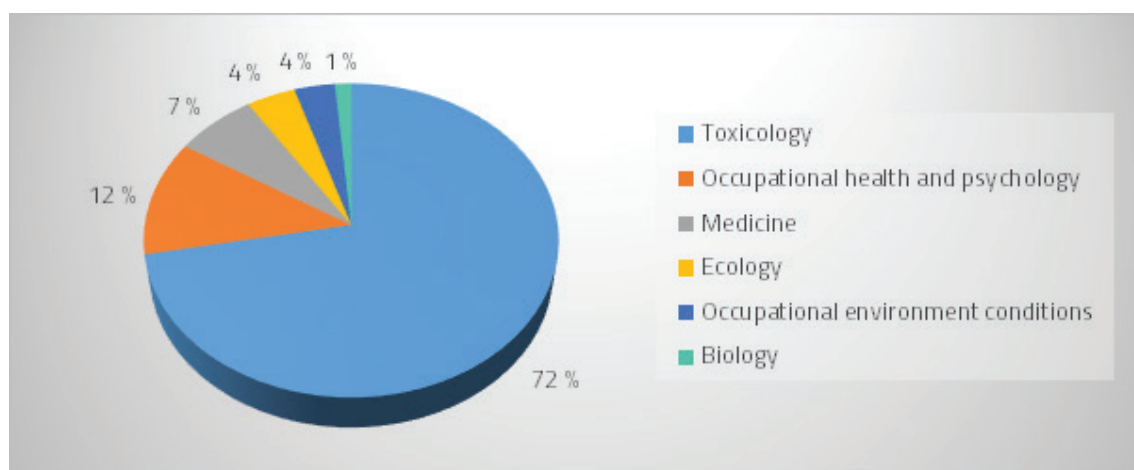
Year	IF	5-years IF
<b>2018</b>	<b>1.436</b>	<b>1.606</b>
2017	1.117	1.335
2016	1.395	1.320
2015	0.971	1.019
2014	0.932	1.120
2013	0.727	0.980
2012	0.674	—
2011	1.048	—
2010	0.826	—

*Ranking of Croatian journals according to IF (Clarivate Analytics)*

Select All	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	Croatian Journal of Forest Engineering	567	2.258	0.00069
2	Biochemia Medica	1,810	2.202	0.00331
3	CROATIAN MEDICAL JOURNAL	1,675	1.624	0.00177
4	FOOD TECHNOLOGY AND BIOTECHNOLOGY	2,039	1.517	0.00129
5	Arhiv za Higijenu Rada i Toksikologiju-Archives of Industrial Hygiene and Toxicology	780	1.436	0.00097

The citation of the *Archives* in 2019 was very good. As of 2 Jan 2020, the *Web of Science* database recorded 4,132 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 - 2019 according to the *Web of Science* database is 27.

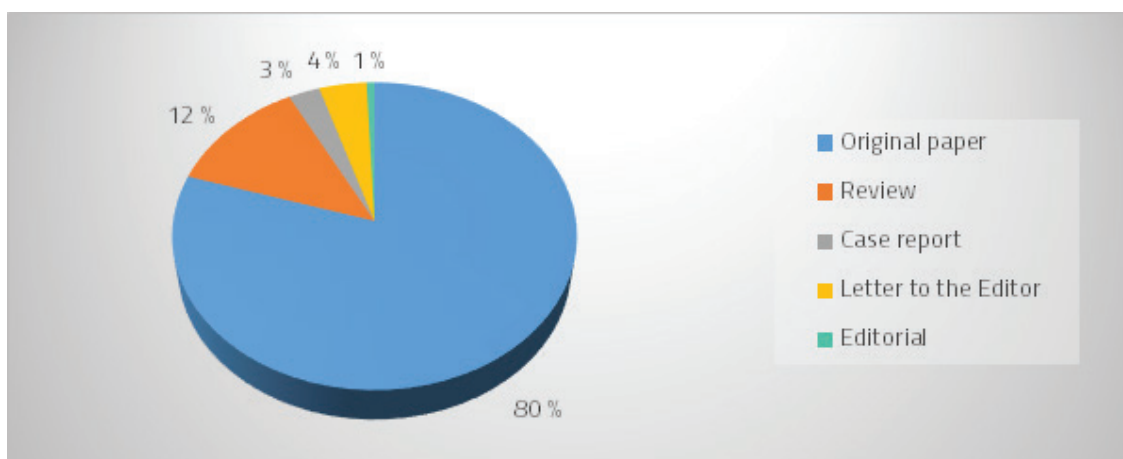
During 2019, the Editorial Office of the *Archives* received a total of 144 submissions, most of which were submitted through the journal's online system available at <https://arhiv.imi.hr> and the remainder by e-mail ([arhiv@imi.hr](mailto:arhiv@imi.hr)). Most of the submissions covered topics from toxicology, while occupational health and psychology followed with a somewhat smaller number of submissions.



*Distribution of articles submitted in 2019 according to research areas*

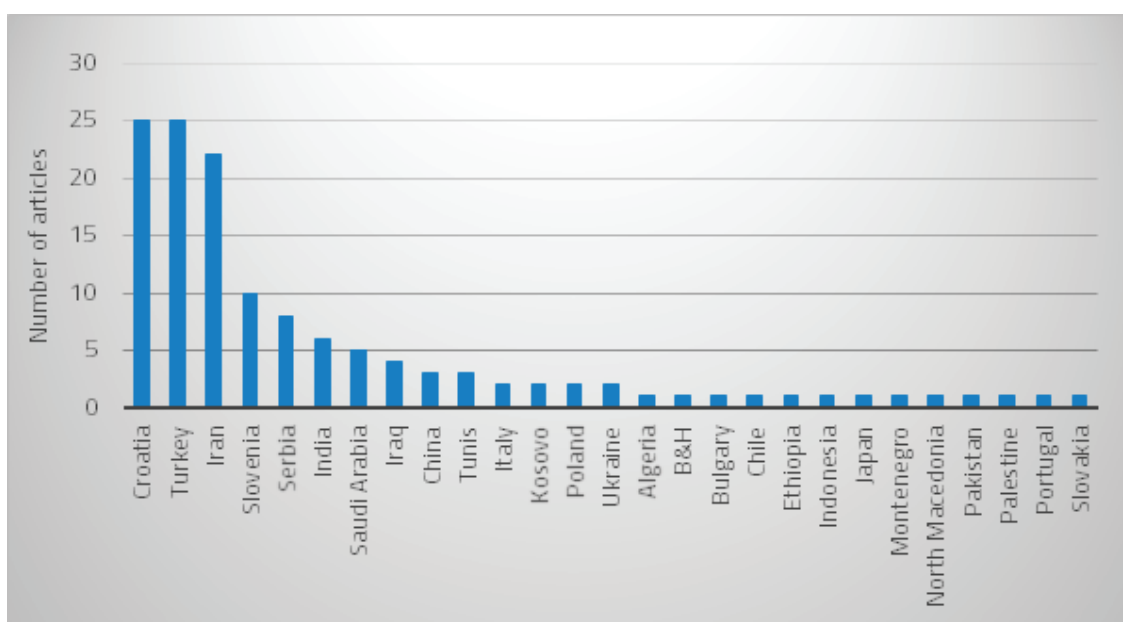
Most of the manuscripts received (80 %) referred to original scientific papers and review papers (12 %), while other categories of manuscripts were less represented.





*Distribution of manuscripts submitted in 2019 according to article type*

The manuscripts were submitted by authors from 27 different countries. The largest number of manuscripts was submitted from Croatia (17 %) and Turkey (17 %), followed by authors from Iran (15 %), Slovenia (7 %), and Serbia (6 %), while other countries were represented by less than 5 %.



*Distribution of articles submitted in 2019 according to origin country*

The rejection rate was 60 % (86 of 144 manuscripts received were rejected). Most of them (67 %) were rejected by the Editor-in-Chief or an Editorial Board decision because of poor quality or failure to meet the minimum criteria for review, while others were rejected due to negative reviews.

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 2019, four regular issues of Volume no. 70 were published, containing articles published in six categories: Original article (29), Review/Mini-Review (9), Letter to the Editor (2), Note (1), Technical Paper (1) and Editorial (1). In addition to regular manuscripts, articles in the *In memoriam* and *Reports* categories were also published. According to the attendance on the Portal of Scientific Journals of the Republic of Croatia (HRČAK) during 2019, 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 2,114,339 on 2 Jan 2020.



*Cover pages of all Archives' issues published in 2019 (Volume 70)*

Throughout 2019, 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 journal's editors work continuously to promote the reputation of the journal domestically and internationally, which includes contacts with researchers and professional associations. For participants of the Specialisation in Occupational Health and Sports, which takes place at the Institute under the mentorship of Dr J. Macan, on 29 Nov 2019, a workshop entitled *How to write and publish a good case report or case series* was held by D. Čakalo, I. Brčić Karačonji, and N. Kopjar. The regular publication of the journal and its successful operation during 2019 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 also available through Sciendo's service (<https://content.sciendo.com/view/journals/aiht/aiht-overview.xml>).

**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 zaštite okoliša i energetike RH – dozvola za obavljanje djelatnosti praćenja kvalitete zraka. Ovlaštenje vrijedi do 20. prosinca 2020.

● Ministarstvo zaštite okoliša i energetike 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  $PM_{10}$  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  $PM_{10}$  frakciji lebdećih čestica
- SIS-TP CENT/TR 16243:2011 (CEN/TR 16243:2011): Određivanje masenih koncentracija elementnog i organskog ugljika u lebdećim česticama u vanjskome zraku
- HRN EN 15549:2008 (EN 15549:2008): Određivanje koncentracija benzo(a)pirena u vanjskome zraku
- SIS-TP CENT/TR 16269:2011 (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.

Ovlaštenje vrijedi do 20. prosinca 2020.

● Državni zavod za radiološku i nuklearnu sigurnost – ovlaštenje za obavljanje stručnih poslova zaštite od ionizirajućeg zračenja:

- mjerenje osobnog vanjskog ozračenja izloženih radnika ili osoba koje se obučavaju ili obrazuju za rad s izvorima ionizirajućeg zračenja
- ispitivanje rendgenskih uređaja, akceleratora i drugih uređaja koji proizvode ionizirajuće zračenje te davanje mišljenja s procjenom opasnosti na osnovi mjerenja i proračuna
- ispitivanje zatvorenih radioaktivnih izvora i uređaja sa zatvorenim radioaktivnim izvorima te davanje mišljenja s procjenom opasnosti na osnovi mjerenja i proračuna
- ispitivanje prostorija u kojima se radi s izvorima ionizirajućeg zračenja te izrada dokumenata iz kojih je vidljivo udovoljava li prostorija propisanim uvjetima zaštite od ionizirajućeg zračenja
- ispitivanje i praćenje vrste i aktivnosti radioaktivnih tvari u zraku, tlu, moru, rijekama, jezerima, podzemnim vodama, oborinama, vodi za piće, hrani i predmetima opće uporabe
- ispitivanje koncentracije radona i potomaka radona u zraku.

Ovlaštenje vrijedi do 10. prosinca 2020.

● Ministarstvo poljoprivrede RH - ovlaštenje za obavljanje analiza: hrana, hrana za životinje, prirodna mineralna, prirodna izvorska i stolna voda.

Ovlaštenje od 26. 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.	AVANCO d. o. o.	2019.

**Ostale znanstvenoistraživačke i stručne suradnje***USTANOVE U REPUBLICI HRVATSKOJ*

1. Agencija za zaštitu okoliša, Zagreb
2. Agronomski fakultet Sveučilišta u Zagrebu
3. CARNet, Zagreb
4. Državni hidrometeorološki zavod, Zagreb
5. Ekonerg d. o. o., Zagreb
6. Fakultet elektrotehnike i računarstva Sveučilišta u Zagrebu
7. Fakultet kemijskog inženjerstva i tehnologije Sveučilišta u Zagrebu
8. Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu
9. Fond za zaštitu okoliša i energetske učinkovitost, Zagreb
10. Gekom d. o. o., Zagreb
11. Hrvatski institut za istraživanje mozga, Zagreb
12. Hrvatski sindikat male privrede, obrtništva, uslužnih djelatnosti i stranih predstavništava, Zagreb
13. Hrvatski veterinarski institut, Zagreb
14. Institut „Ruđer Bošković“, Zagreb
15. Kaznionica u Lepoglavi

16. Klinička bolnica Merkur, Zagreb
17. Klinički bolnički centar Osijek
18. Klinički bolnički centar „Sestre milosrdnice“, Zagreb
19. Klinički bolnički centar Zagreb (KBC Zagreb)
20. Klinika za dječje bolesti, Zagreb
21. Klinika za ženske bolesti i porode, KBC Zagreb
22. Medicinski fakultet Sveučilišta u Rijeci
23. Medicinski fakultet Sveučilišta u Zagrebu
24. Ministarstvo unutarnjih poslova RH, Ravnateljstvo civilne zaštite,
25. Sektor za radiološku i nuklearnu sigurnost
26. Ministarstvo zaštite okoliša i energetike RH, Zagreb
27. Nastavni zavod za javno zdravstvo „Dr. Andrija Štampar“, Zagreb
28. Nastavni zavod za javno zdravstvo Primorsko-goranske županije, Rijeka
29. Nezavisni sindikat znanosti i visokog obrazovanja, Zagreb
30. Odgojni zavod Turopolje, Velika Gorica
31. Odjel za biotehnologiju Sveučilišta u Rijeci
32. Petrokemija d. d., Kutina
33. Prehrambeno-biotehnološki fakultet Sveučilišta u Zagrebu
34. Prehrambeno-tehnološki fakultet, Sveučilište J. J. Strossmayera u Osijeku
35. Prirodoslovno-matematički fakultet Sveučilišta u Splitu
36. Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu
37. Sabor RH, Zagreb
38. Stomatološki fakultet Sveučilišta u Zagrebu
39. Sveučilište J. J. Strossmayera u Osijeku, Odjel za kemiju
40. Veterinarski fakultet Sveučilišta u Zagrebu
41. Zavod za javno zdravstvo Brodsko-posavske županije, Slavonski Brod
42. Zavod za javno zdravstvo Istarske županije, Pula
43. Zavod za javno zdravstvo Koprivničko-križevačke županije, Koprivnica
44. Zavod za javno zdravstvo Osječko-baranjske županije, Osijek
45. Zavod za javno zdravstvo Zadarske županije, Zadar

#### *USTANOVE U INOZEMSTVU*

1. Academic Medical Centre, Amsterdam, Nizozemska
2. Bundesamt für Strahlenschutz, Salzgitter, Njemačka
3. Fakulteta za kemiju in kemijsko tehnologiju Univerza v Ljubljani, Slovenija
4. Florida State University, Tallahassee, FL, SAD
5. Helmholtz Zentrum München Deutsches Forschungszentrum für Gesundheit und Umwelt, München, Njemačka
6. Hungarian Institute for Public Health, Budimpešta, Mađarska
7. Institut für Chemie, Universität Graz, Austrija
8. Institut für Physikalische und Theoretische Chemie, Technische Universität Graz, Graz, Austrija
9. Institut für Soziale Ökologie, Alpen-Adria-Universität Klagenfurt, Austrija
10. Inštitut za biokemiju, Medicinska fakulteta, Univerza v Ljubljani, Ljubljana, Slovenija
11. Inštitut za patološko fiziologiju, Medicinska fakulteta, Univerza v Ljubljani, Ljubljana, Slovenija
12. Institute for Nuclear Research, Hungarian Academy of Sciences, Debrecen, Mađarska
13. Institute of Basic Medical Sciences, University of Oslo, Oslo, Norveška
14. Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic, Prag, Češka
15. Institute of Nature Conservation of Polish Academy of Sciences, Krakow, Poljska

16. International Atomic Energy Agency, Beč, Austrija
17. Joint Research Centre of the European Commission, Bruxelles, Belgija
18. Malopolski Voivodeship Inspectorate of Environmental Protection, Krakow, Poljska
19. Mazovian Voivodeship Inspectorate of Environmental Protection, Varšava, Poljska
20. Nacionalni inštitut za biologijo, Ljubljana, Slovenija
21. National Reference Laboratory of CIEP, Krakow, Poljska.
22. NMR laboratórium, Pannon Egyetem, Veszprém, Mađarska
23. Polish Chamber of Commerce for Sustainable Development (PIGE), Varšava, Poljska
24. Prirodno-matematički fakultet, Univerzitet u Kragujevcu, Srbija
25. Umweltbundesamt (UBA), Langen, Njemačka
26. UHasselt University Belgium, Campus Diepenbeek, Agoralaan Gebouw H, Diepenbeek, Belgija
27. Universidad Autónoma de Tlaxcala, Universidad Nacional Autónoma de México, Meksiko
28. Universität Osnabrück, Osnabrück, Njemačka
29. Universitätsklinikum Hamburg-Eppendorf (UKE), Hamburg, Njemačka
30. University of California at San Diego, La Jolla, CA, SAD
31. University of Rouen, Mont-Saint-Aignan, Francuska
32. Univerzita Hradec Králové, Hradec Králové, Češka
33. VITO- Vlaamse Instelling voor Technologisch Onderzoek, Mol, Belgija

**C. PRIHODI INSTITUTA**

RED.BR.	VRSTA PRIHODA	IZNOS (HRK)	%
<b>A</b>	<b>PRIHODI IZ DRŽAVNOG PRORAČUNA</b>	<b>42.030.966</b>	<b>75,68</b>
1.	Plaće i prijevoz na posao za zaposlenike	25.314.386	45,58
2.	Plaće, prijevoz i naknade za znanstvene novake	411.174	0,74
3.	Programsko financiranje Instituta	3.617.568	6,51
4.	Jubilarne nagrade, otpremnine, potpore za opremanje doktorata	164.936	0,30
5.	Regres za godišnji odmor, božićnica i dar djeci za Dan svetog Nikole	411.750	0,74
6.	Pomoći zaposlenicima za rođenje djeteta, bolovanje i smrtne slučajeve	45.518	0,08
7.	Povrat naknade zbog nezapošljavanja osoba s invaliditetom	37.125	0,07
8.	Nacionalno sufinanciranje Projekta ReC-IMI	83.253	0,15
9.	Bilateralni projekti	106.398	0,19
10.	Potpore za prijavu projekata i za popularizaciju znanosti	25.631	0,05
11.	Ministarstvo zaštite okoliša i energetike RH - financiranje projekta AIRQ	9.147.287	16,47
12.	Projekti Hrvatske zaklade za znanost	2.665.940	4,80
<b>B</b>	<b>PRIHODI OD PRUŽENIH USLUGA NA TRŽIŠTU</b>	<b>5.702.144</b>	<b>10,27</b>
1.	Gradski ured za gospodarstvo, energetiku i zaštitu okoliša, Zagreb	804.214	1,45
2.	Klinički bolnički centar Zagreb	491.067	0,88
3.	Državni zavod za radiološku i nuklearnu sigurnost, Zagreb	48.521	0,09
4.	Klinički bolnički centar „Sestre milosrdnice“, Zagreb	396.198	0,71
5.	Zagrebačke otpadne vode d. o. o., Zagreb	257.652	0,46
6.	Klinička bolnica Dubrava, Zagreb	283.890	0,51
7.	Zavod za javno zdravstvo Koprivničko-križevačke županije, Koprivnica	212.064	0,38
8.	Ekonerg - Institut za energetiku i zaštitu okoliša d. o. o., Zagreb	143.120	0,26
9.	Hrvatski zavod za zdravstveno osiguranje, Zagreb	170.733	0,31
10.	Ministarstvo unutarnjih poslova RH, Zagreb	496.750	0,89
11.	Zavod za javno zdravstvo Brodsko-posavske županije, Slavonski Brod	64.000	0,12
12.	Grad Vinkovci	73.227	0,13
13.	Međunarodna zračna luka Zagreb d. d.	107.520	0,19
14.	Syngenta Agro d. o. o. Zagreb	48.125	0,09
15.	Nastavni zavod za javno zdravstvo „Dr. Andrija Štampar“	41.097	0,07
16.	Dom zdravlja Splitsko-dalmatinske županije, Split	78.050	0,14
17.	Cesta d. o. o. Pula	91.250	0,16
18.	HEP Proizvodnja d. o. o., Zagreb	69.400	0,12
19.	Opća bolnica Varaždin	67.450	0,12
20.	Opća bolnica Šibensko-kninske županije, Šibenik	83.960	0,15
21.	Bayer d. o. o. Zagreb	110.000	0,20
22.	Crosco naftni servisi d. o. o.	45.467	0,08
23.	Ispitivanje i mjerenje radioaktivnosti uzoraka	83.452	0,15
24.	Ocjena ekološke prikladnosti objekata	189.781	0,34
25.	Dozimetrija izvora zračenja	712.225	1,28
26.	Laboratorijske usluge - pacijenti	133.991	0,24
27.	Laboratorijske analize i toksikološke ocjene uzoraka	368.693	0,66
28.	Arhiv – pretplata	5.787	0,01
29.	Izbori u zvanja, etičko povjerenstvo, konzultantske usluge	24.460	0,04



<b>C</b>	<b>PRIHODI OSTVARENI IZ OSTALIH IZVORA</b>	<b>7.804.483</b>	<b>14,05</b>
1.	DHMZ - Program mjerenja razine onečišćenosti u Državnoj mreži	3.939.626	7,09
2.	Međunarodni projekti	620.688	1,12
3.	Prihodi iz EFRR-a za financiranje Projekta REC-IMI	471.764	0,85
4.	Fond za zaštitu okoliša - sufinanciranje projekta AIRQ	1.588.393	2,86
5.	Prihodi od dividendi, kamata i pozitivnih tečajnih razlika	54.698	0,10
6.	Refundacije troškova	146.011	0,26
7.	Prihodi od prodaje stanova i automobila	22.978	0,04
8.	Donacije i pomoći	780.000	1,40
9.	Ostali prihodi i sufinanciranje troškova	180.325	0,32
<b>A+B+C</b>	<b>UKUPNI PRIHOD</b>	<b>55.537.593</b>	<b>100,00</b>

**D. PUBLIKACIJE DJELATNIKA INSTITUTA**

KATEGORIJA PUBLIKACIJE	BROJ RADOVA
<b>D.1. Znanstveni, pregledni i stručni radovi (+ prihvaćeni za objavu u 2020.)</b>	<b>130 (+26)</b>
Radovi u časopisima indeksiranim u bazi WoS	89
Radovi u časopisima indeksiranim u bazi WoS prihvaćeni za objavu u 2020.	26
Radovi u časopisima indeksiranim u ostalim bazama	5
Radovi u neindeksiranim časopisima	3
Radovi u zbornicima skupova održanih u RH	25
Radovi u zbornicima skupova održanih u inozemstvu	8
<b>D.2. Knjige, časopisi, zbornici</b>	<b>20</b>
Autor ili urednik knjige	1
Rad ili poglavlje u knjizi	16
Urednik časopisa ili zbornika	3
<b>D.3. Ostale publikacije</b>	<b>4</b>
Tiskana izdanja	3
Elektronička izdanja	1
<b>D.4. Kvalifikacijski radovi</b>	<b>18</b>
Radovi djelatnika Instituta	2
Radovi pristupnika s mentorom/komentorom na Institutu	16
<b>D.5. Kongresna priopćenja na skupovima održanim u RH</b>	<b>65</b>
Sažetci u časopisima indeksiranim u bazi WoS	0
Sažetci u ostalim časopisima i knjigama sažetaka	65
Sažetci u elektroničkom izdanju	0
<b>D.6. Kongresna priopćenja na skupovima održanim u inozemstvu</b>	<b>76</b>
Sažetci u časopisima indeksiranim u bazi WoS	12
Sažetci u ostalim časopisima i knjigama sažetaka	62
Sažetci u elektroničkom izdanju	2
<b>D.7. Izvještaji stručne djelatnosti</b>	<b>23</b>
Nacionalni projekti, ugovori i suradnje	21
Međunarodni projekti, ugovori i suradnje	2
<b>UKUPNO PUBLIKACIJA OBJAVLJENIH U 2019. (+ prihvaćenih za objavu u 2020.)</b>	<b>336 (+26)</b>

**D.1. ZNANSTVENI, PREGLEDNI I STRUČNI RADOVI*****Radovi u časopisima indeksiranim u bazi WoS***

- AGHAJANYAN A, FUCIC A, TSKHOVREBOVA L, GIGANI O, KONJEVODA P. Genome damage in children with classical Ehlers-Danlos syndrome - An *in vivo* and *in vitro* study. Eur J Med Genet 2019;62(11):103546. (znanstveni rad, Q3)
- ARENAS-HUERTERO F, ZARAGOZA-OJEDA M, SÁNCHEZ-ALARCÓN J, MILIĆ M, ŠEGVIĆ KLARIĆ M, MONTIEL-GONZÁLEZ JM, VALENCIA-QUINTANA R. Involvement of AhR pathway in toxicity of Aflatoxins and other mycotoxins. Front Microbiol 2019;10:2347. (pregledni rad, Q1)
- AZQUETA A, MURUZABAL D, BOUTET-ROBINET E, MILIC M, DUSINSKA M, BRUNBORG G, MØLLER P, COLLINS AR. Technical recommendations to perform the alkaline standard and enzyme-modified comet assay in human biomonitoring studies. Mutat Res Gen Tox En 2019;843:24-32. (pregledni rad, Q3)
- BABIĆ Ž, FRANIĆ Zr, MACAN J. Keeping children safe from harmful household products: a survey on safety practices in Croatia. Arh Hig Rada Toksikol 2019;70:60-1. (pismo uredniku, Q3)
- BABIĆ Ž, KEŽIĆ S, MACAN J. Individual susceptibility to contact sensitization: the role of TNF alpha 308G>A polymorphism and atopy. Eur J Dermatol 2019;29:75-80. (znanstveni rad, Q1)
- BAĆANI M, NOVAK M, KOKANOVIĆ I, BABIĆ D. Composites of multiwall carbon nanotubes and conducting polyaniline: Bulk samples and films produced from a solution in chloroform. Curr Appl Phys 2019;19:775-9. (znanstveni rad, Q2)

7. BARBIR R, GOESSLER W, ČURLIN M, MICEK V, MILIĆ Mi, VUKOVIĆ B, MILIĆ Ma, LJUBOJEVIĆ M, DOMAZET JURAŠIN D, VINKOVIĆ VRČEK I. Protein corona modulates distribution and toxicological effects of silver nanoparticles *in vivo*. Part Part Syst Charact 2019;36:1900174. (znanstveni rad, Q1)
8. BAŠICA B, MIHALJEVIĆ I, MARAKOVIĆ N, KOVAČEVIĆ R, SMITAL T. Molecular characterization of zebrafish Gstr1, the only member of teleost-specific glutathione S- transferase class. Aquat Toxicol 2019;208:196-207. (znanstveni rad, Q1)
9. BAUMANN K, KORDIĆ L, MOČIBOB M, ŠINKO G, TOMIĆ S. Synthesis and *in vitro* screening of novel heterocyclic  $\beta$ -D-gluco- and  $\beta$ -D-galactoconjugates as butyrylcholinesterase inhibitors. Molecules 2019;24:2833-47. (znanstveni rad, Q2)
10. BOSAK A, OPSENICA DM, ŠINKO G, ZLATAR M, KOVARIK Z. Structural aspects of 4-aminoquinolines as reversible inhibitors of human acetylcholinesterase and butyrylcholinesterase. Chem Biol Interact 2019;308:101-9. (znanstveni rad, Q2)
11. CEDILAK M, BANJANAC M, BELAMARIC D, RADICEVIC AP, FARAHO I, ILIC K, CUZIC S, GLOJNARIC I, HABER VE, BOSNAR M. Precision-cut lung slices from bleomycin treated animals as a model for testing potential therapies for idiopathic pulmonary fibrosis. Pulm Pharmacol Ther 2019;55:75-83. (znanstveni rad, Q2)
12. COLLINS A, MILIĆ M, BONASSI S, DUSINSKA M. The comet assay in human biomonitoring: Technical and epidemiological perspectives. Mutat Res 2019;843:1-2. (uvodnik, Q3)
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