EDIAQI

Evidence Driven Indoor
Air Quality Improvement

Deliverable D7.5

Ethical guidelines, including informed consent procedures

Work Package 7

EXPLOIT- Dissemination, communication and exploitation

Version: Final

This project has received funding from the European Union's
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Deliverable Overview

This deliverable provides guidelines for the ethics review and impact assessments of the pilots and other relevant outputs of the project, including guidelines for the involvement of an independent appointed ethical and legal expert.

Additional Information

Type: R – Document, report

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Disclaimer

Document Revision History (Please update)

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V1.1	20th of April 2023	1st draft of the deliverable	SCH
V2.0	20th May 2023	Peer review of the deliverable	KNOW + IMROH + NIB
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Statement of Originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

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List of Terms and Abbreviations

Abbreviation	Description
EDIAQI	Evidence Driven Indoor Air Quality Improvement
SCH	Srebrnjak Children`s Hospital
IMROH	Institute for Medical Research and Occupational Health
ANT	Institute for Anthropological Research
EAB	External Advisory Board
WP	Work Package
IAQ	Indoor air quality
IAP	Indoor air pollution
RegionH	Region Hovedstaden
STC	Scientific and Technical Committee
COEH	Chief Officer Ethics and Health
DPO	Data Protection Officer
ANT	Institute of Anthropological Research
FP7 ATOPICA	European Union Seventh Framework Programme Atopic disease in changing climate, land use and air quality
COPSAC	Copenhagen Prospective Study on Asthma in Childhood
NIB	National Institute of Biology (Slovenia)
OECD	Organization for Economic Cooperation and Development
GLP	Good Laboratory Practice

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Executive Summary

The main objective of this deliverable (D7.5 Ethical guidelines, including informed consent procedures) is to provide an ethics assessment overview of all activities within the pilots and other relevant outputs of the project. This deliverable provides:

- an overview of the ethics related aspects of the EDIAQI project,
- assessment of the involvement of human (clinical) studies,
- assessment of the involvement of *in vivo* and *in vitro* studies,
- relevant guidelines for informed consent procedures,
- appointment of an independent ethical and legal expert within an External Advisory Board with members in the fields of research, including ethics related issues.

The EDIAQI consortium concludes that all pilot project activities, including the preclinical, clinical and human biomonitoring studies will be conducted according to all relevant ethics guidelines and professional codes of conduct. All the study protocols for the different cohorts and respective approvals from the ethical committees have been submitted as part of deliverables 2.7 Clinical Study Submission Package and 2.8 Clinical Studies Submission Package. They are therefore not included in this deliverable.

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1. Ethics related aspects of the EDIAQI project

The EDIAQI project aim is to improve indoor air quality (IAQ) guidelines and awareness based on scientific evidence. One of the main objectives of the EDIAQI project is to assess the levels and sources of exposure to indoor air pollution (IAP) and its effects on human health using a multidisciplinary approach. This will be done using several pilots and measurement and awareness campaigns, clinical and human biomonitoring studies (data from past and new prospective clinical cohorts), as well as *in vitro* and *in vivo* studies (in model cells and animals), focusing on the effects of IAP exposure on human health, primarily on vulnerable and at risk-populations - children and patients with chronic respiratory conditions such as asthma.

1.1 Ethics related principles of the EDIAQI project

Following the Regulation (EU) No 1291/2013 of the European Parliament and of the Council of 11th of December 2013 establishing Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020) and repealing Decision No 1982/2006/EC Text with EEA relevance, the EDIAQI project research and consortium will always comply with relevant ethical principles and national, Union and international legislation on ethics related matters. All members of the EDIAQI consortium have well established and long-lasting extensive experience and expertise in carrying our research activities in accordance with principles of good clinical, laboratory and data management practices.

The EDIAQI consortium will adhere to all relevant fundamental research and ethical principles, including: i) research integrity, ii) using state-of-the-art and standardized methodology and research procedures (including research reproducibility), iii) data availability (open access and using open data repositories, when applicable), iv) collaborative work, v) professional codes of conduct, vi) data management, storage and protection, vii) health and safety measures.

To ensure this, a project specific External Advisory Board (EAB) will be appointed, with members being experts in the fields of research, including (bio)ethics related issues.

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2. Clinical and human biomonitoring studies

The EDIAQI research will involve both past and existing (retrospective) cohorts and new and prospective cohorts. The retrospective cohort data will be analysed on associations and non-linear relationship by means of machine learning (within work package 5, WP5), while the prospective cohorts will encompass further procedures (including participant recruitment), measurements and analyses (within WP5, tasks T5.2 and 5.3) and association to IAQ.

Human studies in Croatia (SCH, IMROH) and Denmark (RegionH) will be conducted and regulated according to all relevant international and national ethical legislative.

Each institution included in participant recruitment, human material sampling and analysis will seek an approval from relevant authorities (Ethics committees), before the start of the any clinical study related activities, elaborating recruitment strategy, inclusion/exclusion criteria, number of participants, informed consent, questionnaire and other patient related documentation design, sample storage and handling and data management. Additionally, EDIAQI partners will report to the EAB.

The EDIAQI project will aim at conducting the clinical studies according to all relevant national, European and international laws and ethical rules in research, including:

- The Nuremberg Code (1946) addressing volunteer consent and proper acting.
- The Revised Declaration of Helsinki in its last version of 2013 (Ethical Principles for Medical Research Involving Human Subjects).
- The "Convention on Human Rights and Biomedicine" (Council of Europe, 1997) and the additional protocol on the prohibition of cloning human beings (1998); its additional protocol on biomedical research (2005).
- Recommendation CM/Rec (2016)6 on research on biological materials of human origin adopted by the Committee of Ministers of the Council of Europe.
- Regulation (EU) 2016/679 of the European Parliament and of the Council on the protection of natural persons regarding the processing of personal data and on the free movement of such data.

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- Code of practice on secondary use of medical data in scientific research projects, 2014.
- UN Convention on the Rights of the Child (1990).
- Opinions of the European Group on Ethics in Science and New Technologies (Commission Decision (2021/156)-
- The Royal Decree establishing basic requirements for the authorisation and functioning of biobanks with biomedical research purpose and for the processing of human samples and regulating the functioning and organisation of the National Register of Biobanks for Biomedical Research (1716/2011).

2.1 Retrospective clinical cohorts

EDIAQI plans to utilize data from 3 retrospective (FP7 ATOPICA, COPSAC2000 and COPSAC2010 mother-child cohort) and 2 new and prospective cohorts (SCH2021 and Severe childhood asthma). These clinical studies have already been approved by the relevant Ethics committees. These approvals have been included in the deliverable 2.8 Clinical Studies Submission Package.

2.2 Prospective clinical cohorts

The EDIAQI project plans to utilize 2 prospective cohorts - a new SCH2021 cohort (Croatia, partner SCH) and the Severe childhood asthma (Denmark, partner RegionH). The Severe childhood asthma cohort is an ongoing cohort with an existing ethics approval. The SCH2021 cohort applied for approval from the local Ethics committee and the study was approved on 1st February 2023. These approvals have also been included in the deliverable 2.8 Clinical Studies Submission Package.

Both prospective cohorts are non-interventional.

2.2.1 Participant recruitment

For the **SCH2021 cohort**, participants (children aged 6-18 years) will be recruited from the outpatient clinic at the Srebrnjak Children`s Hospital in Zagreb, Croatia, which is the national Referral Centre of the Croatian Ministry of Health for Clinical Allergy in children to an observational case-control type of study. Following an expert (physician, experienced

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allergy/pulmonology specialist) confirmed diagnosis of asthma for at least 1 year prior to recruitment as well as being on a stable dose of anti-inflammatory treatment for at least a month, and after obtaining an informed consent from the children`s legal guardians and children themselves (according to local legislation), participants will undergo a standard battery of diagnostic tests, examinations and procedures as a part of their individual asthma management plan. Additional inclusion criteria involve proven sensitization to at least one inhaled allergen.

Exclusion criteria include: known inborn or perinatal pulmonary disease, pulmonary malformation, oxygen therapy after birth with a duration of more than 24 h, ventilator support or mechanical ventilation after birth, diagnosis of cystic fibrosis, primary ciliary dyskinesia, heart failure diagnosed after birth affecting pulmonary circulation, major respiratory diseases such as interstitial lung disease, acute respiratory infection at recruitment, use of systemic corticosteroids, recent asthma-related visit to the emergency department (in the past three weeks) and coexistence of other serious chronic illness. Moreover, children will be excluded from study visits and biomaterial collection in the case of a fever of at least 38.5 °C during the last two weeks prior to the planned visit.

Additionally, a subset of control participants (non-asthmatic), age and gender matched to the case subjects, will be recruited by SCH and its other outpatient clinics and through the project campaigns vial local media, social networks, public lectures, promotional materials etc.

The sample size was assessed at 200 (when accounting for 5-10% drop-out rate), to reach an adequate level of significance in the results of the toxicological studies by a power analysis.

This study will also involve clinical follow-up visits (approximately every 3-6 months, according to Global Initiative for Asthma- GINA guidelines). As a part of this research, certain biological samples (including peripheral blood samples - at baseline and at the end of the study; buccal cell swabs, induced sputum and exhaled breath condensate - at baseline) will be collected both at baseline and follow-up visits, aiming at using biological samples left over from routine diagnostics whenever possible, using minimally invasive methods at all times and minimizing discomfort for the participants and their legal guardians as much as possible.

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For the **Severe childhood asthma cohort (RegionH)**, the primary objectives are a standardized cross-sectional examination of the children, collection of bio-samples from multiple compartments, and perform assessments and bio-sampling during acute exacerbations. The aim within this project is to identify the underlying disease mechanisms driving severe uncontrolled asthma. This will be done by combining data from detailed clinical phenotyping with multi-omics data including genomics, metabolomics, the microbiome, and immunological profiles of the children. The secondary objective included in the EDIAQI project is re-use of the same data alongside indoor air pollution data in children's home to analyse the association to asthma and wheezing.

The Severe childhood asthma cohort consists of up to 300 children aged 6-16 years with severe asthma requiring recurrent hospitalization and 150 healthy controls additionally will be recruited. The study will involve school aged participants with asthma (6- 16 yrs) as well as matching control subjects with a signed informed consent, i.e. those who have agreed to participate

in a clinical study and meet the criteria for inclusion. Criteria for inclusion will be assessed by an experienced paediatric allergy/pulmonology specialist physician. The children will be enrolled in the study after their legal guardians have read, agreed to, and signed the informed consent form. The subjects will be assessed for inclusion and exclusion criteria on the first study visit (at the respective clinic) after signing the informed consent. Additional inclusion criteria include: a verified asthma diagnose and treatment with either high dose inhaled corticosteroids or systemic treatment with oral corticosteroids OR a previously established severe asthma diagnose requiring treatment.

For healthy controls inclusion criteria include: willingness to participate and age matching the affected participants.

Exclusion criteria include: known inborn or perinatal pulmonary disease; pulmonary malformation; oxygen therapy after birth with a duration of more than 24 h; ventilator support or mechanical ventilation after birth; diagnosis of cystic fibrosis; primary ciliary dyskinesia; heart failure diagnosed after birth affecting pulmonary circulation; major respiratory diseases such as e.g. interstitial lung disease, acute respiratory infection at recruitment, use of systemic corticosteroids, recent asthma-related visit to emergency

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department (in the past three weeks) and coexistence of other serious chronic illness. Moreover, children will be excluded from study visits and biomaterial collection in the case of fever of at least 38.5 °C during the last two weeks prior to the planned visit.

The sample size was assessed at up to 300 children with asthma requiring recurrent hospitalization. This number is required to reach an adequate level of significance in the results of the toxicological studies and was calculated by Sample Size Calculator, which presented as a public service of the Creative Research Systems survey software.

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3. *In vitro* studies

The *in vitro* studies proposed within WP5 of the EDIAQI research for the evaluation of cytotoxic and genotoxic effects of IAP and their mixtures will involve commercially available, immortalized cell lines already routinely in use at NIB and IMROH. More specifically, HepG2 cell line (ID ATCC® HB-8065™) and A549 cell line (ID CCL-185™) both obtained from American Type Culture Collection and/or peripheral blood cells from donors for which IMROH has ethical permission. These studies will include informed consent signed by blood donors and will be done in accordance with Declaration of Helsinki.

As these cell lines are commercially available, this part of the project does not raise any ethical issues. These cell lines are not genetically modified and are classified as Biosafety Level I. They will be accordingly used in cell culture facilities authorized to use Class-1 biological materials, including standardized disposal procedures required for risk-I level laboratories.

Both partners (NIB and IMROH) involved in *in vitro* studies have a long-standing expertise in working with cell culture, and have all the necessary equipment, personnel, know-how and certificates for these types of studies. NIB holds the quality management standard ISO 9001:2000. The Department for Genetic Toxicology and Cancer Biology (GEN) at NIB has a certificate for mutagenicity testing in accordance with the OECD Principles of Good Laboratory Practice.

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4. *In vivo* studies

In vivo studies will be carried out within the scope of the Zagreb pilot and WP5 at IMROH. All in vivo experiments will be approved by the relevant Ethics Committees at national level prior to the start (the Ethics Committee at IMROH and The Croatian Ministry of Agriculture – Veterinary and Food Safety Directorate), ensuring they will be done in accordance with the 3R guidelines of replacement, reduction and refinement.

The experiments with mammalian species will include Wistar Han strain rats (lat. *Rattus norvegicus*; HsdBrlHan), an ideal general multipurpose model for studying compound safety, which will be purchased from the breeding colony at IMROH. Animals will be bred and maintained according to the Directive 2010/63/EU. The research team and facilities at IMROH have a long-standing experience in working with animal models and they have all relevant permits and certificates required for in vivo studies.

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5. Guidelines for informed consent procedures

The EDIAQI consortium recognizes that children represent a vulnerable population in research and clinical studies. However, since they are a vulnerable population, the health risks of IAP are likely to be far more pronounced in children than in adults. Moreover, since EDIAQI believes that exposure to IAP may act in a cumulative manner over a longer period, the involvement of paediatric participants is necessary.

Adequate measures will be undertaken to minimize the risks and discomfort for children and their legal guardians. Their legal guardians and the children themselves (if older than 12 years of age) will receive a full verbal and written explanation about the intent, significance, implications, and risks of the EDIAQI project. Their agreement to participate in the study is mandatory. Children >12 years have the right to abandon the study even if their legal guardians had previously agreed to join the study. They will also be informed that their participation is voluntary, anonymous, and that they have rights to revoke their consent at any point without any additional explanations.

General procedures that will be included in the research protocol to safeguard the privacy of participants:

- Written and verbal informed consents will include how participants' data is treated and stored, the research purpose, a data protection officer (DPO) at each institution, and their rights and requirements during the study.
- Pseudo-anonymization will be implemented for all material obtained in the framework of the project. The master key file linking the centre's study numbers with personal identifiers will be maintained in a password protected file with limited access.
- All files containing personal data will be stored in password-locked files. Access to these files will be limited to authorized project personnel.
- Only researchers linked to specific project tasks (clinical study and IAQ measurements in households) will have access to personal data.
- Personal data will not be transferred, except in the cases considered by law.

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- Reported study results will pertain to analyses of aggregate data. No individual's name will be associated with any published or unpublished report of this study.
- All project personnel will be trained in the importance of confidentiality of individual records and required to sign a confidentiality agreement.
- Incidental findings policies- all incidental data, especially that related to the participants` health and wellbeing will be discussed with the participants themselves (according to age) and their legal guardians, and the decision of recording or not of incidental findings will be made according to the participants' and their parents'/caregivers' wishes.

The informed consent document contains the following information:

- **Overview of the informed consent form**: This section informs the participant what the research is about, who will conduct it, where it will take place, and what the consent form entails. It also expresses that participation in the research is voluntary and can be terminated by the participant at any time.
- **Description and objectives of the research**: the objectives are to determine: i) whether there is an association between indoor air pollution and clinical analyses (inflammation, expression profiles) and damage to the subject's genome; ii) whether there is an association between indoor air pollution space and outdoor air pollution; iii) whether there is an association between indoor air pollution and chemical analysis and microbiological characterization of household dust. The informed consent form further states that the samples may also be used for additional methods (not mentioned above) and are in accordance with the research objectives of the EDIAQI project. The expected results could contribute significantly to understanding of how air quality affects the risk of disease occurrence and manifestations in children.
- **Role of the child as participant and parent/guardian in the research**: the participants are children. Participation in the study requires collection of blood, exhalation, sputum, and buccal mucosa swabs. Whole blood will be collected by venepuncture by highly trained personnel to minimise risks and discomfort (risks and discomfort are described in the informed consent form), and the remaining methods

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of sample collection will be minimally invasive. Participants and their legal guardians will be asked to complete questionnaires that provide information on basic anthropometric and medical information about the participants, as well as data on socioeconomic status and exposure relevant to this research. Completion of the questionnaires and sampling will occur twice (at the beginning and end of the study, after 24 months). After the analysis is conducted, there is a possibility that IMROH staff, in consultation with the participants, will install measuring devices in their households (mainly pumps and sensors) to monitor air quality and dust levels. These devices are used to measure the content of particles, gases, dust compounds, microplastics and radon. They are silent, energy friendly, and have no harmful effects on the participants and their families. The estimated duration of the sampling is 3 to 7 days and 3 months for radon. All personal data and analysis of results will be protected and coded and only project collaborators will have access to them. The measurements will be performed by employees of the Unit for environmental hygiene at IMROH.

- **The advantages and benefits of participation for the child and legal guardians**: the participants will receive information about the clinical and other procedures and analyses within the scope of the EDIAQI research for their child and, if that part of the research will be carried out at their homes, detailed information about the air quality of the participant's households. This research will generate new knowledge that may contribute to the understanding of the risk of air pollution to the paediatric population and the development of diseases such as asthma.
- **The possible risks of participating in the research**: the study team does not anticipate that the participants will be exposed to increased health or safety risks within the scope of this research. Blood will be drawn in from the cubital vein under sterile conditions and in volumes required for standard tests (a maximum of 12,5 mL at a single timepoint, twice during the study). Other procedures are non-invasive and cause minimal discomfort to participants and their legal guardians.
- **Obligation to participate in the research**: participants decide completely freely and independently whether or not to participate in this research. Participants have the

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right to withdraw from the research voluntarily and at any time, without giving any reason, without any consequences for them or their family. If a participant decides to stop participating in the research, they will be asked to inform the study principal investigator.

- **Confidentiality and right of inspection of documentation**: all personal data will be stored and processed in electronic form, and the research manager and their associates are obliged to fully comply with the prescribed procedures for the protection of personal data. The participant will be entered into the study databases using a special code. The coded medical documentation will be reviewed only by the work package leader and his/her colleagues. Names or other personal information will never be disclosed to third parties.
- **What will the data in the scientific research be used for**: the data obtained in this scientific research may be useful in clinical practice and for the purpose of further scientific knowledge. Therefore, it is expected that these data will be published in appropriate scientific journals and other publications. Thereby, the identity of the participant will remain completely anonymous and protected.
- **Who organises and funds this research?** this research is carried out as part of the European project EDIAQI - Evidence Driven Indoor Air Quality Improvement Horizon Europe (8 million EUR), and was organized as part of the work packages WP3 Identification and characterization of indoor air pollution) and WP5 (Population, health effects and toxicology).
- **Who approved this research?** this research has been approved by the Ethics Committee of the Institute for Medical Research and Occupational Medicine and the Srebrnjak Children's Hospital after thorough review of the submitted research proposal and supporting documentation. The research will be conducted in accordance with all applicable guidelines, whose goal is to ensure the proper conduct of the research and the safety of the subjects participating in it, including the "Fundamentals of Good Clinical Practice" and the "Declaration of Helsinki".
- **Contact information**: if the participants need any additional information or have enquiries, they can contact: Ph.D. Goran Gajski, B.Sc. in Biol, Mutagenesis Unit,

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Institute for Medical Research and Occupational Medicine, Ksaverska cesta 2, 10000 Zagreb, Phone number: +38514682500, Email: ggajski@imi.hr
Lead of SCH2021: prof. Mirjana Turkalj, PhD, MD, Department for Allergy and Pulmonology, Srebrnjak Children`s Hospital, Srebrnjak 100, 10000 Zagreb, Phone number: +38516391178.

- **Information about written consent**: In the context of the Croatian pilot, a copy of the signed document can be issued upon your request. The original of the document will be kept and stored by the study principal investigators.

To ensure understanding, the documentation will be made available to participants in Croatian and in easy-to-understand language. Participants and their legal guardians will be able to ask any questions about their involvement in the study, either in person or in writing, and it will be made clear that their participation in the study is completely on a voluntary basis and that they may withdraw their consent to participate at any time, without affecting their legal rights and medical care. The full informed consent documents and information sheets (in Croatian and English translations) can be found in Annexes 1-10. According to national (Croatian) legislation participants will be required to sign a separate informed consent form for children aged 12 years and older and an additional informed consent form for genetic analyses for their legal guardians, after being informed in writing and in person to their satisfaction. This means that participants and their legal guardians will have the right not to consent to the part of the research involving genetic analysis. Moreover, participants aged 12 years and older have the option to withhold consent to participate in the study even if their legal guardians agree to it, but they will not be able to participate in the study if they wish to do so, but their legal guardians do not wish so and do not sign the informed consent form.

As for the other pilots (Estonian pilot, Ferrara pilot and filtration pilot) and campaigns (Evaluation of low cost sensors, Measurement Campaign Sevilla, Measurement Campaign Vilnius), no informed consent procedures will be involved as these do not involve human participants in any way, thus won`t require the application of ethical principles that guarantee the rights of research subjects, the protection of their rights and welfare, health risks, discrimination, justice and other. The pilots and campaigns will take

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place in public (municipal) or private buildings and facilities (project partners` facilities) and adequate permits will be obtained by local authorities. Any data collected during the pilots and campaigns will be stored securely and no personal information will be collected or visible.

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6. Appointment of an independent ethical and legal expert within an External Advisory Board

As a part of the Scientific and Technical Committee (STC) the EDIAQI project has appointed a Chief Officer Ethics and Health (COEH) whose role is to ensure that the project progress and activities are in accordance with the objectives outlined in the work plan and executed according to all relevant national and international legislation, and ethical rules and guidelines. COEH for EDIAQI is Goran Gajski, PhD, BSc in Biol. Goran Gajski is a Senior Scientific Associate at IMROH in the field of genetic and environmental toxicology with special emphasis in human biomonitoring and has more than 15 years of experience in the field. He is a full member of the Croatian Toxicological Society and the Croatian Genetic Society as well as EUROTOX and EEMGS, and a Chair of the International Comet Assay Working Group (ICAWG). To date, he has published more than 100 research papers and book chapters mainly covering genetic and environmental toxicology issues, with more than 3000 citations and an h-index of 30 (Google scholar). He has been involved in several national and international projects and collaborations as principal investigator, work package leader or team member.

Additionally, a project specific External Advisory Board (EAB) is appointed, with members being experts in the fields of research as well as (bio)ethic issues. EAB meetings will be organised annually (at EDIAQI progress meetings).

Within the EAB, an independent ethics and legal expert is appointed to monitor the respect and adherence to main ethical principles by the EDIAQI consortium. This independent expert is prof. Adnan Čustović, MD, PhD, FRCP. Prof. Čustović leads the Paediatric Allergy Group within the Centre for Paediatrics and Child Health at Imperial College London and is Honorary Consultant in Paediatric Allergy at St. Mary's Hospital and Royal Brompton Hospital. He is the Director of the Imperial College London/Imperial College Healthcare Trust Allergy Centre, one of the World Allergy Organization (WAO) Centres of Excellence. His research focuses on the origins and natural history of asthma and allergy throughout life, with an emphasis on prevention and translation for patient benefit. His research findings are of great practical significance and have influenced and changed national and international

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guidelines on asthma prevention and management. His studies on food allergy have substantially impacted clinical practice. His discovery that the IgE-response to the peanut allergen Arah2 is much more predictive of true peanut allergy than standard tests using whole allergen extract marked the start of the component-resolved diagnostics as the new gold standard in clinical practice.

Prof Čustović pioneered the use of data-driven methodologies in the analysis of complex data, including the first use of machine learning in respiratory medicine/allergy. To gain more from birth cohorts across the UK, he led a multidisciplinary MRC-funded STELAR consortium, combining the world-leading expertise in birth cohorts with statistical machine learning and health informatics. This effort enabled the discovery of latent subtypes of childhood asthma, allergies, and developmental patterns of lung function from pre-school age to early adulthood. He currently leads MRC UNICORN programme, which integrates birth cohorts with patient cohorts and randomised controlled trials for joint analyses, offering opportunity for a step change in understanding mechanisms underlying different asthma endotypes.

In 2020, prof Čustović was elected to the Fellowship of the UK Academy of Medical Sciences. In 2019, he was awarded membership in the Academy of Sciences and Arts of Bosnia and Herzegovina (ANUBiH). In 2015, he received the highly prestigious European Respiratory Society Gold Medal in Asthma, which is awarded to a researcher who has made an outstanding contribution to the field of asthma research. In 2013, he received the BSACI William Frankland Medal for outstanding contributions to clinical allergy research in the UK. He is an Associate Editor of the American Journal of Respiratory and Critical Care Medicine and a member of the International Advisory Board of the Lancet Child and Adolescent Health. He has served as a Secretary of the British Society of Allergy and Clinical Immunology for two terms, and as President of Asthma section of the European Academy of Allergy and Clinical Immunology. He is a member of the UKRI Future Leaders Fellowships PRC and the MRC PSMB.

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7. Annexes

Annex 1 Information sheet - IMROH

INSTITUT ZA MEDICINSKA ISTRAŽIVANJA I MEDICINU RADA ZAGREB
Informirani pristanak za sudjelovanje u znanstvenom istraživanju
„EDIAQI - Evidence Driven Indoor Air Quality Improvement"

Poštovani,
pozivamo Vas da sudjelujete u znanstvenom istraživanju čiji je glavni cilj utvrditi povezanost onečišćenja zraka i biomarkera izloženosti i učinka u maloljetnoj populaciji Hrvatske. Voditelj projekta je dr. sc. Francesco Moreddu, dok je voditelj radnog paketa unutar kojeg se istraživanje odvija dr. sc. Goran Gajski. Istraživanje će se provesti u Dječjoj bolnici Srebrnjak pod nadzorom prof. dr. sc. Mirjane Turkalj, na Institutu za medicinska istraživanja i medicinu rada te potencijalno u Vašem domu. Molimo Vas, pažljivo pročitajte ovaj Informirani pristanak za sudjelovanje u istraživanju u kojem se objašnjava zašto se ispitivanje provodi i koji bi mogli biti mogući rizici i koristi za Vas i Vaše dijete kao ispitanika. U slučaju da ne razumijete bilo koji dio ovog Informiranog pristanka, molimo Vas da se za objašnjenje obratite ispitivaču u istraživanju. Sudjelovanje u istraživanju je dobrovoljno i može se u bilo kojem trenutku prekinuti. Ukoliko odlučite da želite sudjelovati u ovom istraživanju, od Vas će se tražiti da potpišete Informirani pristanak uz naznaku datuma. Informirani pristanak potpisuje i istraživač, a potpisanu presliku Informiranog pristanka možete dobiti prije početka istraživanja. Original Informiranog pristanka ostaje kod istraživača ovog ispitivanja.

OPIS I CILJEVI ISTRAŽIVANJA

Ciljevi ovog istraživanja su utvrditi: (i) postoji li povezanost između onečišćenja zraka u zatvorenom prostoru i kliničkih analiza (upala, ekspresijski profili) i oštećenja genoma ispitanika (ii) postoji li povezanost između onečišćenja zraka u zatvorenom prostoru s onečišćenjem zraka na otvorenom i (iii) postoji li povezanost između onečišćenja zraka u zatvorenom sa kemijskom analizom i mikrobiološkom karakterizacijom kućne prašine. Uzorci se mogu koristiti i za dodatne metode koje nisu ovdje navedene, a u skladu su s ciljevima istraživanja. Očekivani rezultati mogli bi značajno doprinijeti razumijevanju kako kvaliteta zraka utječe na razine rizika pojavnosti bolesti kod djece.

ULOGA DJETETA KAO ISPITANIKA i RODITELJA/SKRBNIKA U ISTRAŽIVANJU

U ovom istraživanju ispitanici su djeca. Suradnici s DB Srebrnjak, provest će uzimanje uzoraka krvi, izdaha, sputuma i stanica usne šupljine djece. Krv će biti vađena u za to predviđene spremnike iz vene ruke u adekvatnim uvjetima, a sve preostale metode minimalno su invazivne. Prije uzimanja uzoraka, ispitanici će zajedno s roditeljima ispuniti upitnike koji daju uvid u osnovne antropometrijske i medicinske informacije o ispitanicima te podatke o socio-ekonomskom statusu te izloženosti, a koje su relevantne za ovo istraživanje. Ispunjavanje upitnika te uzorkovanje uzoraka vršit će se dvaput (sada i za oko 2 god). Po odrađivanju analiza, postoji mogućnost da, u dogovoru s Vama, suradnici s IMI-ja u Vaš dom postave mjerne uređaje (uglavnom pumpice i senzore) za praćenje kvalitete zraka te usišu prašinu. Ti uređaji služe za mjerenje razine čestica, plinova, spojeva iz prašine, mikroplastike i radona. Oni nisu bučni, energetski su prihvatljivi i nemaju štetne učinke na stanare. Predviđeno vrijeme sakupljanja uzoraka je 3 do 7 dana te 3 mjeseca za radon jednokratno. Svi će osobni podaci te rezultati analiza biti zaštićeni i kodirani te će uvid u njih imati samo suradnici projekta. Mjerenja će odraditi djelatnici Jedinice za higijenu okoline dr.sc. Silvije Davila i Marija Jelena Lovrić (a u slučaju više sile, njihova zamjena iz iste jedinice).

KOJE SU ZA VAS i VAŠE DIJETE MOGUĆE PREDNOSTI I KORISTI OD SUDJELOVANJA?

Sudjelovanjem u ovom istraživanju dobit ćete informacije o kliničkim analizama Vašeg djeteta te, ukoliko će taj dio istraživanja biti proveden kod Vas, detaljne informacije o kvaliteti zraka Vašeg doma. Ujedno nama omogućujete nove analize koje će doprinijeti razumijevanju rizika onečišćenja zraka na maloljetnoj populaciji te na razvoj bolesti poput astme. Istraživanja će obuhvaćati veliki broj biomedicinskih i citogenetičkih biomarkera koji će se povezivati sa onečišćenjem zraka u Hrvatskoj, a koja do sada nisu provedena na ovakvom nivou.

KOJI SU ZA VAS MOGUĆI RIZICI SUDJELOVANJA U ISTRAŽIVANJU?

Ne očekujemo da ćete u ovom istraživanju biti izloženi povećanim rizicima za zdravlje ili sigurnost. Krv će biti vađena u za to predviđene spremnike iz vene ruke u sterilnim uvjetima i volumenima koji su potrebni u standardnim pretragama (maksimalno 12 mL). Ostale procedure nisu invazivne i ne utječu na Vašu životnu rutinu.

MORATE LI SUDJELOVATI U ISTRAŽIVANJU?

Vi ćete u potpunosti slobodno i samostalno odlučiti hoćete li u ovom istraživanju sudjelovati ili ne. Vaše sudjelovanje je dragovoljno i u bilo koje vrijeme, bez navođenja razloga, imate se pravo, bez ikakvih posljedica povući iz istraživanja. Ako odlučite prekinuti sudjelovanje u istraživanju, lijepo Vas molimo da o tome na vrijeme obavijestite voditelja istraživanja i njegove suradnike.

POVJERLJIVOST I PRAVO UVIDA U DOKUMENTACIJU

Svi osobni podaci bit će pohranjeni i obrađivani u elektroničkom obliku, a voditelj istraživanja i njegovi suradnici su dužni u potpunosti poštivati propisane postupke za zaštitu osobnih podataka. U naše baze podataka bit ćete uneseni s pomoću posebnog koda. Kodiranu medicinsku dokumentaciju pregledavat će samo voditelj radnog paketa i njegovi suradnici, a Vaša imena nikada neće biti otkrivena trećim osobama.

ZA ŠTO ĆE SE KORISTITI PODACI DOBIVENI U OVOM ZNANSTVENOM ISTRAŽIVANJU?

Podaci dobiveni u ovom znanstvenom istraživanju mogu biti korisni u kliničkoj praksi te u svrhu daljnjeg razvoja i unapređenja znanosti. Stoga se očekuje da se ti podaci objave u odgovarajućim znanstvenim časopisima i ostalim publikacijama. Pri tome će Vaš identitet ostati u potpunosti anoniman i zaštićen.

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

TKO ORGANIZIRA I FINANCIRA OVO ISTRAŽIVANJE?

Ovo istraživanje provodi se u sklopu europskog EDIAQI - *Evidence Driven Indoor Air Quality Improvement* Obzor Europa projekta vrijednog 8 mil. EUR, a organizirano je u sklopu radnog paketa (WP3) Identifikacija i karakterizacija unutarnjeg onečišćenja zraka i (WP5) Populacija, učinci na zdravlje i toksikologija.

TKO JE ODOBRIO OVO ISTRAŽIVANJE?

Ovo istraživanje odobrilo je Etičko povjerenstvo Instituta za medicinska istraživanja i medicinu rada i Dječje bolnice Srebrnjak nakon temeljite analize dostavljenog prijedloga istraživanja i prateće dokumentacije. Istraživanje se provodi u skladu sa svim primjenjivim smjernicama čiji je cilj osigurati pravilno provođenje istraživanja te sigurnost osoba koje u njemu sudjeluju, uključujući „Osnove dobre kliničke prakse" i „Helsinšku deklaraciju".

KOGA MOŽETE KONTAKTIRATI ZA DODATNE OBAVIJESTI I UPITE?

Ako su Vam potrebne bilo kakve dodatne informacije, ili imate dodatnih pitanja, slobodno se obratite na kontakt koji slijedi:

Ime i prezime istraživača: dr. sc. Goran Gajski, dipl. ing. biol.
Adresa: Jedinica za mutagenezu, Institut za medicinska istraživanja i medicinu rada, Ksaverska cesta 2, 10000 Zagreb
Broj telefona: 01/4682500
Email: ggajski@imi.hr
Ime i prezime istraživača: prof. dr. sc. Mirjana Turkalj, dr. med.
Adresa: Dječja bolnica Srebrnjak, 10000 Zagreb
Broj telefona: 01/6391100

O VAŠOJ PISANOJ SUGLASNOSTI ZA SUDJELOVANJE U OVOM ISTRAŽIVANJU

Preslika potpisanog dokumenta može biti izdana na Vaš zahtjev. Izvorni primjerak dokumenta će zadržati i čuvati voditelj istraživanja.

Hvala Vam što ste pročitali ovaj dokument i razmotrili mogućnost sudjelovanja u ovom znanstvenom istraživanju.

Ova obavijest je sastavljena u skladu s odredbama Zakona o zdravstvenoj zaštiti Republike Hrvatske (NN 121/03) i Zakona o pravima pacijenata Republike Hrvatske (NN 169/04).

Prema zakonu o zaštiti podataka Europske unije (Direktiva o zaštiti podataka, koja je 25. svibnja 2018. zamijenjena općom uredbom o zaštiti podataka), Vaš istraživač donosi važne odluke u korištenju Vaših osobnih podataka te će kao „kontrolor" biti zajednički odgovoran za poštivanje tog zakona. Putem istraživača imate pravo pristupiti svim podacima prikupljenim o Vama te ako su netočni, tražiti njihove ispravke tijekom provođenja istraživanja. Imate pravo na pritužbu na način kako se postupa s Vašim podacima, a možete je uputiti nadležnom odgovornom tijelu za provođenje Zakona o zaštiti osobnih podataka. Popis nadležnih tijela u Europskoj uniji dostupan je na ovoj poveznici: http://ec.europa.eu/justice/data-protection/article29/structure/data-protection-authorities/index_en.htm. Za Republiku Hrvatsku nadležno tijelo kojem možete uputiti pritužbu je Agencija za zaštitu osobnih podataka, Martićeva ulica 14, HR - 10 000 Zagreb.

Svojim potpisom potvrđujem da sam kao roditelj informiran/a o ciljevima, prednostima i rizicima ovog istraživanja i pristajem u njemu sudjelovati. Svojim potpisom pristajete da se uzorci Vaše djece i doma koriste i u daljnjim znanstvenim istraživanjima u skladu sa ciljevima ovog projekta.

SUGLASNOST

IME I PREZIME DJETETA:_____

IME I PREZIME RODITELJA: _____

ADRESA STANOVANJA: _____

KONTAKT (TELEFON/E-MAIL ADRESA): _____

_____

Potvrđujem da sam upoznat/a sa svrhom ispitivanja i obradom podataka, razumio/razumjela ga i da sam voljan/voljna ispuniti upitnik i dati uzorke za potrebe istraživanja. Također sam upoznat/a s činjenicom da imam pravo bez posebnog obrazloženja odustati od sudjelovanja u ovom istraživanju u bilo kojem trenutku i fazi istraživanja te da se u tom slučaju naši podaci ne smiju dalje obrađivati. Podaci se smiju koristiti samo u znanstvene svrhe (objavljivanje znanstvenih radova), bez objave privatnih podataka (imena, prezimena, adresa, a podaci za kontakt neće se objaviti i bit će zaštićeni u registru podataka bez pristupa neovlaštenih osoba).

DATUM: _____

_____ _____

IME I PREZIME RODITELJA/SKRBNIKA te POTPIS IME I PREZIME DJETETA te POTPIS (12 g i starije)

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 2 Information Sheet - IMROH (English translation)

Dear Sir/Madam,

we invite you to participate in a scientific study whose main goal is to determine the connection between air pollution and biomarkers of exposure and effect in the juvenile population of Croatia. The project leader is Ph.D. Francesco Mureddu, while the head of the work package within which the research takes place is Ph.D. Goran Gajski. The research will be conducted at the Srebrnjak Children's Hospital under the supervision of prof. Ph.D. Mirjane Turkalj, at the Institute for Medical Research and Occupational Medicine and potentially in your home. Please read this Informed Consent for Research Participation carefully, which explains why the study is being conducted and what the possible risks and benefits might be for you and your child as a subject. If you do not understand any part of this Informed Consent, please contact the research investigator for clarification. Participation in the research is voluntary and can be terminated at any time. If you decide that you want to participate in this research, you will be asked to sign and date the Informed Consent. The informed consent is also signed by the researcher, and you can get a signed copy of the informed consent before the start of the research. The original of the Informed Consent remains with the researcher of this trial.

DESCRIPTION AND OBJECTIVES OF THE RESEARCH

The goals of this research are to determine: (i) whether there is a connection between indoor air pollution and clinical analyzes (inflammation, expression profiles) and damage to the examinee's genome (ii) whether there is a connection between indoor air pollution and outdoor air pollution and (iii) whether there is a connection between indoor air pollution with chemical analysis and microbiological characterization of house dust. The samples can also be used for additional methods that are not listed here and are in accordance with the research objectives. The expected results could significantly contribute to the understanding of how air quality affects the risk levels of disease occurrence in children.

THE ROLE OF THE CHILD AS A PARTICIPANT AND PARENT/GUARDIAN IN THE RESEARCH

In this research, the respondents are children. Collaborators from DB Srebrnjak will take samples of children's blood, exhalation, sputum and oral cavity cells. Blood will be drawn into containers provided for this from a vein in the arm under adequate conditions, and all

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remaining methods are minimally invasive. Before taking the samples, the test subjects together with their parents will fill out questionnaires that provide insight into basic anthropometric and medical information about the test subjects, as well as data on socio-economic status and exposure, which are relevant for this research. Filling in the questionnaire and sampling samples will be done twice (now and in about 2 years). After carrying out the analysis, there is a possibility that, in agreement with you, colleagues from IMI will install measuring devices (mainly pumps and sensors) in your home to monitor the air quality and vacuum the dust. These devices are used to measure the level of particles, gases, compounds from dust, microplastics and radon. They are not noisy, are energy-friendly and have no harmful effects on the tenants. The estimated time of sample collection is 3 to 7 days and 3 months for radon once. All personal data and analysis results will be protected and coded, and only project collaborators will have access to them. Measurements will be made by employees of the Environmental Hygiene Unit, Ph.D. Silvije Davila and Marija Jelena Lovrić (and in case of force majeure, their replacement from the same unit).

WHAT ARE THE POSSIBLE ADVANTAGES AND BENEFITS OF PARTICIPATION FOR YOU AND YOUR CHILD?

By participating in this research, you will receive information about the clinical analyzes of your child and, if that part of the research will be conducted at your place, detailed information about the air quality in your home. At the same time, you provide us with new analyzes that will contribute to understanding the risk of air pollution on the minor population and the development of diseases such as asthma. The research will include many biomedical and cytogenetic biomarkers that will be associated with air pollution in Croatia, which have not been conducted at this level so far.

WHAT ARE THE POSSIBLE RISKS OF PARTICIPATING IN RESEARCH FOR YOU?

We do not expect that you will be exposed to increased health or safety risks in this research. Blood will be drawn into containers provided for this from a vein in the arm under sterile conditions and in volumes required for standard tests (maximum 12 mL). Other procedures are not invasive and do not affect your daily routine.

DO YOU HAVE TO PARTICIPATE IN RESEARCH?

This project has received funding from the European Union's
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You will decide completely freely and independently whether you want to participate in this research or not. Your participation is voluntary, and you have the right to withdraw from the research at any time, without giving any reason, without any consequences. If you decide to discontinue your participation in the research, we kindly ask you to inform the research manager and his associates about this in time.

CONFIDENTIALITY AND RIGHT OF INSPECTION OF DOCUMENTATION

All personal data will be stored and processed in electronic form, and the research manager and his colleagues are obliged to fully comply with the prescribed procedures for the protection of personal data. You will be entered into our databases using a special code. Coded medical documentation will only be reviewed by the work package manager and his colleagues, and your names will never be revealed to third parties.

WHAT WILL THE DATA OBTAINED IN THIS SCIENTIFIC RESEARCH BE USED FOR?

The data obtained in this scientific research can be useful in clinical practice and for the purpose of further development and improvement of science. Therefore, it is expected that these data will be published in appropriate scientific journals and other publications. Your identity will remain completely anonymous and protected.

WHO ORGANIZES AND FINANCES THIS RESEARCH?

This research is carried out as part of the European EDIAQI - Evidence Driven Indoor Air Quality Improvement Horizon Europe project worth EUR 8 million and is organized as part of the work package (WP3) Identification and characterization of indoor air pollution and (WP5) Population, health effects and toxicology.

WHO APPROVED THIS RESEARCH?

This research was approved by the Ethics Committee of the Institute for Medical Research and Occupational Medicine and the Srebrnjak Children's Hospital after a thorough analysis of the submitted research proposal and accompanying documentation. The research is conducted in accordance with all applicable guidelines aimed at ensuring the proper conduct of the research and the safety of the persons participating in it, including the "Basics of Good Clinical Practice" and the "Declaration of Helsinki".

WHO CAN YOU CONTACT FOR ADDITIONAL INFORMATION AND INQUIRIES?

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

If you need any additional information, or have additional questions, feel free to contact the following contact:

Name and surname of the researcher: Ph.D. Goran Gajski, B.Sc. ing biol.

Address: Mutagenesis Unit, Institute for Medical Research and Occupational Medicine, Ksaverska cesta 2, 10000 Zagreb

Phone number: 01/4682500

Email: ggajski@imi.hr

Name and surname of the researcher: prof. Ph.D. Mirjana Turkalj, MD.

Address: Children's Hospital Srebrnjak, 10000 Zagreb

Phone number: 01/6391100

ABOUT YOUR WRITTEN CONSENT TO PARTICIPATE IN THIS RESEARCH

A copy of the signed document can be issued upon your request. The original copy of the document will be kept and kept by the research manager.

Thank you for reading this document and considering the possibility of participating in this scientific research.

This notice has been compiled in accordance with the provisions of the Act on Health Care of the Republic of Croatia (Official Gazette 121/03) and the Act on Patients' Rights of the Republic of Croatia (Official Gazette 169/04).

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 3 Information sheet for participants - SCH

DJEČJA BOLNICA SREBRNJAK

ETIČKO POVJERENSTVO

Prilog 1: Obavijest za ispitanika

Poštovani/poštovana,

Pozivamo Vas da Vi/Vaše dijete u svojstvu ispitanika sudjelujete u znanstvenom istraživanju pod nazivom **EDIAQI „Evidence Driven Indoor Air Quality Improvement“**, čiji je cilj istražiti i karakterizirati razinu izloženosti onečišćenju zraka u unutrašnjim prostorima te njen utjecaj na ljudsko zdravlje kroz razvoj i kliničke osobitosti astme, kao i specifičnih podtipova bolesti identificirajući nove patofiziološke mehanizme uključene u razvoj i progresiju bolesti. Istraživanje se provodi u sklopu projekta financiranog sredstvima Europske unije za istraživanje i inovacije u sklopu okvirnog programa Obzor 2020 (Horizon 2020), Grant agreement ID: 101057497. Voditelj projekta je izv.prof.dr.sc. Mirjana Turkalj, dr.med., a predviđeno trajanje projekta je od 12. mjeseca 2022. godine do 12. mjeseca 2026. godine. Projekt se provodi u Dječjoj bolnici Srebrnjak, Zagreb.
Vaše sudjelovanje u istraživanju treba se temeljiti na jasnom razumijevanju ciljeva istraživanja i načina i postupaka za njegovo provođenje te mogućih koristi ili rizika za Vas/Vaše dijete kao ispitanika. Stoga Vas molimo da, prije donošenja odluke, pažljivo pročitate i proučite ovu obavijest, a ako u njoj naiđete na bilo kakve nejasnoće ili nepoznate riječi i izraze da o tome pitate istraživače i liječnike koji u istraživanju sudjeluju i dužni su Vam i spremni odgovoriti na svako pitanje.

OPIS KLJUČNOG PROBLEMA I HIPOTEZE ISTRAŽIVANJA
Brojna su istraživanja potvrdila da loša kvaliteta zraka (onečišćenja zraka) ima značajnu ulogu u razvoju određenih bolesti, uključujući astmu, osobito u osjetljivim populacijama (djeca). Astma je najčešća kronična bolest u djece, a brojne epidemiološke studije pokazuju stalan porast pojavnosti astme, uz gotovo izvjestan nastavak sličnog trenda u budućnosti. Zbog kompleksnog i heterogenog svojstva bolesti, lijek za astmu još uvijek ne postoji, pa je terapija prije svega simptomatska. Lijekovi služe za olakšavanje trenutnih simptoma i kontrolu upalnih procesa u podlozi bolesti te sprječavanje akutnih pogoršanja. Sam učinak terapije je izrazito varijabilan te uvelike ovisi o individualnim svojstvima pacijenata. Unatoč brojnim istraživanjima pojedinih podtipova astme, znanje o uzročniku i etiološkim čimbenicima još uvijek je nedostatno te je stoga onemogućeno donošenje odluke o vrsti terapije na personaliziranoj bazi i adekvatno praćenje kontrole bolesti. Astma predstavlja značajan javnozdravstveni problem jer se, uz direktne troškove liječenja, značajan dio sredstava gubi i kroz smanjenu kvalitetu života pacijenata i njihove obitelji (izostanci s posla, iz škole, smanjena produktivnost itd.).
Prema podacima Europske agencije za zaštitu okoliša (eng. *European Environmental Agency*, EEA) dugotrajna izloženost onečišćenju zraka uzrok je smrti u više od 400 000 slučajeva godišnje u velikim europskim gradovima. Riziku za razvojem zdravstvenih problema uzrokovanih okolišnim čimbenicima osobito su podložne osjetljive populacije, poput djece. Moderan način života, osobito uslijed velikih promjena u istome zbog nedavne COVID-19 pandemije, podrazumijeva da gotovo 90% vremena provodimo u zatvorenim prostorima. Istraživanja su pokazala kako je kvaliteta zraka u unutrašnjim prostorima čak lošija od kvalitete vanjskog zraka, a

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dodatno, smjernice i zakonodavstvo za razine izloženosti onečišćenju zraka u unutrašnjim prostorima značajno su slabije regulirani od onih za kvalitetu vanjskog zraka. Štoviše, za određene onečišćivače, zakonska regulativa gotovo da ni ne postoji. S obzirom na navedeno, izvjesno je da onečišćenje zraka u unutrašnjim prostorima ima jednak, ako ne i veći utjecaj na razvoj određenih bolesti (uključujući astmu) kao vanjsko onečišćenje zraka.

Ovim istraživanjem planira se ostvariti bolji uvid u učinak loše kvalitete zraka u unutrašnjim prostorima na ljudsko zdravlje i razvoj određenih bolesti, ali i u heterogenost svih bolesti koje se kategoriziraju pod zajednički termin astme te patofiziološke mehanizme pojedinih podtipova bolesti. Nadalje, provedbom istraživačkih aktivnosti u sklopu ovog projekta nastojat će se omogućiti bolje praćenje napretka, stupnja kontrole i težine astme te samog terapeutskog učinka u svrhu poboljšanog i personaliziranog pristupa liječenju koje ne karakterizira usmjerenost na simptome, već izravno na uzroke bolesti. Nadalje, implementacijom rezultata ovog istraživanja omogućit će se pravovremena i precizna dijagnostika bolesti i njezinih specifičnih podtipova te potencijalno prepoznavanje predispozicija za razvoj istih. Razvojem personaliziranog programa liječenja potencijalno se mogu unaprijediti dijagnostičke i terapeutske procedure u procesu liječenja astme i pojedinih podtipova bolesti.

CILJ I SVRHA ISTRAŽIVANJA

Primjenjujući koncept translacijske medicine i kombinirajući golemu ekspertizu u pedijatrijskoj alergologiji kao Referentni centar za kliničku alergologiju u djece s iskustvom drugih partnera u projektu EDIAQI, Dječja bolnica Srebrnjak i partnerske institucije istraživat će razmjere utjecaja onečišćenja zraka u unutrašnjim prostorima. Ovakvim translacijskim multidisciplinarnim pristupom koji podrazumijeva blisku suradnju kliničkih i temeljnih istraživača omogućit će se individualni pristup svakom pacijentu i medicinskom problemu, a potencijalno će se omogućiti i optimizacija i personalizacija terapijskih režima na izravnu dobrobit ciljnih skupina.

Cilj ovog istraživanja je steći bolji uvid u učinke onečišćenja zraka u unutrašnjim prostorima na razvoj astme, težinu bolesti, ishode liječenja i određene podtipove bolesti, detaljnim profiliranjem pacijenata s astmom. Kombinirajući kliničke podatke s rezutatima različitih analiza (transkriptoma, metaboloma, mikrobioma itd.) planira se istražiti heterogenost i patogenezu specifičnih podtipova astme te identificirati nove patofiziološke mehanizme uključene u razvoj i progresiju bolesti. Također, bazom podataka prikupljenom kroz ovo istraživanje stvara se dodana vrijednost u smislu istraživanja i razvoja novih metoda liječenja astme te prevencije istih.

ULOGA VAS KAO ISPITANIKA U ISTRAŽIVANJU

Kako bi se pružio bolji uvid u kompleksnu prirodu astme i povezanost onečišćenja zraka u unutrašnjim prostorima s razvojem astme, osobito određenih podtipova/fenotipova bolesti, osoblje Dječje bolnice Srebrnjak će Vas/Vaše dijete, prilikom rutinske kliničke posjete u Bolnici, zamoliti za sudjelovanje u ovom istraživanju. Ovo će istraživanje poštivati sve nacionalne, europske i međunarodne zakone i etička pravila u istraživanju. Istraživanje će uključivati djecu školske dobi 6 do 14 godina, koji su pacijenti Dječje bolnice Srebrnjak. Ukoliko (nakon detaljnog informiranja o studiji) pristanete sudjelovati u istraživanju, u sklopu rutinske posjete

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Bolnici i rutinske dijagnostičke obrade, prikupit će se relevantni klinički podaci, podaci o Vašem kućanstvu radi procjene izloženosti onečišćenju zraka u unutrašnjem prostoru, demografski i drugi podaci. U sklopu ove kliničke posjete i rutinske dijagnostičke obrade, Vaše dijete će se podvrgnuti uobičajenim dijagnostičkim testovima i procedurama kako bi se ustanovila dijagnoza astme, uključujući: uzimanje osobne i obiteljske anamneze, plućne funkcijske testove, kožne ubodne testove, rutinske laboratorijske testove, što podrazumijeva i vađenje krvi. Uzorci krvi uzet će se postupkom venepunkcije iz podlaktice, a vađenje krvi obavljat će kvalificirano osoblje Dječje bolnice Srebrnjak u skladu sa svim primjenjivim smjernicama etičkog kodeksa struke. Za potrebe ovog istraživanja od uzoraka periferne krvi za rutinsku laboratorijsku dijagnostiku, odvojit će se manji dio (maksimalno 2 ml) za naknadne analize. Također, moguće je da će prilikom vađenja krvi biti prikupljeni dodatni uzorci periferne krvi za transkriptomske analize u tzv. Paxgene epruvete (ukupno 2,5 ml) i za naknadna toksikološka istraživanja (ukupno 8 ml). Budući da će se u istraživanju koristiti anamneze i rezultati pretraga već obavljenih pri Vašem pregledu (pregledu Vašeg djeteta), a uzimanje dodatnih maksimalno 12,5 mL periferne krvi iz podlaktice obavit će se u sklopu uzimanja krvi pri standardnoj obradi ispitanika, sudjelovanje u istraživanju ne pruža dodatni rizik za Vas/Vaše dijete. Vađenje krvi metodom venepunkcije i drugi dijagnostički testovi koje podrazumijeva ovo istraživanje, ukoliko ga provodi educirano i stručno osoblje kao ono u DBS (Referentnom centru za kliničku alergologiju djece), ne predstavlja dodatni rizik za ispitanika. Također, zamolit će Vas se da se djetetu uzme uzorak brisa sluznice usne šupljine (nježnim prelaskom posebnom četkicom po unutrašnjoj strani djetetovog obraza) te uzorci kondenzata izdaha (koji podrazumijeva pasivno disanje djeteta kroz određeni period, cca 15 minuta) i induciranog sputuma (iskašljaja). Navedene su procedure potrebne za analizu mogućih tragova onečišćivača zraka uobičajeno prisutnih u unutrašnjim prostorima i njihovog potencijalnog toksikološkog učinka te su minimalno invazivne i ne predstavljaju dodatni rizik niti značajnu neugodnost za Vas/Vaše dijete. Dodatno, u sklopu ovog istraživanja bit ćete zamoljeni da se u Vašem kućanstvu na određeni period (nekoliko dana) postave mjerni uređaji koji će mjeriti razinu izloženosti onečišćenju zraka u unutrašnjem prostoru (plinovi, lebdeće čestice, volatilni spojevi, radon, kućna prašina prikupljena usisavačima s posebnim nastavcima s kreveta itd.). Ovakvo mjerenje ne predstavlja nikakav dodatni rizik niti za Vas niti za Vaše dijete, jedino će biti potrebno da se osigura jedan manji dio prostora u kojem se borabi za uređaje te mogućnost da isti stvaraju vrlo niske razine buke dok rade.
U prvom dijelu istraživanja, u vremenskoj točki 0 (točki uključivanja u studiju), u svrhu postavljanja dijagnoze astme, provest će se rutinska (ili po potrebi proširena) alergološka obrada koja uključuje kožne ubodne testove, određivanje ukupnog i alergen-specifičnih imunoglobulina E u serumu, plućne-funkcijske i bronhoprovokacijske testove itd. te će se prikupiti relevantni klinički i drugi podaci. Također, Vašem djetetu će se uzeti spomenuti uzorak pune krvi (periferne krvi) za naknadne genske (transkriptomske) i toksikološke analize, kao i uzorci brisa sluznice usne šupljine, kondenzata izdaha i induciranog sputuma (iskašljaja).

U drugom dijelu istraživanja provodit će se kontrolne posjete u sklopu rutinskog praćenja i liječenja astme Vašeg djeteta, u prosjeku svakih 3-6 mjeseci. Tijekom tog razdoblja, na redovitim kliničkim kontrolnim posjetama, provodit će se antropometrijska mjerenja, fizikalni pregledi, procjena kontrole bolesti, komorbiditeta, plućno-funkcijska mjerenja te ostali dijagnostički postupci, ukoliko isto bude potrebno tijekom liječenja Vašeg djeteta dok traje ovo istraživanje. Dodatno, tijekom ovog

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perioda obavit će se i mjerenja kvalitete zraka u Vašem kućanstvu prema gore navedenom protokolu. Tijekom ovog istraživanja moguće je da ćete biti zamoljeni i da se u kraćem periodu u Vašem kućanstvu postavi pročišćavač zraka kako bi se ustanovilo imaju li takvi pročišćavači utjecaj na kvalitetu zraka u unutrašnjim prostorima i posljedično, na astmu i kliničke osobitosti bolesti kod Vašeg djeteta, kao i kontrolu astme i terapijske ishode.

U trećem dijelu istraživanja, analizirat će se rezultati dijagnostičke obrade, antropometrijskih i drugih mjerenja te usporediti s kliničkim i molekularno-genetičkim, toksikološkim i drugim podacima prikupljenima tijekom provedbe istraživanja, te će se svi rezultati integrirati na inovativnoj (bio)informatičkoj platformi. U konzultaciji s ekspertima liječničke, molekularno-genetičke, bioinformatičke i specijalnosti okolišnih znanosti definirat će se klinički značaj dobivenih rezultata i njihova važnost za pojedine skupine pacijenata što može dovesti do optimizacije liječenja astme i izrade preciznijih i personaliziranih režima liječenja. Po završetku projekta relevantni rezultati istraživanja služit će za edukaciju i podizanje svijesti o izloženosti onečišćenju zraka u unutrašnjim prostorima, kao i izradu nacionalnih i europskih smjernica i zakonskih regulativa o dozvoljenim razinama onečišćenja zraka u zatvorenim prostorima.

KOJE SU ZA VAS MOGUĆE PREDNOSTI I KORISTI OD SUDJELOVANJA?

Astma je jedna od najčešćih kroničnih bolesti današnjice općenito i najčešći kronični poremećaj u djece, a studije pokazuju kako je pojavnost iste u stalnom porastu posljednjih godina. Astma je izrazito kompleksna i heterogena bolest koja obuhvaća više različitih podtipova zbog čega je liječenje i prevencija izrazito otežana i zbog čega predstavlja značajan javnozdravstveni i društveni problem jer u velikoj mjeri i dugoročno utječu na kvalitetu života pacijenata s astmom. Pacijenti s astmom i njihove obitelji nerijetko se susreću i s psihološkim problemima, ali i s poteškoćama u svakodnevnom životu i obavljanju svakodnevnih aktivnosti (posao, školovanje), zbog čega je teško uopće procijeniti stvarni socio-ekonomski učinak astme. Podaci i saznanja proizašli iz ovog istraživanja pridonijeli bi uspostavi pravovremene dijagnoze i liječenja astme i pojedinih podtipova/fenotipova bolesti, učinkovitijoj prevenciji akutnih pogoršanja, a potencijalno i uštedi troškova u zdravstvenom sustavu budući da se primjenjuje personaliziran pristup liječenja.

Unatoč brojnim istraživanjima razumijevanje patofizioloških mehanizama u podlozi astme i određenih podtipova bolesti još je uvijek ograničeno. Sudjelovanjem u ovom istraživanju Vi/Vaše dijete kao pacijent možete imati direktnu korist kroz podizanje svijesti o učincima izloženosti onečišćenju zraka u unutrašnjim prostorima na zdravlje te mogućnostima smanjenja iste kroz određene mehanizme (primejrice primjenu pročišćivača zraka). Također, očekujemo da će ovo istraživanje mehanizama uključenih u razvoj astme i određenih fenotipova bolesti, te Vaše sudjelovanje u njemu, pomoći prepoznati čimbenike rizika za bolest, pojedine podtipove bolesti te uzroke i posljedice neadekvatnog liječenja, s obzirom na to da velik broj pacijenata danas nema zadovoljavajući odgovor na terapiju i u riziku su od akutnih pogoršanja (egzacerbacija) zbog neadekvatne kontrole bolesti uzrokovane, između ostalog, okolišnim čimbenicima. To je od presudnog značaja za znanstvenu, medicinsku i opću društvenu zajednicu, kako bi se planirala učinkovita prevencija i omogućilo individualizirano liječenje astme i pojedinih podtipova bolesti te, u konačnici, razvile nove i bolje terapije, kao temelj potpuno personalizirane translacijske medicine.

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KOJI SU ZA VAS MOGUĆI RIZICI SUDJELOVANJA U ISTRAŽIVANJU?
Ovo će istraživanje ne uključuje nikakve intervencijske postupke. Sudjelovanje u ovom istraživanju neće ni na koji način utjecati na niti ugroziti liječenje astme kod Vašeg djeteta.
Budući da će se u istraživanju koristiti podaci i rezultati pretraga pri rutinskim posjetima Vas/Vašeg djeteta, a uzimanje dodatnih maksimalno 12,5 mL periferne krvi iz podlaktice obavit će se u sklopu uzimanja krvi pri standardnoj obradi ispitanika, sudjelovanje u istraživanju ne pruža dodatni rizik za Vas/Vaše dijete. Vađenje krvi metodom venepunkcije i drugi dijagnostički testovi koje podrazumijeva ovo istraživanje, ukoliko ga provodi educirano i stručno osoblje, ne predstavlja poseban rizik za ispitanika. Sam postupak eventualno može uzrokovati kratkotrajnu bol na mjestu uboda te u rijetkim slučajevima može izazvati strah, nesvjesticu, te podljev na mjestu uboda. Plućni funkcijski i bronhoprovkacijski testovi ne predstavljaju nikakav rizik za Vas/Vaše dijete kao ispitanika te su stoga prihvatljivi i za malu djecu kao pacijente jer ne zahtijevaju minimalnu suradnju. Kožni ubodni testovi su također potpuno sigurna dijagnostička procedura, s minimalnim nuspojava, koje eventualno uključuju blagu nelagodu/manju bol i/ili strah kod manje djece. Uzimanje uzorka brisa sluznice usne šupljine provodi se nježnim četkanjem unutrašnje strane obraza, te ga praktički možete provoditi i Vi ili dijete samo. Sam postupak ne uzrokuje bol niti posebnu nelagodu, a ne predstavlja niti ikakav dodatni rizik za Vas/Vaše dijete. Uzimanje uzoraka kondenzata izdaha i induciranog sputuma (iskašljaja) također ne uzorkuju posebnu nelagodu niti predstavljaju poseban rizik za Vas/Vaše dijete. Ukoliko do eventualnih neželjenih nuspojava dođe kod Vas/Vašeg djeteta, pružit će Vam se sva neophodna medicinska pomoć i njega.

POSTOJE LI DRUGI LIJEKOVI, DRUGE DIJAGNOSTIČKE METODE ILI DRUGI OPERATIVNI PRISTUPI?
Ovo istraživanje ne podrazumijeva nikakve intervencijske postupke. Dodatno, u kontekstu astme, Vaš liječnik specijalist (liječnik Vašeg djeteta) će prema kliničkim parametrima i trenutnim smjernicama Vama/Vašem djetetu po potrebi propisati terapiju (ukoliko ista postoji) te će se kontrolnim kliničkim posjetama pratiti Vaš odgovor (odgovor Vašeg djeteta) na tu terapiju. Vaš liječnik specijalist će eventualno, ukoliko za tim bude potrebe (prema Vašim/Vašeg djeteta kliničkim parametrima) korigirati terapiju: promijeniti dozu, klasu terapije ili uvesti dodatnu terapiju (ukoliko dođe do pogoršanja bolesti).

MORATE LI SUDJELOVATI U ISTRAŽIVANJU?
Ne. Vaša je odluka želite li da Vi/Vaše dijete sudjelujete u ovom istraživanju ili ne, odnosno želite li dozvoliti da se rezultati pretraga koriste kao vrijedni podaci iz kojih će se ovo istraživanje učiniti znanstveno vjerodostojnijim. Vaše/sudjelovanje Vašeg djeteta je dragovoljno. Bez posljedica možete promijeniti svoje mišljenje u bilo koje vrijeme. Ukoliko odlučite prekinuti sudjelovanje, molimo Vas da o tome obavijestite glavnog istraživača/suradnika ili mentora (kontakti na sljedećoj stranici). Vi ćete u potpunosti slobodno i samostalno odlučiti hoćete li u ovom istraživanju sudjelovati ili ne. Vaše sudjelovanje je dragovoljno i u bilo koje vrijeme, bez navođenja razloga, imate se pravo bez ikakvih posljedica povući iz istraživanja. U tom slučaju ćete se nastaviti dalje liječiti na način koji je uobičajen za Vašu bolest (bolest Vašeg djeteta).

POVJERLJIVOST I PRAVO UVIDA U DOKUMENTACIJU

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Svi Vaši osobni podaci (podaci Vašeg djeteta) biti će pohranjeni i obrađivani u elektroničkom obliku, a voditelj projekta i njegovi suradnici su dužni u potpunosti poštivati propisane postupke za zaštitu osobnih podataka. U naše baze podataka Vi/Vaše dijete ćete biti uneseni pomoću posebnog koda. Vašu medicinsku dokumentaciju će pregledavati samo voditelj projekta i njegovi suradnici, a Vaše ime nikada neće biti otkriveno trećim osobama. Pristup Vašoj dokumentaciji mogu imati i predstavnici Etičkog povjerenstva u ustanovi u kojoj se liječite (lokalno etičko povjerenstvo).
Osobni podaci, uključujući Vaše ime (ime Vašeg djeteta), datum rođenja, adresu, spol i datum uključivanja u studiju će se zabilježiti, kao i medicinski i drugi podaci, poput visine, težine, povijesti bolesti, obiteljske povijesti bolesti, upotrebi lijekova, prehrambene navike i dr. podaci dobiveni tijekom istraživanja te će isti biti u potpunosti zaštićeni i anonimni (osim za nadležnog liječnika), prema dobroj kliničkoj i pravnoj praksi. Svim će se pacijentima, uzorcima i pripadajućim podacima u studiji dodijeliti jedinstvena šifra, pod kojom će Vaš identitet (identitet Vašeg djeteta) ostati skriven i kojom će se osigurati maksimalna povjerljivost podataka. Svi će uzorci i ostali podaci dobiveni tijekom studije biti obilježeni isključivo tom šifrom i čuvat će se adekvatan način, odvojeno od originalnih podataka koji otkrivaju identitet pacijenta, prema nacionalnoj legislativi. Svo će osoblje koje barata uzorcima i drugim podacima imati pristup samo šifriranim podacima, osim nadležnog liječnika i, u posebnim slučajevima, ovlaštenom osoblju koje će potencijalno provoditi provjeru etičke ispravnosti i standarda istraživanja, poput etičke komisije, audita, inspektora i sl.
S obzirom na to da ovo istraživanje uključuje gensku analizu, kao sudionik ovog istraživanja, trebate imati na umu da se Vaš genetički materijal (genetički materijal Vašeg djeteta) neće koristiti ni u koje druge svrhe osim u sklopu navedenog istraživanja, te će biti posebno zaštićen, prema načelima dobre medicinske i pravne prakse, prema svim nacionalnim, europskim i međunarodnim zakonima i etičkim pravilima u istraživanju: EC-GCP smjernicama (smjernice Europske komisije o dobroj kliničkoj praksi i njihove dopune, eng. European Community – Good Clinical Practice, Note for Guidance, III/3976/88-EN iz 1990.g.; Općom odredbom o zaštiti podataka 2016/679 Europskog parlamenta i Vijeća od 27. travnja 2016. godine; Direktivom 98/44/EC Europskog parlamenta i vijeća o zakonskoj zaštiti biotehnoloških izuma i patenata od 6.7.1998.g.; konvencijom Europskog vijeća o ljudskim pravima i biomedicini iz Ovieda u travnju 1997.g.; Helsinškom deklaracijom; mišljenjem Europske skupine o etici u znanosti i novim tehnologijama iz 1998.g. itd. Također, sama priroda metodologije istraživanja podrazumijeva da će Vaš uzorak (uzorak Vašeg djeteta), odnosno genetički materijal, nakon provedene analize za ovo znanstveno istraživanje biti uništen te da neće biti korišten u druge svrhe.

Dodatno, postoji mogućnost da će tijekom istraživanja biti potrebno provesti dodatne analize, no za isto ćete biti pravovremeno obaviješteni te ćete moći odlučiti želite li na iste pristati,a ukoliko želite, bit će potrebno da za dodatne postupke potpišete dodatni informirani pristanak.

Vi/Vaše dijete, kao pacijenti, nećete ni na koji način biti plaćeni za sudjelovanje u ovom istraživanju niti će se bilo kakvi podaci i materijali dobiveni njime koristiti u komercijalne svrhe.

ZA ŠTO ĆE SE KORISTITI PODACI DOBIVENI U OVOM ZNANSTVENOM ISTRAŽIVANJU?

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Podaci dobiveni u ovom znanstvenom istraživanju mogu biti korisni u kliničkoj praksi (npr. spoznaje o novim interakcijama lijekova, novim dijagnostičkim i terapijskim postupcima, itd.) ali i u svrhu daljnjeg razvoja i unapređenja znanosti. Stoga se očekuje da se ti podaci objave u odgovarajućim znanstvenim časopisima i publikacijama. Pri tome će Vaš identitet (identitet Vašeg djeteta) ostati u potpunosti anoniman i zaštićen.

TKO ORGANIZIRA I FINANCIRA OVO ISTRAŽIVANJE?
Ovo istraživanje organizira i financira Dječja bolnica Srebrnjak, kroz projekt financiran sredstvima Europske unije za istraživanje i inovacije u sklopu okvirnog programa Obzor 2020 (Horizon 2020), Grant agreement ID: 101057497.

TKO JE ODOBRIO OVO ISTRAŽIVANJE?
Ovo istraživanje je odobrilo Etičko povjerenstvo Dječje bolnice Srebrnjak, kao ustanove u kojoj se istraživanje provodi, nakon temeljite analize dostavljenog prijedloga istraživanja i prateće dokumentacije. Istraživanje se provodi u skladu sa svim primjenljivim smjernicama čiji je cilj osigurati pravilno provođenje istraživanja te sigurnost osoba koje u njemu sudjeluju, uključujući «Osnove dobre kliničke prakse», «Helsinšku deklaraciju», „Opću uredbu (EU) 2016/679 Europskog parlamenta i Vijeća“ i „Zakone o zaštiti prava pacijenata Republike Hrvatske“.

KOGA MOŽETE KONTAKTIRATI ZA DODATNE OBAVIJESTI I UPITE?
Ako su Vam potrebne bilo kakve dodatne informacije, ili imate dodatnih pitanja, slobodno se obratite voditelju projekta ili njegovim suradnicima, kako slijedi:

Ime i prezime voditelja projekta: izv.prof.dr.sc. Mirjana Turkalj, dr.med.
Adresa voditelja projekta: Dječja bolnica Srebrnjak, Srebrnjak 100, 10 000 Zagreb
Broj telefona voditelja projekta: 01/ 6391 178

TKO ĆE JOŠ BITI OBAVIJEŠTEN O OVOM ISTRAŽIVANJU?
O Vašem sudjelovanju u ovom znanstvenom istraživanju biti će obaviješten i Vaš obiteljski liječnik/pedijatar, ukoliko je isto relevantno za zdravlje Vašeg djeteta/štićenika i ukoliko Vi isto odobravate.

O VAŠOJ PISANOJ SUGLASNOSTI ZA SUDJELOVANJE U OVOM ISTRAŽIVANJU
Presliku dokumenta (potpisne stranice) koji trebate potpisati ako pristajete sudjelovati u ovom istraživanju dobit ćete Vi i voditelj istraživanja. Izvorni primjerak dokumenta će zadržati i čuvati voditelj istraživanja.

Hvala Vam što ste pročitali ovaj dokument i razmotrili mogućnost Vašeg sudjelovanja u ovom znanstvenom istraživanju.

Oba obavijest je sastavljena u skladu s odredbama Zakona o zdravstvenoj zaštiti Republike Hrvatske (NN 121/03), Opće uredbe (EU) 2016/679 Europskog parlamenta i Vijeća te Zakona o pravima pacijenata Republike Hrvatske (NN 169/04).

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 4 Information sheet for participants - SCH (English translation)

Annex 1: Notice for the participant

Dear Sir or Madam,

We invite you/your child as a subject to participate in a scientific study called EDIAQI "Evidence Driven Indoor Air Quality Improvement", the aim of which is to investigate and characterize the level of exposure to air pollution in indoor spaces and its impact on human health through development and clinical characteristics asthma, as well as specific subtypes of the disease, identifying new pathophysiological mechanisms involved in the development and progression of the disease. The research is carried out as part of a project funded by the European Union for research and innovation within the framework program Horizon Europe, Grant agreement ID: 101057497. The principal investigator is associate professor, Ph.D. Mirjana Turkalj, MD, and the projected duration of the project is from the 12th month of 2022 to the 12th month of 2026. The project is carried out in the Srebrnjak Children's Hospital, Zagreb.

Your participation in the research should be based on a clear understanding of the goals of the research and the methods and procedures for its implementation, as well as the possible benefits or risks for you/your child as a subject. Therefore, we ask that, before deciding, you carefully read and study this notification, and if you come across any ambiguities or unfamiliar words and expressions in it, to ask about it the researchers and doctors participating in the research, who are obliged to you and ready to answer any Question.

DESCRIPTION OF THE KEY PROBLEM AND HYPOTHESES OF THE RESEARCH

Numerous studies have confirmed that poor air quality (air pollution) plays a significant role in the development of certain diseases, including asthma, especially in sensitive populations (children). Asthma is the most common chronic disease in children, and numerous epidemiological studies show a constant increase in the incidence of asthma, with an almost certain continuation of a similar trend in the future. Due to the complex and heterogeneous nature of the disease, there is still no cure for asthma, so therapy is primarily symptomatic. Medicines serve to alleviate current symptoms and control inflammatory processes

underlying the disease and prevent acute exacerbations. The effect of the therapy itself is extremely variable and largely depends on the individual characteristics of the patients. Despite a large amount of research on certain subtypes of asthma, knowledge about the causative agent and etiological factors is still insufficient, and therefore it is impossible to decide on the type of therapy on a personalized basis and to adequately monitor the control of the disease. Asthma represents a significant public health problem because, in addition to the direct costs of treatment, a significant part of funds is lost through the reduced quality of life of patients and their families (absences from work, school, reduced productivity, etc.). According to data from the European Environmental Agency (EEA), long-term exposure to air pollution is the cause of death in more than 400,000 cases per year in large European cities. Sensitive populations, such as children, are particularly susceptible to the risk of developing health problems caused by environmental factors. A modern way of life, especially due to major changes in it due to the recent COVID-19 pandemic, means that we spend almost 90% of our time indoors. Research has shown that indoor air quality is even worse than outdoor air quality, and additionally, guidelines and legislation for indoor air pollution exposure levels are significantly less regulated than those for outdoor air quality. Moreover, for certain pollutants, legal regulation is almost non-existent. Considering the above, it is certain that indoor air pollution has an equal, if not greater, impact on the development of certain diseases (including asthma) as outdoor air pollution.

With this research, it is planned to achieve a better insight into the effect of poor indoor air quality on human health and the development of certain diseases, but also into the heterogeneity of all diseases that are categorized under the common term asthma and the pathophysiological mechanisms of certain subtypes of the disease. Furthermore, the implementation of research activities as part of this project will aim to enable better monitoring of progress, degree of asthma control and severity, and the therapeutic effect itself for the purpose of an improved and personalized approach to treatment that is not characterized by a focus on symptoms, but directly on the causes of the disease. Furthermore, the implementation of the results of this research will enable timely and precise diagnosis of the disease and its specific subtypes, as well as the potential recognition of predispositions for their development. The development of a personalized treatment

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program can potentially improve diagnostic and therapeutic procedures in the process of treating asthma and certain subtypes of the disease.

GOAL AND PURPOSE OF THE RESEARCH

Applying the concept of translational medicine and combining vast expertise in paediatric allergology as a Reference Centre for Clinical Allergology in Children with the experience of other partners in the EDIAQI project, Srebrnjak Children's Hospital and partner institutions will investigate the extent of the impact of indoor air pollution. Such a translational multidisciplinary approach, which implies a close collaboration of clinical and basic researchers, will allow an individual approach to each patient and medical problem, and will potentially enable the optimization and personalization of therapeutic regimens for the direct benefit of target groups.

The goal of this research is to gain a better insight into the effects of indoor air pollution on the development of asthma, severity of the disease, treatment outcomes and certain subtypes of the disease, by detailed profiling of patients with asthma. By combining clinical data with the results of various analyses (transcriptome, metabolome, microbiome, etc.), it is planned to investigate the heterogeneity and pathogenesis of specific subtypes of asthma and to identify new pathophysiological mechanisms involved in the development and progression of the disease. Also, the database collected through this research creates added value in terms of research and development of new methods of asthma treatment and prevention.

YOUR ROLE AS A PARTICIPANT IN THE RESEARCH

To provide a better insight into the complex nature of asthma and the connection between indoor air pollution and the development of asthma, especially certain subtypes/phenotypes of the disease, the staff of the Srebrnjak Children's Hospital will ask you/your child, during a routine clinical visit at the Hospital, to participate in this research. This research will respect all national, European and international laws and ethical rules in research. The research will include children of school age 6 to 14 years old, who are patients of the Srebrnjak Children's Hospital. If (after detailed information about the study) you agree to participate in the research, as part of a routine visit Hospitals and routine diagnostic procedures, relevant clinical data, data about your household to assess exposure

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to indoor air pollution, demographic and other data will be collected. As part of this clinical visit and routine diagnostic workup, your child will undergo the usual diagnostic tests and procedures to establish a diagnosis of asthma, including: taking a personal and family history, pulmonary function tests, skin prick tests, routine laboratory tests, which includes blood extraction. Blood samples will be taken by venipuncture from the forearm, and blood will be drawn by qualified staff of the Srebrnjak Children's Hospital in accordance with all applicable guidelines of the profession's ethical code. For the purposes of this research, a smaller part (maximum 2 ml) will be separated from peripheral blood samples for routine laboratory diagnostics for subsequent analyses. Also, it is possible that additional peripheral blood samples will be collected during the blood collection for transcriptomic analysis in the so-called Paxgene test tubes (total 2.5 ml) and for subsequent toxicological studies (total 8 ml). Since the research will use the anamnesis and the results of tests already performed during your examination (examination of your child), and the taking of an additional maximum of 12.5 mL of peripheral blood from the forearm will be done as part of the blood collection during the standard processing of the examinee, participation in the research does not provides additional risk for you/your child. Taking blood by venipuncture and other diagnostic tests that this research entails, if it is carried out by trained and professional staff like those at DBS (Reference Center for Clinical Allergology for Children), does not represent an additional risk for the examinee. You will also be asked to take a swab sample of the child's oral mucosa (by gently brushing the inside of the child's cheek with a special brush) and samples of exhaled breath condensate (which implies passive breathing of the child over a certain period, approx. 15 minutes) and induced sputum (cough). The mentioned procedures are necessary for the analysis of possible traces of air pollutants commonly present in indoor spaces and their potential toxicological effect and are minimally invasive and do not represent an additional risk or significant inconvenience for you/your child. Additionally, as part of this research, you will be asked to install measuring devices in your household for a certain period (several days) that will measure the level of exposure to indoor air pollution (gases, floating particles, volatile compounds, radon, house dust collected by vacuum cleaners' special extensions from the bed, etc.). This kind of measurement does not represent any additional risk either for you or your child, it will only

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be necessary to ensure a smaller part of the space in which the devices fight and the possibility that they create very low noise levels while they are working.

In the first part of the study, at time point 0 (the point of inclusion in the study), for the purpose of establishing a diagnosis of asthma, a routine (or extended, if necessary) allergology treatment will be carried out, which includes skin prick tests, determination of total and allergen-specific immunoglobulin E in the serum , lung-function and bronchoprovocation tests, etc., and relevant clinical and other data will be collected. In addition, your child will have the mentioned sample of whole blood (peripheral blood) taken for subsequent genetic (transcriptomic) and toxicological analyses, as well as swab samples of the mucous membrane of the oral cavity, exhaled breath condensate and induced sputum (cough).

In the second part of the research, control visits will be carried out as part of the routine monitoring and treatment of your child's asthma, on average every 3-6 months. During this period, at regular clinical control visits, anthropometric measurements, physical examinations, assessment of disease control, comorbidities, pulmonary function measurements and other diagnostic procedures will be carried out, if the same is necessary during the treatment of your child while this research is ongoing. Additionally, during this period, air quality measurements will be performed in your household according to the above protocol. During this research, it is possible that you will be asked to install an air purifier in your household for a short period of time to determine whether such purifiers have an impact on the air quality in the interior spaces and, consequently, on asthma and the clinical features of the disease in your child, such as and asthma control and therapeutic outcomes.

In the third part of the research, the results of diagnostic processing, anthropometric and other measurements will be analysed and compared with clinical and molecular genetics, toxicological and other data collected during the research, and all results will be integrated on an innovative (bio)informatics platform. In consultation with experts in medical, molecular genetics, bioinformatics and environmental sciences, the clinical significance of the obtained results and their importance for certain groups of patients will be defined, which can lead to the optimization of asthma treatment and the creation of more precise

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and personalized treatment regimens. Upon completion of the project, the relevant research results will serve to educate and raise awareness about exposure to air pollution in indoor spaces, as well as the development of national and European guidelines and legal regulations on permitted levels of air pollution in closed spaces.

WHAT ARE THE POSSIBLE ADVANTAGES AND BENEFITS OF PARTICIPATION FOR YOU?

Asthma is one of the most common chronic diseases today in general and the most common chronic disorder in children, and studies show that its incidence has been steadily increasing in recent years. Asthma is an extremely complex and heterogeneous disease that includes several different subtypes, which makes treatment and prevention extremely difficult, and which is why it represents a significant public health and social problem, as it has a large and long-term effect on the quality of life of patients with asthma. Asthma patients and their families often face psychological problems, as well as difficulties in everyday life and daily activities (work, school), which makes it difficult to assess the real socio-economic impact of asthma. Data and knowledge derived from this research would contribute to the establishment of timely diagnosis and treatment of asthma and certain subtypes/phenotypes of the disease, more effective prevention of acute exacerbations, and potentially cost savings in the health care system since a personalized treatment approach is applied.

Despite numerous studies, the understanding of the pathophysiological mechanisms underlying asthma and certain subtypes of the disease is still limited. By participating in this research, you/your child as a patient can benefit directly by raising awareness of the effects of exposure to indoor air pollution on health and the possibilities of reducing it through certain mechanisms (for example, the use of air purifiers). We also expect that this research into the mechanisms involved in the development of asthma and certain phenotypes of the disease, and your participation in it, will help identify risk factors for the disease, certain subtypes of the disease, and the causes and consequences of inadequate treatment, given that a large number of patients today do not have satisfactory response to therapy and are at risk of acute deterioration (exacerbation) due to inadequate control of the disease caused by, among other things, environmental factors. This is of crucial importance for the scientific, medical and general social community, to plan effective prevention and enable

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individualized treatment of asthma and certain subtypes of the disease and, ultimately, to develop new and better therapies, as the basis of completely personalized translational medicine.

WHAT ARE THE POSSIBLE RISKS OF PARTICIPATING IN RESEARCH FOR YOU?

This research will not include any intervention procedures. Participation in this research will in no way affect or jeopardize your child's asthma treatment.

Since the research will use data and test results during routine visits to you/your child, and the collection of an additional maximum of 12.5 mL of peripheral blood from the forearm will be performed as part of the blood collection during the standard processing of the examinee, participation in the research does not provide additional risk for you/your child. Taking blood by venipuncture and other diagnostic tests that this research entails, if it is carried out by trained and professional staff, does not represent a particular risk for the subject. The procedure itself may possibly cause short-term pain at the injection site, and in rare cases it may cause fear, fainting, and swelling at the injection site. Pulmonary function and bronchoprovocation tests do not pose any risk to you/your child as a test subject and are therefore acceptable for small children as patients as they do not require minimal cooperation. Skin prick tests are also a completely safe diagnostic procedure, with minimal side effects, which may include mild discomfort/minor pain and/or fear in smaller children. Taking a swab sample of the mucous membrane of the oral cavity is carried out by gently brushing the inside of the cheek, and you or the child can practically carry it out. The procedure itself does not cause pain or special discomfort and does not pose any additional risk for you/your child. Sampling of exhaled breath condensate and induced sputum (cough) also do not cause any discomfort or pose any particular risk to you/your child. If you/your child experience any unwanted side effects, you will be provided with all necessary medical help and care.

ARE THERE OTHER MEDICINES, OTHER DIAGNOSTIC METHODS OR OTHER OPERATIONAL APPROACHES?

This research does not imply any intervention procedures. Additionally, in the context of asthma, your specialist doctor (your child's doctor) will, according to the clinical parameters and current guidelines, prescribe therapy for you/your child, if necessary (if it exists), and

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your response (your child's response) to this will be monitored with control clinical visits. therapy. Your specialist doctor will eventually, if necessary (according to your/your child's clinical parameters), correct the therapy: change the dose, class of therapy or introduce additional therapy (if the disease worsens).

DO YOU HAVE TO PARTICIPATE IN RESEARCH?

Not. It is your decision whether you/your child want to participate in this research or not, or whether you want to allow the results of the searches to be used as valuable data that will make this research more scientifically credible. Your/your child's participation is voluntary. You can change your mind at any time without consequence. If you decide to end your participation, please inform the principal researcher/collaborator or mentor (contacts on the next page). You will decide completely freely and independently whether you want to participate in this research or not. Your participation is voluntary, and you have the right to withdraw from the research at any time without giving any reason. In this case, you will **continue to be treated in the manner that is usual for your illness (your child's illness).**

CONFIDENTIALITY AND RIGHT OF INSPECTION OF DOCUMENTATION

All your personal data (your child's data) will be stored and processed in electronic form, and the project manager and his associates are obliged to fully comply with the prescribed procedures for the protection of personal data. You/your child will be entered into our databases using a special code. Your medical documentation will only be reviewed by the project manager and his associates, and your name will never be revealed to third parties. Representatives of the Ethics Committee in the institution where you are being treated (local ethics committee) may also have access to your documentation.

Personal data, including your name (your child's name), date of birth, address, gender and date of inclusion in the study will be recorded, as well as medical and other data, such as height, weight, medical history, family medical history, medication use, dietary habits and other data obtained during the research and will be fully protected and anonymous (except for the competent doctor), according to good clinical and legal practice. All patients, samples and associated data in the study will be assigned a unique code, under which your identity (the identity of your child) will remain hidden and which will ensure maximum data confidentiality. All samples and other data obtained during the study will be marked

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exclusively with that code and will be stored in an adequate manner, separately from the original data that reveal the patient's identity, according to national legislation. All personnel who handle samples and other data will only have access to encrypted data, except for the competent physician and, in special cases, authorized personnel who will potentially carry out checks on ethical correctness and research standards, such as ethics commissions, audits, inspectors, etc.

Given that this research includes genetic analysis, as a participant in this research, you should keep in mind that your genetic material (your child's genetic material) will not be used for any other purpose than as part of the aforementioned research and will be specially protected. according to the principles of good medical and legal practice, according to all national, European and international laws and ethical rules in research: EC-GCP guidelines (European Commission guidelines on good clinical practice and their amendments, Eng. European Community – Good Clinical Practice, Note for Guidance , III/3976/88-EN from 1990; General Data Protection Regulation 2016/679 of the European Parliament and the Council of April 27, 2016; Directive 98/44/EC of the European Parliament and the Council on the legal protection of biotechnological inventions and of patents from July 6, 1998; the Convention of the European Council on Human Rights and Biomedicine from Oviedo in April 1997; the Declaration of Helsinki; the opinion of the European Group on Ethics in Science and New Technologies from 1998 etc. Also, the very nature of the research methodology implies that your sample (your child's sample), i.e. genetic material, will be destroyed after the analysis for this scientific research and will not be used for other purposes.

In addition, there is a possibility that during the research it will be necessary to carry out additional analyses, but you will be informed about this in a timely manner and you will be able to decide whether you want to agree to them, and if you wish, you will need to sign an additional informed consent for additional procedures.

You/Your child, as patients, will not be paid in any way for participating in this research, nor will any data and materials obtained from it be used for commercial purposes.

WHAT WILL THE DATA OBTAINED IN THIS SCIENTIFIC RESEARCH BE USED FOR?

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement Nº 101057497.

The data obtained in this scientific research can be useful in clinical practice (eg knowledge about new drug interactions, new diagnostic and therapeutic procedures, etc.) but also for the purpose of further development and advancement of science. Therefore, it is expected that these data will be published in appropriate scientific journals and publications. In doing so, your identity (your child's identity) will remain completely anonymous and protected.

WHO ORGANIZES AND FINANCES THIS RESEARCH?

This research is organized and financed by the Srebrnjak Children's Hospital, through a project funded by the European Union for Research and Innovation within the framework program Horizon 2020, Grant agreement ID: 101057497.

WHO APPROVED THIS RESEARCH?

This research was approved by the Ethics Committee of the Srebrnjak Children's Hospital, as the institution where the research is conducted, after a thorough analysis of the submitted research proposal and accompanying documentation. The research is conducted in accordance with all applicable guidelines aimed at ensuring the proper conduct of the research and the safety of the persons participating in it, including the "Basics of Good Clinical Practice", the "Declaration of Helsinki", "General Regulation (EU) 2016/679 of the European Parliament and the Council " and "Laws on the Protection of Patients' Rights of the Republic of Croatia".

WHO CAN YOU CONTACT FOR ADDITIONAL INFORMATION AND INQUIRIES?

If you need any additional information, or have additional questions, feel free to contact the project manager or his associates, as follows:

WHO CAN YOU CONTACT FOR ADDITIONAL INFORMATION AND INQUIRIES?

If you need any additional information, or have additional questions, feel free to contact the project manager or his associates, as follows:

Name and surname of the project manager: associate professor, Ph.D. Mirjana Turkalj, MD.

Address of the project manager: Srebrnjak Children's Hospital, Srebrnjak 100, 10 000 Zagreb

Phone number of the project manager: 01/ 6391 178

WHO ELSE WILL BE NOTIFIED ABOUT THIS RESEARCH?

Your family doctor/pediatrician will also be informed about your participation in this scientific research, if it is relevant for the health of your child/ward and if you approve it.

ABOUT YOUR WRITTEN CONSENT TO PARTICIPATE IN THIS RESEARCH

You and the research manager will receive a copy of the document (signature page) that you need to sign if you agree to participate in this research. The original copy of the document will be kept and kept by the research manager.

Thank you for reading this document and considering the possibility of your participation in this scientific research.

Both notices were compiled in accordance with the provisions of the Law on Health Care of the Republic of Croatia (Official Gazette 121/03), General Regulation (EU) 2016/679 of the European Parliament and of the Council, and the Law on Patients' Rights of the Republic of Croatia (Official Gazette 169/04).

This project has received funding from the European Union's
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Annex 5 Informed consent form for minors under the age of 12 years signed by their legal guardians - SCH

DJEČJA BOLNICA SREBRNJAK

ETIČKO POVJERENSTVO

Prilog 2:
Suglasnost za sudjelovanje maloljetne osobe u znanstvenom istraživanju pod nazivom EIDAQI (Evidence Driven Indoor Air Quality Improvement)

Ako je ispitanik u znanstvenom istraživanju maloljetna osoba (osoba mlađa od 18 godina), pristanak za sudjelovanje u istraživanju treba dati roditelj ili zakonski zastupnik to jest skrbnik. Istraživači su dužni s djecom u dobi od 8 do 18 godina razgovarati o predloženom znanstvenom istraživanju i uzeti u obzir njihovu želju i odluku o sudjelovanju u istraživanju.

1. Potvrđujem da sam dana (upisati dan/mjesec/godinu) u (upisati mjesto) pročitao/pročitala Obavijest za ispitanika za gore navedeno znanstveno istraživanje te sam imao/imala priliku postavljati pitanja.
2. Razumijem da je sudjelovanje mog djeteta/mog štićenika dragovoljno i da se iz sudjelovanja u istraživanju može povući u bilo koje vrijeme, bez navođenja razloga i bez ikakvih posljedica za svoje zdravstveno stanje ili pravni status.
3. Razumijem da medicinskoj dokumentaciji mog djeteta/mog štićenika pristup imaju samo odgovorne osobe, to jest voditelj istraživanja i njegovi suradnici te članovi Etičkog povjerenstva ustanove u kojoj se istraživanje obavlja i Etičkog povjerenstva koje je odobrilo ovo znanstveno istraživanje. Tim osobama dajem dopuštenje za pristup medicinskoj dokumentaciji mog djeteta/mog štićenika.
4. Pristajem da obiteljski liječnik mog djeteta/mog štićenika bude upoznat s njegovim sudjelovanjem u navedenom znanstvenom istraživanju, ukoliko je to relevantno za njegovo/njezino zdravlje.
5. Želim i pristajem da moje dijete/moj štićenik sudjeluje u navedenom znanstvenom istraživanju.

Ime i prezime roditelja/zakonskog zastupnika/skrbnika: (upisati **tiskanim slovima**)
Vlastoručni potpis: (potpisati)
Mjesto i datum: (upisati)

Ime i prezime osobe koja je vodila postupak Obavijesti za ispitanika i Suglasnosti za sudjelovanje: (upisati **tiskanim slovima**)

Ime i prezime voditelja projekta: izv.prof.dr.sc. Mirjana Turkalj, dr.med.
Vlastoručni potpis: (potpisati)
Mjesto i datum: (upisati)

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 6 Informed consent form for minors under the age of 12 years signed by their legal guardians - SCH (English translation)

CHILDREN'S HOSPITAL SREBRNJAK

ETHICS COMMITTEE

Appendix 2:

Consent for the participation of a minor in scientific research called EIDAQI (Evidence Driven Indoor Air Quality Improvement)

If the subject in scientific research is a minor (a person under 18 years of age), consent to participate in the research must be given by a parent or legal representative, i.e. a guardian. Researchers are obliged to discuss the proposed scientific research with children between the ages of 8 and 18 and consider their desire and decision to participate in the research.

1. confirm that on (insert day/month/year) in (insert place) I have read the Notice for respondents for the above-mentioned scientific research and had the opportunity to ask questions.
2. I understand that the participation of my child/my ward is voluntary and that I can withdraw from the research at any time, without giving a reason and without any consequences for my health or legal status.
3. I understand that only responsible persons have access to the medical documentation of my child/my ward, i.e. the head of the research and his colleagues and members of the Ethics Committee of the institution where the research is conducted and the Ethics Committee that approved this scientific research. I give these people permission to access the medical records of my child/my ward.
4. I agree that my child's/my ward's family doctor will be informed of his/her participation in the mentioned scientific research if it is relevant for his/her health.
5. I wish and agree that my child/my ward participates in the mentioned scientific research.

Name and surname of parent/legal representative/guardian: (write in block letters)

Handwritten signature: (sign)

Place and date: (enter)

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Name and surname of the person who conducted the process of Notification for the respondent and Consent to participate: (write in block letters)

Name and surname of the project manager: associate professor, Ph.D. Mirjana Turkalj, MD.

Handwritten signature: (sign)

Place and date: (enter)

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 7 Informed consent form for genetic analysis- SCH

DJEČJA BOLNICA SREBRNJAK

ETIČKO POVJERENSTVO

Prilog 4:

SUGLASNOST ZA SUDJELOVANJE U DIJELU ISTRAŽIVANJA VEZANOM UZ GENETIKU

Potvrđujem da sam pročitao/pročitala obavijest za znanstveno istraživanje pod nazivom: **EDIAQI „Evidence Driven Indoor Air Quality Improvement"**

Imao/imala sam dovoljno vremena o svemu razmisliti, na sva pitanja koja sam postavio/postavila, dobio/dobila sam zadovoljavajuće odgovore.
Razumijem da sam slobodan/na prihvatiti, odbiti ili u bilo kojem trenutku prekinuti svoje sudjelovanje/sudjelovanje mog djeteta u istraživanju, bez navođenja razloga i bez ikakvih posljedica po zdravstvenom ili pravnom pitanju.

Razumijem da ovo istraživanje uključuje gensku analizu. Razumijem da podaci o genskoj analizi mog uzorka/uzorka mog djeteta neće biti otkriveni niti dostupni trećim osobama, niti osobnom liječniku mog djeteta, te da će uzorak krvi za gensku analizu nakon provedene analize za ovo znanstveno istraživanje biti uništen i da neće biti korišten u druge svrhe.

Razumijem da pristup mojoj medicinskoj dokumentaciji (dokumentaciji mog djeteta) imaju odgovorni pojedinci, tj. glavni istraživač i njegovi suradnici, članovi Etičkog povjerenstva ustanove u kojoj se istraživanje obavlja te članovi Etičkog povjerenstva koje je odobrilo ovo znanstveno istraživanje, kao i druga nadležna tijela zadužen a za audit i reviziju istraživanja. Dajem dozvolu tim pojedincima za pristup medicinskoj dokumentaciji mog djeteta.

Izjavljujem da sam suglasan/suglasna da ja/moje dijete sudjelujemo u znanstvenom istraživanju pod nazivom: EDIAQI „Evidence Driven Indoor Air Quality Improvement" u dijelu vezanom uz genetiku.

Ime i prezime ispitanika (tiskanim slovima): _____
Ime i prezime roditelja/staratelja ispitanika (tiskano): _____
Potpis roditelja/staratelja ispitanika: _____

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

Datum: _____

Osoba koja je vodila postupak obavijesti za ispitanika i suglasnost za sudjelovanje:

Ime i prezime liječnika (tiskanim slovima)_____

Potpis: _____

Datum:_____

Ime i prezime voditelja projekta: izv.prof.dr.sc. Mirjana Turkalj, dr.med.

Vlastoručni potpis: _____

Mjesto i datum: _____

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 8 Informed consent form for genetic analysis – SCH (English translation)

CHILDREN'S HOSPITAL SREBRNJAK

ETHICS COMMITTEE

Appendix 4:

CONSENT FOR PARTICIPATION IN PART OF THE RESEARCH RELATED TO GENETICS

I confirm that I have read the notice for the scientific research entitled: EDIAQI "Evidence Driven Indoor Air Quality Improvement"

I had enough time to think about everything, I got satisfactory answers to all the questions I asked.

I understand that I am free to accept, refuse or terminate my/my child's participation in research at any time, without giving any reason and without any health or legal consequences.

I understand that this research involves genetic analysis. I understand that the data on the genetic analysis of my sample/my child's sample will not be disclosed or made available to third parties, nor to my child's personal doctor, and that the blood sample for genetic analysis after the analysis for this scientific research will be destroyed and will not be used in other purposes. I understand that responsible individuals have access to my medical documentation (my child's documentation), i.e. the principal investigator and his associates, members of the Ethics Committee of the institution where the research is conducted, and members of the Ethics Committee that approved this scientific research, as well as other competent bodies in charge of for audit and revision of research. I give permission to these individuals to access my child's medical records.

I declare that I agree that I/my child participate in the scientific research entitled: EDIAQI "Evidence Driven Indoor Air Quality Improvement" in the part related to genetics.

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Name and surname of the respondent (printed letters):

_____

Name and surname of the respondent's parent/guardian (printed):

_____

Signature of the respondent's parent/guardian:

_____

Date: _____

The person who managed the notification procedure for the respondent and consent to participate:

Doctor's name and surname (printed letters)_____

Signature: _____

Date:_____

Name and surname of the project manager: associate professor, Ph.D. Mirjana Turkalj, MD.

Signature: _____

Place and date: _____

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 9 Informed consent for minors 12 years or older signed by the participants themselves - SCH

DJEČJA BOLNICA SREBRNJAK

ETIČKO POVJERENSTVO

Prilog 3:
Suglasnost za sudjelovanje starijeg maloljetnika u istraživanju pod nazivom EDIAQI (Evidence Driven Indoor Air Quality Improvement)

1. Potvrđujem da sam dana (upisati dan/mjesec/godinu) u (upisati mjesto) pročitao/pročitala Obavijest za ispitanika za gore navedeno znanstveno istraživanje te sam imao/imala priliku postavljati pitanja.
2. Razumijem da je moje sudjelovanje dragovoljno i da se iz sudjelovanja u istraživanju mogu povući u bilo koje vrijeme, bez navođenja razloga i bez ikakvih posljedica za moje zdravstveno stanje ili pravni status.
3. Razumijem da mojoj medicinskoj dokumentaciji pristup imaju samo odgovorne osobe, to jest voditelj istraživanja i njegovi suradnici te članovi Etičkog povjerenstva ustanove u kojoj se istraživanje obavlja i Etičkog povjerenstva koje je odobrilo ovo znanstveno istraživanje. Tim osobama dajem dopuštenje za pristup mojoj medicinskoj dokumentaciji.
4. Pristajem da moj obiteljski liječnik (odnosno član obitelji) bude upoznat s mojim sudjelovanjem u navedenom znanstvenom istraživanju.
5. Želim i pristajem sudjelovati u navedenom znanstvenom istraživanju.

Ime i prezime ispitanika: (upisati **tiskanim slovima**)
Vlastoručni potpis: (potpisati)

Mjesto i datum: (upisati)

Ime i prezime osobe koja je vodila postupak Obavijesti za ispitanika i Suglasnosti za sudjelovanje: (upisati **tiskanim slovima**)

Ime i prezime voditelja projekta: izv.prof.dr.sc. Mirjana Turkalj, dr.med.

Vlastoručni potpis: (potpisati)
Mjesto i datum: (upisati)

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

Annex 10 Informed consent for minors 12 years or older signed by the participants themselves – SCH (English Translation)

CHILDREN'S HOSPITAL SREBRNJAK

ETHICS COMMITTEE

Appendix 3:

Consent for the participation of an older minor in research called EDIAQI (Evidence Driven Indoor Air Quality Improvement)

1. I confirm that I am on (insert day/month/year) in (insert place) read the Notice for respondents for the above-mentioned scientific research and I had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I can withdraw from participating in the research at any time, without giving a reason and without any consequences for my health or legal status.
3. I understand that only responsible persons have access to my medical documentation, that is, the head of the research and his colleagues and members of the Ethics Committee of the institution where the research is conducted and the Ethics Committee that approved this scientific research. I give these people permission to access my medical records.
4. I agree that my family doctor (that is, a family member) will be informed of my participation in the mentioned scientific research.
5. I want and agree to participate in the mentioned scientific research.

Name and surname of the respondent: (write in block letters)

Handwritten signature: (sign)

Place and date: (enter)

This project has received funding from the European Union's Horizon Europe Framework Programme under grant agreement № 101057497.

Name and surname of the person who conducted the process of Notification for the respondent and Consent to participate: (write in block letters)

Name and surname of the project manager: associate professor, Ph.D. Mirjana Turkalj, MD.

Handwritten signature: (sign)

Place and date: (enter)

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.

Deliverable D7.5

Ethical guidelines, including informed consent procedures

Work Package 7

EXPLOIT: Dissemination, communication and exploitation

Version: Final

This project has received funding from the European Union's
Horizon Europe Framework Programme under grant agreement № 101057497.