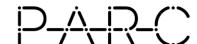
# Aktivnosti v sklopu naloge 4.1

JSI

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## 4.1 Human biomonitoring

### 4.1.1 Design, alignment and fieldwork of HBM studies

### 4.1.1.1 Supporting material

#### In WG1:

- Update of HBM4EU informed consent form in line with GDPR (General Data Protection Regulation)
- SOP for sample collection
- Questionnaires Format-lay out

#### In WG2:

Questionnaires in relation with research and policy questions (in collaboration with 4.1.4 statistical analysis) – Link to codebooks

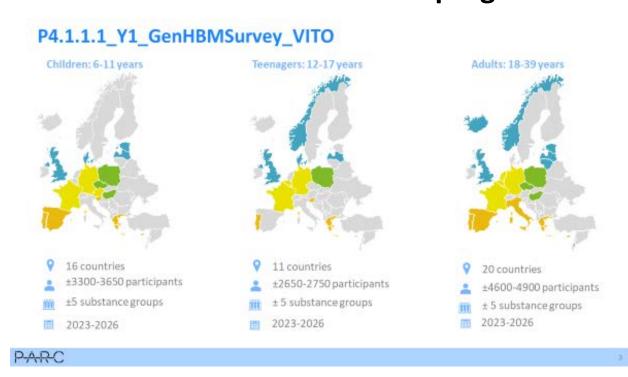
VITO experience from HBM4EU shows that developing the questionnaire in relation to the codebooks and data file layout is very crucial for replicability and comparability of the data results.

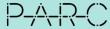
- Definition of a minimal set of obligatory variables related to the substance groups to be measured
- Substance specific questionnaire/ age-group questionnaires

#### In WG3:

- The Digitalization of collection of information

## 4.1.1.3 General HBM survey **Second national HBM program**





## 4.1 Human biomonitoring

### 4.1.3 Link exposure and health related information

### 4.1.3.2 Identification of effect markers

Selection of classical/clinical and novel effect biomarkers: *Kidney function biomarkers* 

Table 1 – Set of effect biomarkers proposed to the study owners for measurement in the PARC general survey

	Children	Teenagers	Adults
Classical/C	Clinical effect biomarkers (1 option to select)		
Option 1	Renal markers in urine (NAG (N-acetyl-β- D glucosaminidase), A1MG (α1- microglobulin), creatinine, albumin (albumin to crt ratio)	Thyroid hormones in serum (FT3, FT4, TSH)	Thyroid hormones in serum (FT3, FT4, TSH)
Option 2	Extended set of renal markers in urine (NAG (N-acetyl-β-D glucosaminidase), A1MG (α1-microglobulin), creatinine, albumin (albumin to crt ratio), Kim-1 (kidney injury molecule-1), RBP4 (Retinol-binding protein 4)	Thyroid hormones in serum (FT3, FT4, TSH); and Blood lipids in serum (Cholesterol, Triglycerides, HDL, LDL)	Thyroid hormones in serum (FT3, FT4, TSH); and Blood lipids in serum (Cholesterol, Triglycerides, HDL, LDL)
Option 3	None of the above	Thyroid hormones in serum (FT3, FT4, TSH); and Blood lipids in serum (Cholesterol, Triglycerides, HDL, LDL); Sexual development markers (LH, FSH, DHEAS, E2, TT, SHBG - note: Specific sampling conditions will apply for sexual development markers, see information leaflet)	Thyroid hormones in serum (FT3, FT4, TSH); and Blood lipids in serum (Cholesterol, Triglycerides, HDL, LDL); and immune (IgG; IgM; IgE; Interleukins (1, 1B, 6, 8); LTB4; TNFα, IFN-G: only the most affordable will be chosen)
Option 4	1	None of the above	None of the above



## 4.1 Human biomonitoring

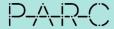
4.1.3 Link exposure and health related information

### 4.1.3.2 Identification of effect markers

Selection of classical/clinical and novel effect biomarkers: *Kidney function biomarkers* 

#### 4.1.3.3 Health outcomes

Selection of endpoints and suggested health measures to be obtained within the General HBM survey: *Arsenic in teenagers (JSI, NIJZ)* 





**Design**: cross-sectional

Implementation level: national (9 regions)

PARC General Survey: 3 out of 9 regions

**Timing of sampling**: started in 2018, across all seasons except summer holidays in July and August

PARC General Survey: 2024 – 2025

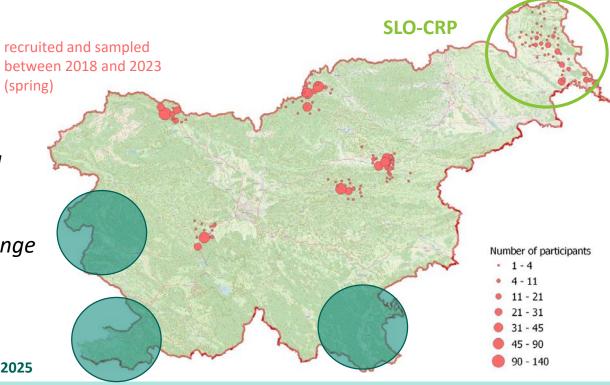
**Age groups**: 6–9 years (children)

12–15 years (adolescents)

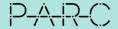
Sample size: 100 children and 100 adolescents per study area

 $\rightarrow$  300 children and 300 adolescents

**Recruitment strategy**: parents with children of chosen age range invited **through schools** in the selected study areas







### Uspešnost nabora:

OBMOČJE	Šola	Število razdeljenih zgibank	Število prijav	Uspešnost rekrutiranja (%)
Idrija s				
Posočjem	OŠ Idrija	440	157	35,7
	OŠ Kanal	170	50	29,4
	OŠ Deskle	130	25	19,2
		740	232	31,4
Koper	OŠ Koper	650	45	6,9
	OŠ Dušana Bordona Koper	450	18	4,0
	OŠ Antona Ukmarja Koper	520	41	7,9
		1620	104	6,4
	Skupaj	3740	495	13,2

#### Opomba:

- Nabor v Beli krajini se še ni začel (sodelovanje z Bonio Miljavec)
- V Kopru bomo vključili dodatne šole (sodelovanje z Agnes Šömen Joksić)

Z vzorčenjem pričnemo v sredini januarja 2024.







**Sample types collected**: first morning urine, peripheral blood (whole blood, plasma and serum), hair (3 cm from scalp)

**Chemical analysis planned**: multi-elemental analysis, phthalates & DINCH, bisphenols, FRs, pesticides, PAHs, PFAS

**In-house laboratory capacity** (multi-elements, As speciation, BPs, phthalates, DINCH) + **external labs** 

**Biobanking of residual sample volume planned**: YES

Children	Teenagers	Adults
Pesticides	PFAS	PFAS
Bisphenols	Pesticides	Pesticides
Metals in urine	Bisphenols	Bisphenols
Mercury in hair	Arsenic species	Metals in urine and blood
Phthalates & substitutes	Phthalates & substitutes	Phthalates & substitutes





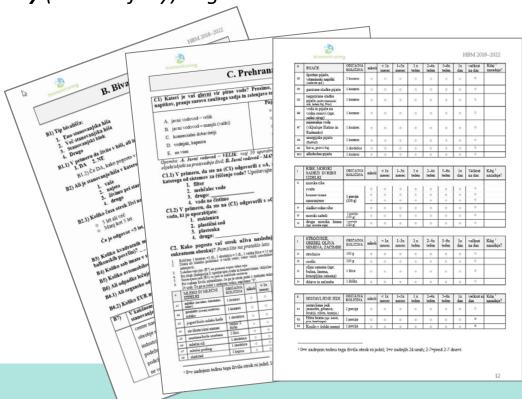
**Questionnaires**: guided interviews (online form)

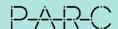
personal information, health status, lifestyle, dietary and environmental characteristics additional questionnaire in regards to gestation, lactation and grand-/parents' pedigree (genetic polymorphisms) and children's sexual maturation

existing questionnaires (aligned with HBM4EU) - **mostly** (but not fully) aligned with PARC materials



Dodatna uskladitev vprašalnikov za potrebe PARC študije (opravljena v sodelovanju z NIJZ)





## P4.1.4.2.a\_Y1\_DataAnalysisHBM4EU\_VITO: Further analysis of data generated within HBM4EU

**Lead: VITO** 

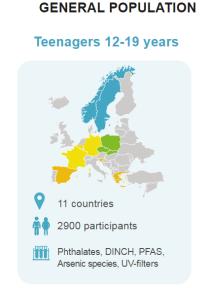
Activity: Exposure sources, routes and determinants of exposure (Lead: JSI)

**Goal**: Further exploitation of the data generated within HBM4EU. In order to make optimal use of the available HBM4EU data and use the results to feed into the design of HBM studies planned under PARC, further statistical analyses will be performed on HBM4EU data.

Legenda:



Northern Europe



Southern Europe

Eastern Europe



Western Europe

**HBM4EU Aligned Studies** 

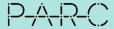
Substance	Available HBM data	Research question	Partners
PFAS	<u>Teenagers</u> , 9 studies	RQ1.1. Explore a link between PFAS concentrations in human samples (serum/plasma), questionnaire data on frequency of consumption and concentration of PFAS in fish and other seafood.	Lead: VITO Contributing:
		RQ1.2. Explore a link between PFAS concentrations in human samples (serum/plasma) and environmental emissions and releases of PFAS.	NIPH, SZU-SK, ISSeP, ISCIII, Sciensano
PAH	Adults, 11 studies	RQ2.1. Explore a link between concentrations of PAH metabolites in urine and Europe-wide data on PAH concentrations in air.	Lead: MU Contributing: AUTH, UBA
Pesticides (pyrethroids)	Adults, 6 studies  Children, 6 studies	RQ3.1. Investigate exposure to pyrethroids associated with proximity of agricultural fields and/or by the proportion of agricultural fields within the respective NUTS areas where the study participants reside. In addition, also use of pyrethroid pesticide on the NUTS or country level would be applied.	
Pesticides (glyphosate, AMPA)	Adults, 3 studies  Children, 5 studies	RQ4.1. Investigate exposure to glyphosate and AMPA associated with proximity of agricultural fields and green space and/or by the proportion of agricultural fields and green spaces within the respective NUTS areas where the study participants reside. In addition, also use of glyphosate-based herbicides on the NUTS or country level would be applied.	
Arsenic species	<u>Teenagers</u> , 6 studies	RQ5.1. Explore HBM data in combination with the available concentrations of arsenic species in fish and seafood on the national level.  RQ5.2. Explore HBM data in relation with the emissions of as from industry sector on the NUTS level.	Lead: JSI  VITO, ISCIII, Sciensano, ISSeP
Cadmium	Adults, 10 studies	RQ6.1. Further explore Cd concentrations in crops in different EU areas and combine it with mineral fertilizers use in the respective areas. Focus will be on domestic crops use.	Lead: JSI
ALL	<u>Children</u> , 14 studies <u>Teenagers</u> , 11 studies <u>Adults</u> , 13 studies	RQ7.1. Grouping of chemicals according to a specific source (cluster analysis).	Lead: JSI Contributing: VITO

#### Existing databases to be explored within the project:

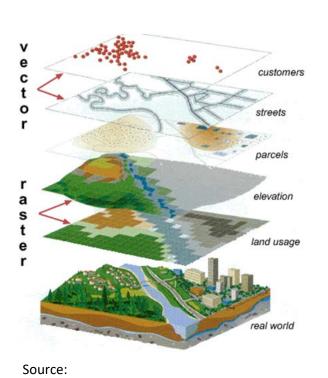
- EFSA Data Reports
- Land use/cover patterns (e.g. CORINE Land Cover, satellite data)
- EUROSTAT
- E-PRTR (European Pollutant Release and Transfer Register)
- EEA (European Environment Agency)
- Air Monitoring Network (MONET)
- FOREGS Geochemical database European Soil Data Centre
- Sector-specific databases: e.g., Eurofer, Galssalliance, Cembureau
- European Space Agency: satellite data on land use, AQ etc.
- Other potential sources to derive proxies: Google maps, Openstreetmap
- Other relevant databases (e.g. heating systems, monitoring of pesticide residues, tap water) to be explored (national, regional, EU-level)

#### Type of analysis to link HBM and geospatial data:

- Each study participant will be assigned a value based on the NUTS area (other area), or based on an exact geolocation
- Use of multilevel mixed regression models, which are able to distinguish within and between group variability (group = country, NUTS,...)



**Geospatial variables** will be obtained based on three different levels:



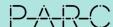






Country	NUTS2, NUTS3	Residential address
Concentrations of chemicals in food items: PFAS, As, Cd (EFSA)	Proportion of agricultural fields (%) (CORINE LAND Cover)	Proximity to agricultural fields (m) (CORINE LAND Cover)
Consumption frequency for food items (EFSA)	Proportion of green space areas (%) (CORINE LAND Cover)	Proximity to green space (m) (CORINE LAND Cover)
	Arsenic (other chemicals) emissions from industry (t/facility) (E-PRTR)	Vicinity of industrial or other facilities (m) ( <i>various sources</i> )
	Annual pesticide use (t/area) (EUROSTAT)	Concentrations of chemicals in soil (mg/kg) (JRC)
	Concentrations of PM10, PM2.5, NO2, SO2, O3 in air ( $\mu g/m^3$ ) ( <b>EEA</b> )	Concentrations of PM10, PM2.5, NO2, SO2, O3 in air ( $\mu g/m^3$ ) ( <b>EEA</b> )
	Annual PFOA and PFOS emissions (t/area) (JRC)	

The list is not final...



Input to:

Partnership for the Assessment of Risks from Chemicals

**Report T4.1.4/** 

Statistical Analysis Plan (SAP) for T4.1 projects

