ManGO

User Day 8 October 2024

EXIMIOUS

Mapping Exposure-Induced Immune Effects

MEMBER OF THE European Human Exposome NETWORK

Data management in human exposome projects: the EXIMIOUS experience and how we plan to use it in the EXPOSIM project

Manosij Ghosh

Environment and Health, Department of Public Health and Primary Care

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 874707.

- ***FAIR Data management in exposome research - a case study from the EU-funded EXIMIOUS project***
- ***Building on the EXIMIOUS experience to use it in the EXPOSIM project***

- ***FAIR Data management in exposome research - a case study from the EU-funded EXIMIOUS project***

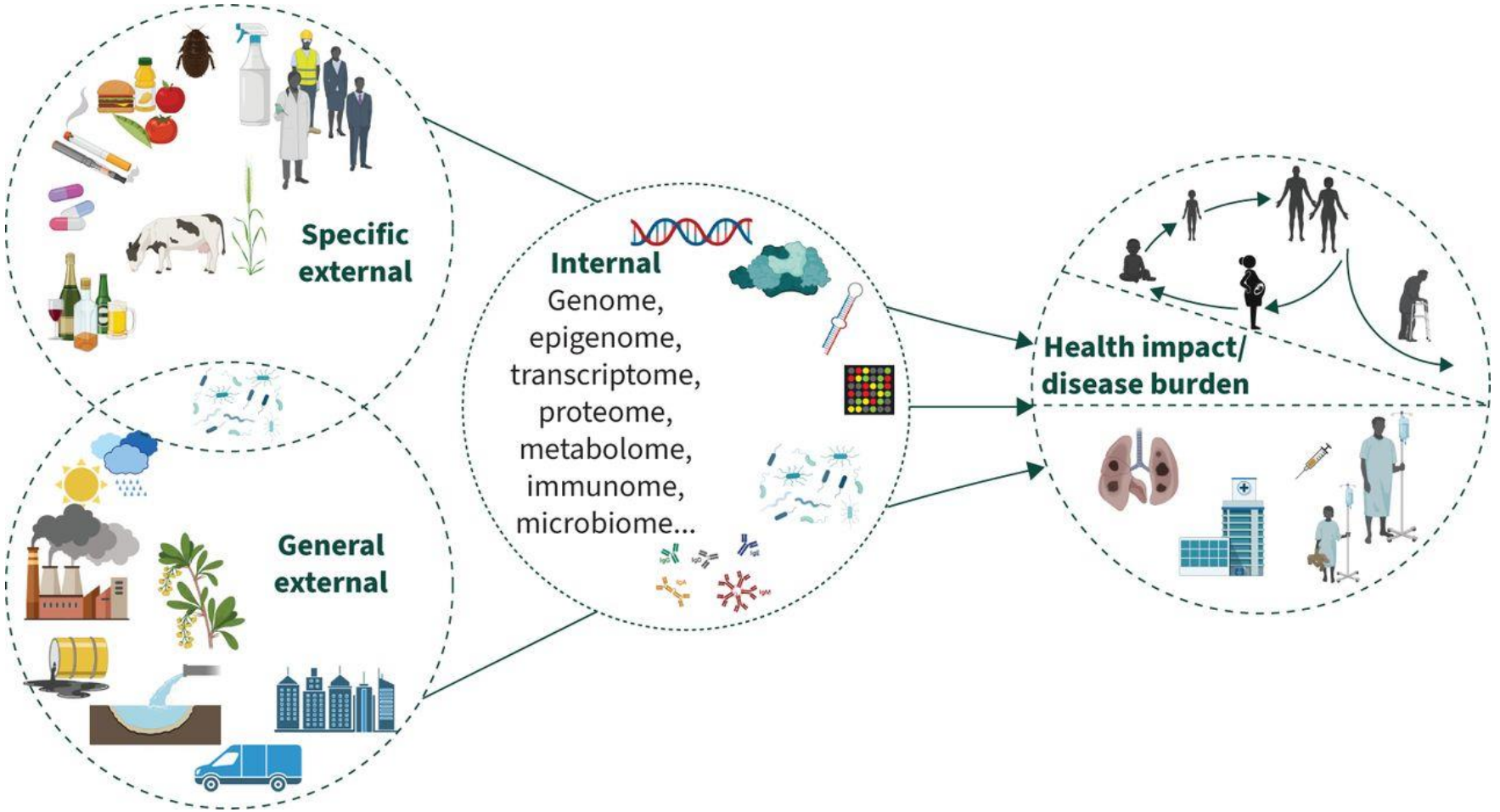
Manosij Ghosh, *Katrijn Broothaerts, Steven Ronsmans, Ingrid Barcena Roig, Jef Scheepers, Mustafa Dikmen, Emily Rose Ciscato, Carolina Blanch, Michelle Plusquin, Unni C. Nygaard, Camilla Sandal Sejbæk, Karin S. Hougaard, Peter HM Hoet*

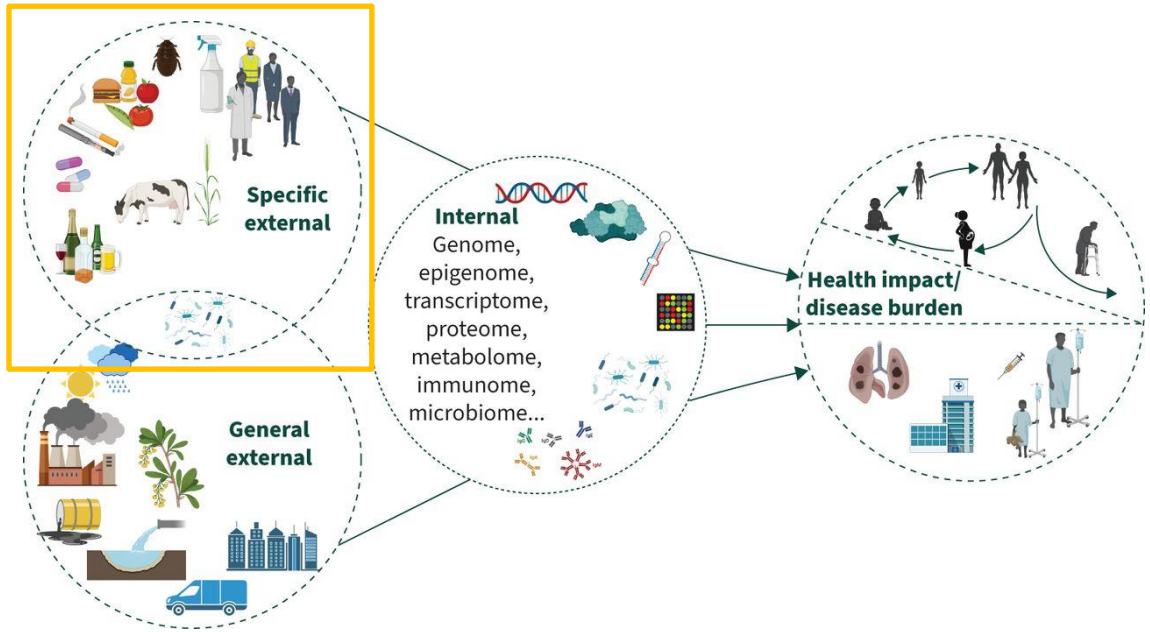
On behalf of the EXIMIOUS consortium#

- ***Building on the EXIMIOUS experience to use it in the EXPOSIM project***

EXPOSOME

"The **cumulative measure of environmental influences and associated biological responses throughout the lifespan**, including exposures from the environment, diet, behavior, and endogenous processes", by including a quantifiable "cumulative measure" of the exposome component and the "differential response" in biological processes.

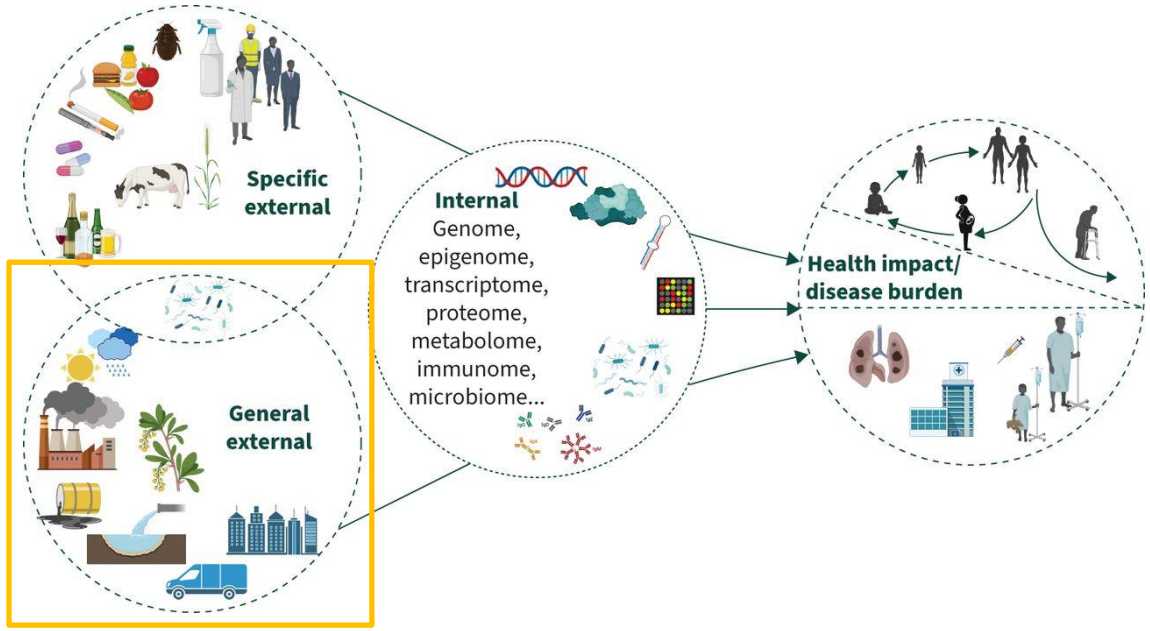




1.Specific external: an individual's immediate local environment, including exposure to chemicals, diet, physical activity, tobacco and infections

2.General external: social, economic factors, the urban environment and climate factors.

3.Internal*:* internal biological processes such as oxidative stress, inflammation, epigenetic changes, metabolism and the internal microbiome.



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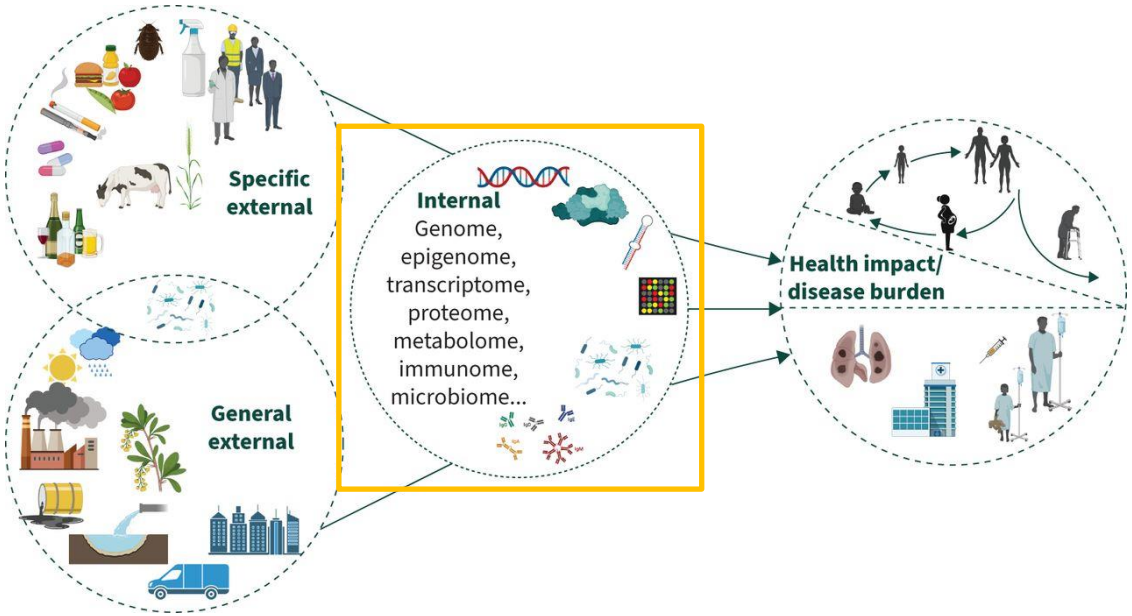

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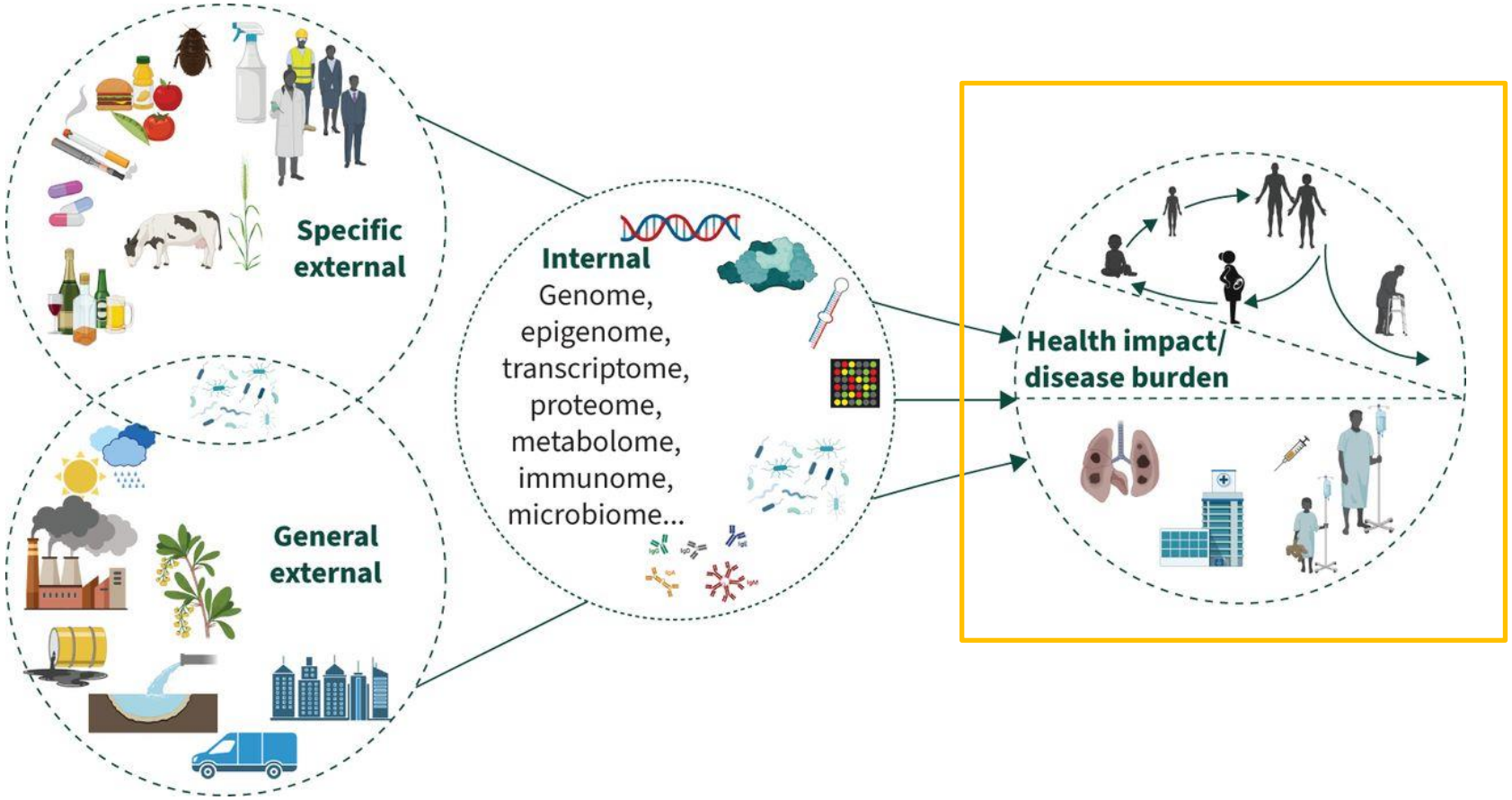
EXPOSOME


Specific external
General external
Internal
Genome,
epigenome,
transcriptome,
proteome,
metabolome,
immunome,
microbiome...
Health impact/
disease burden

Exposome & Human biomonitoring

Human biomonitoring can be defined as the ***method for assessing human exposure to chemicals or their effects by measuring these chemicals, their metabolites or reaction products in human specimens****. Biomonitoring involves measurements of biomarkers in bodily fluids, such as blood, urine, saliva, breast milk, sweat, and other specimens, such as faeces, hair, teeth, and nails [2][3]. In the area of occupational medicine or occupational hygiene, biomonitoring is to be understood* ***as the examination of biological materials of employees for the quantitative determination of hazardous substances, their metabolites or their biochemical and/or biological parameters.***

An exposomic approach differs from traditional biomonitoring in that it can theoretically include all exposures of potential health significance, whether they are derived from exogenous sources (e.g., pollutants, diet, drugs) or endogenous sources (e.g., hormones, human and microbial metabolites)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5381997/

What is EXIMIOUS about?

EXIMIOUS
Mapping Exposure-Induced Immune Effects

‘meet in the middle’

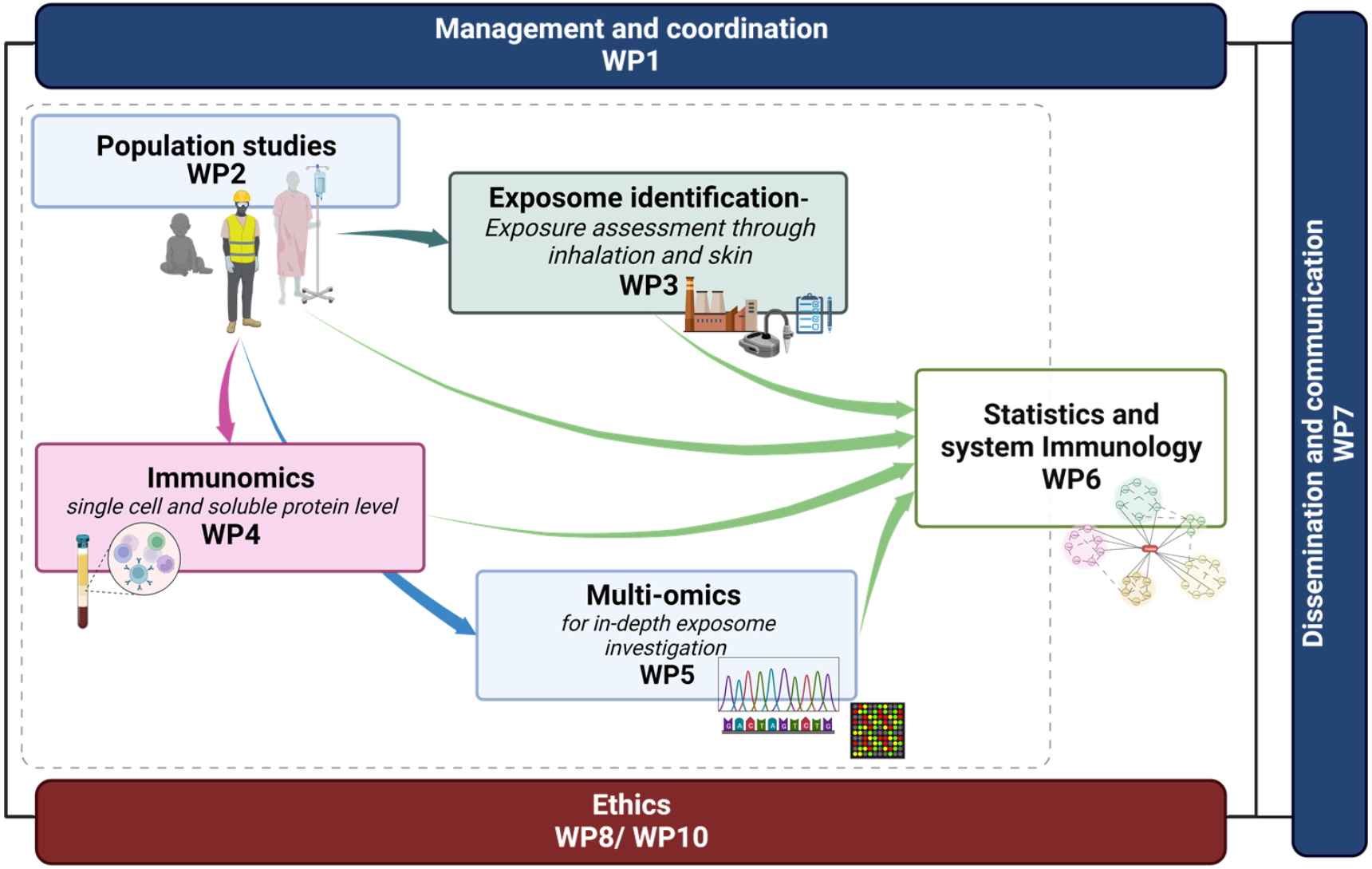
FIRST APPROACH: STARTING FROM THE EXPOSOME

We will begin with cohorts that cover the entire lifespan: general and birth cohorts (LifeLines, DOC*X and DOC*X Generation, ENVIRONAGE) and occupational cohorts (park workers, paint factory workers, miners, metallurgy workers, waste handlers and administrative workers).

SECOND APPROACH: STARTING FROM THE DISEASE

In this approach, we start from cohorts of people that have potentially exposure-related, immune-mediated diseases, like systemic sclerosis (SSc), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), sarcoidosis and hypersensitivity pneumonitis (HP).

How is the project organized…



The origin of the data…..

OCCUPATIONAL COHORTS

- Waste workers – Denmark
- Park workers – Spain
- Workers exposed to mineral dust and organic solvents – Romania

GENERAL POPULATION & BIRTH COHORTS

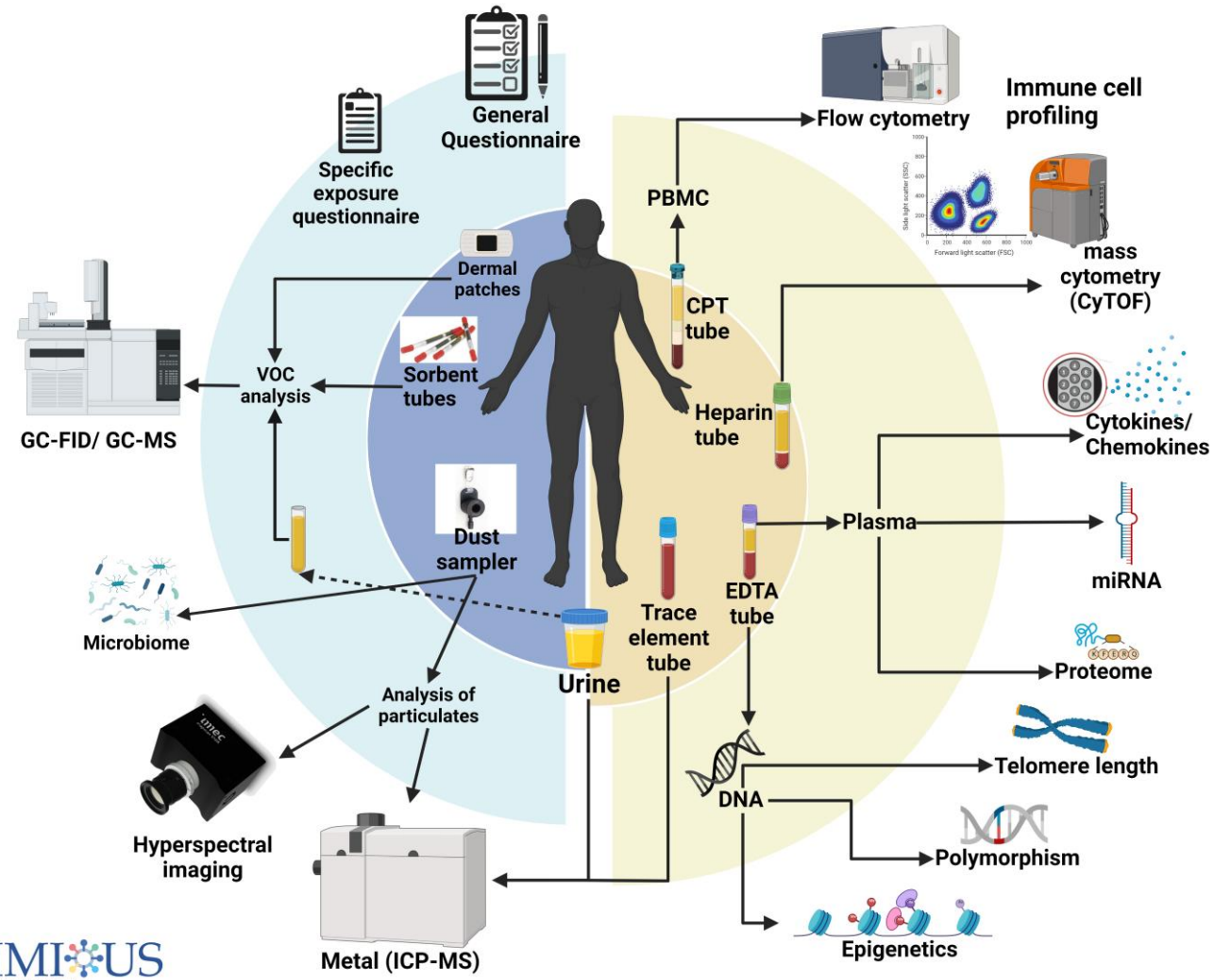
- The LifeLines Cohort Study – The Netherlands
- ENVIRonAGE birth cohort – Belgium
- DOC*X cohort – Denmark
- DOC*X generation – Denmark

DISEASE COHORTS

- Systemic Sclerosis (SS) – Belgium
- Rheumatoid Arthritis (RA) – Belgium
- Sarcoidosis – Belgium
- Systemic Lupus Erythematosus (SLE) – Belgium
- Hypersensitivity Pneumonitis (HP) – Spain

Study Population	Time course			
	Prenatal	0–18 years	18–65 years	> 65 years
The LifeLines Cohort				
ENVIRonAGE				
DOC*X				
DOC*X Generation				
Waste workers				
Park workers				
Workers exposed to mineral dust and organic solvents				
Sarcoidosis				
Hypersensitivity pneumonitis				
Systemic Sclerosis				
Systemic Lupus Erythematosus				
Rheumatoid Arthritis				

What data does EXIMIOUS collect?

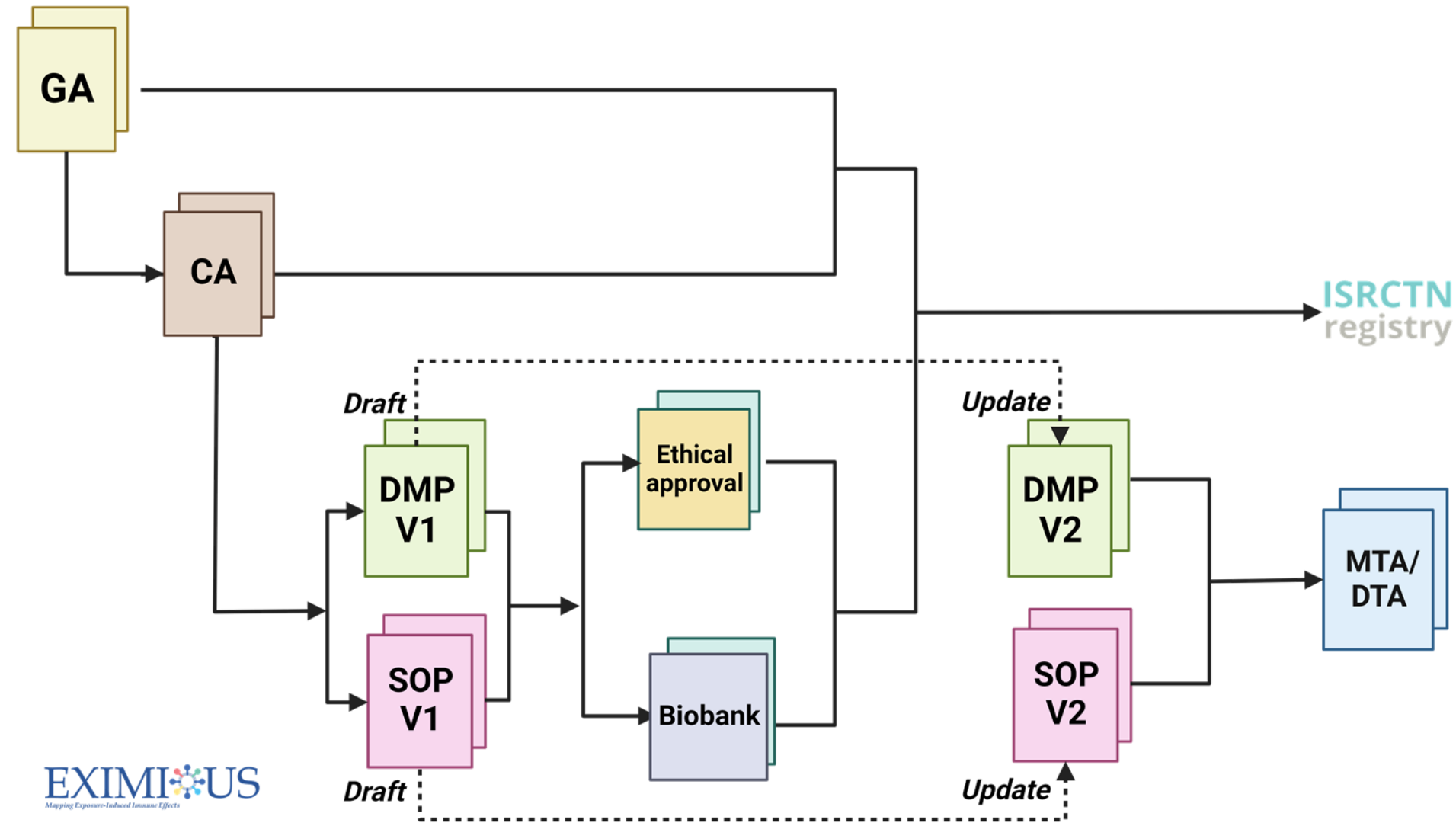


"adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed"

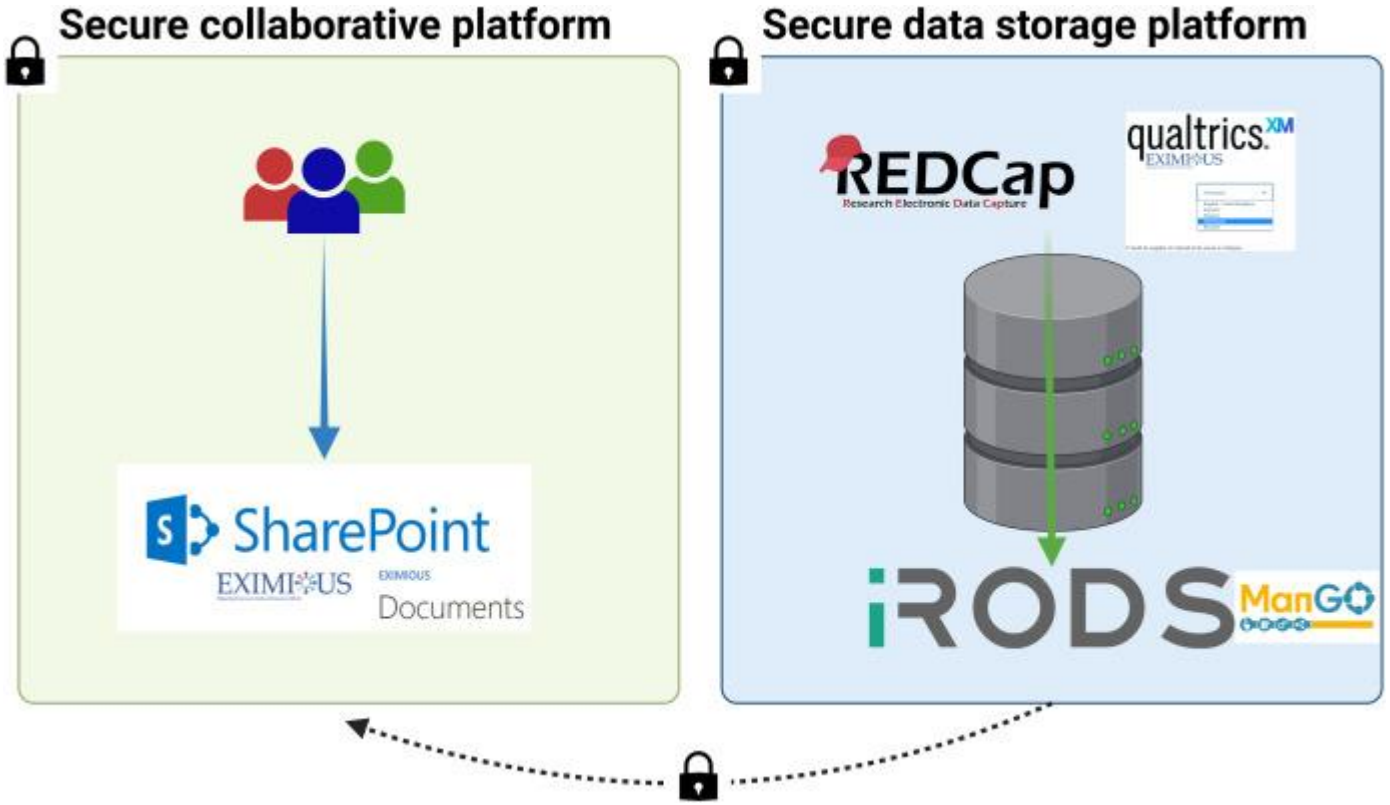
		TYPE OF DATA															
		Primary Biological Samples			Questionnaire Data				Clinical Data		Environmental Samples and Exposure Data						
		Blood	Urine	Other: BAL, ...	Health & medication	Sociodemographics	Lifestyle habits	Current and past exposures	Electronic patient files	Clinical assessment workers	Air	Mineral dust	Dermal patches	Risk assessment	Safety data sheets	Exposure profile
SOURCE OF DATA (PRIMARY / SECONDARY)	**DISEASE COHORTS**															
	Sarcoidosis and systemic sclerosis (KU Leuven)	X (PB)	X	(x)	X	X	X	X	X						(x)	X
	Systemic sclerosis, SLE and RA (UCL)	X (PB)	X	(x)	X	X	X	X	X						(x)	X
	Hypersensitivity Pneumonitis (VHIR)	X (PB)	X	(x)	X	X	X	X	X						(x)	X
	GENERAL AND BIRTH COHORTS															
	LifeLines (Uhasselt)	X (PB)	X		X	X	X	X								
	ENVIRONAGE (Uhasselt)	X (PB+CB)	X		X	X	X	X								
	DOC*X(Generation) (NRCWE/ RegionH)				X	X	X	X								
	OCCUPATIONAL COHORTS															
	Waste workers (NRCWE)	X (PB)	X		X	X	X	X			X	X	X	X	X	X
	Park workers (VHIR)	X (PB)	X		X	X	X	X			X	X	X	X	X	X
	Workers exposed to dust and solvents (UMFST)	X (PB)	X	(x)	X	X	X	X		(x)	X	X	X	X	X	X
	***Objective 1**: Delineating the exposome*	EXPOSOME														
	***Objective 2A**: Immunomics*	IMMUNOME		IMMUNOME					IMMUNOME							
	***Objective 2B**: Multi-omics*	OMICS		OMICS												
	***Objective 3**: Statistics and systems immunology*	COMBINED ANALYSIS														

The data management, legal and ethical workflow of the EXIMIOUS project

In accordance with *Article 5 EU GDPR* principles relating to the processing of personal data, i.e. the "***Data protection by design and by default***"



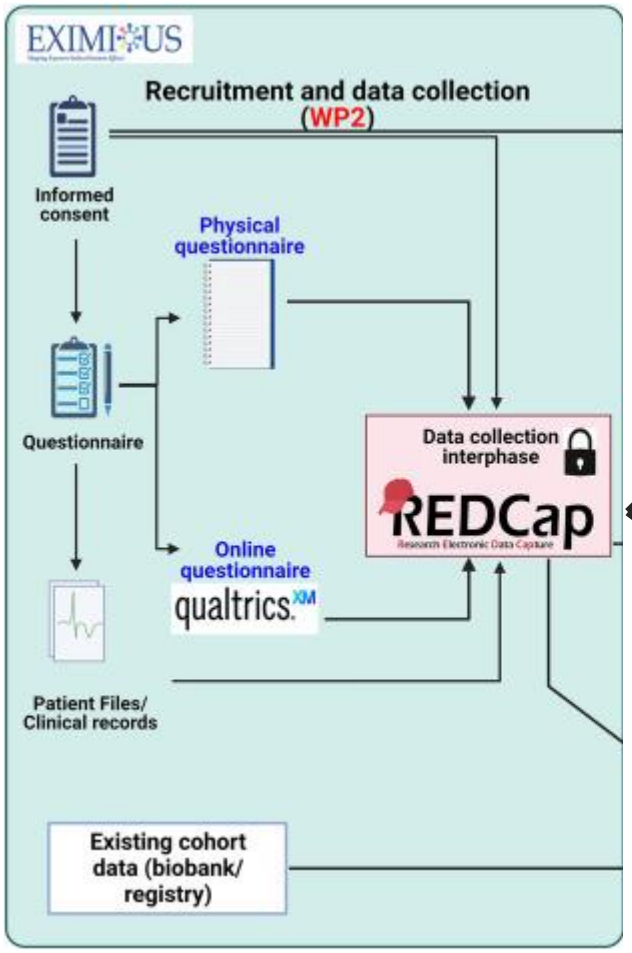
Separation of secure workspace in the EXIMIOUS project



Technical and organizational measures to safeguard data

- ***EXIMIOUS data managers***
- ***Data access groups***
- ***Data governance***
- ***Version control of data***

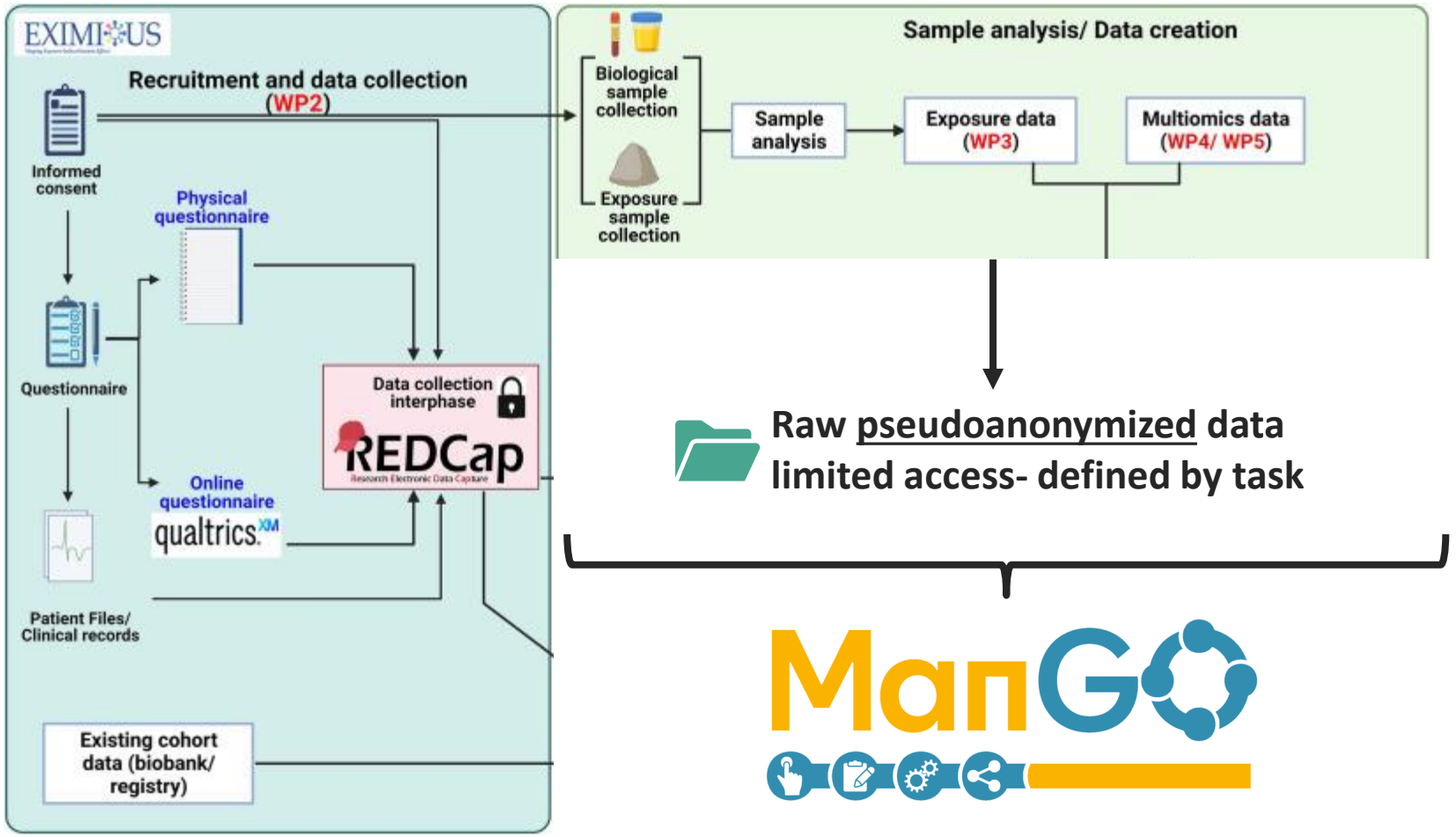
Data collection workflow



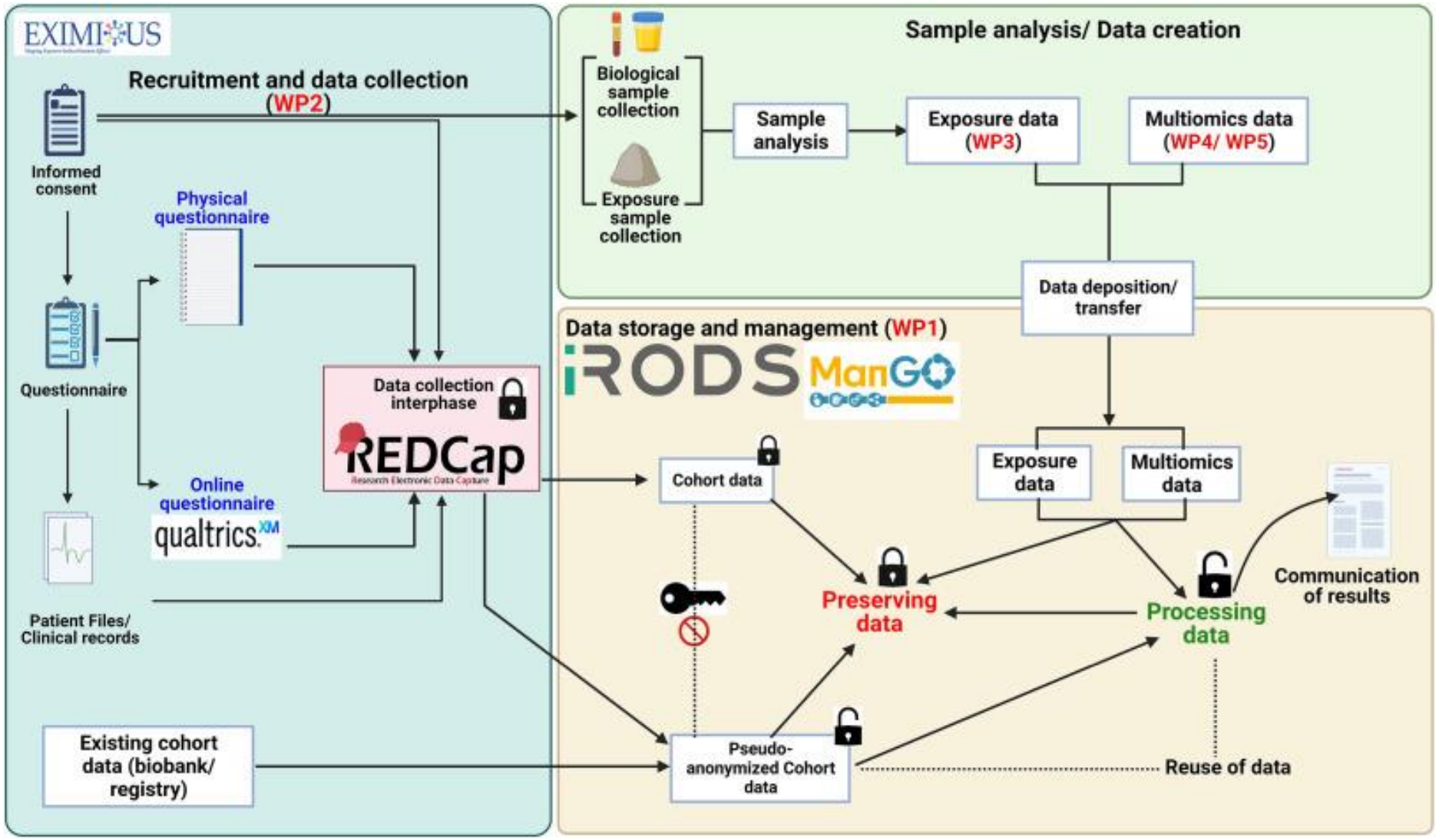
Raw data- no general access
Only Cohort owners have access

Raw <u>pseudoanonymized</u> data
limited access- defined by task

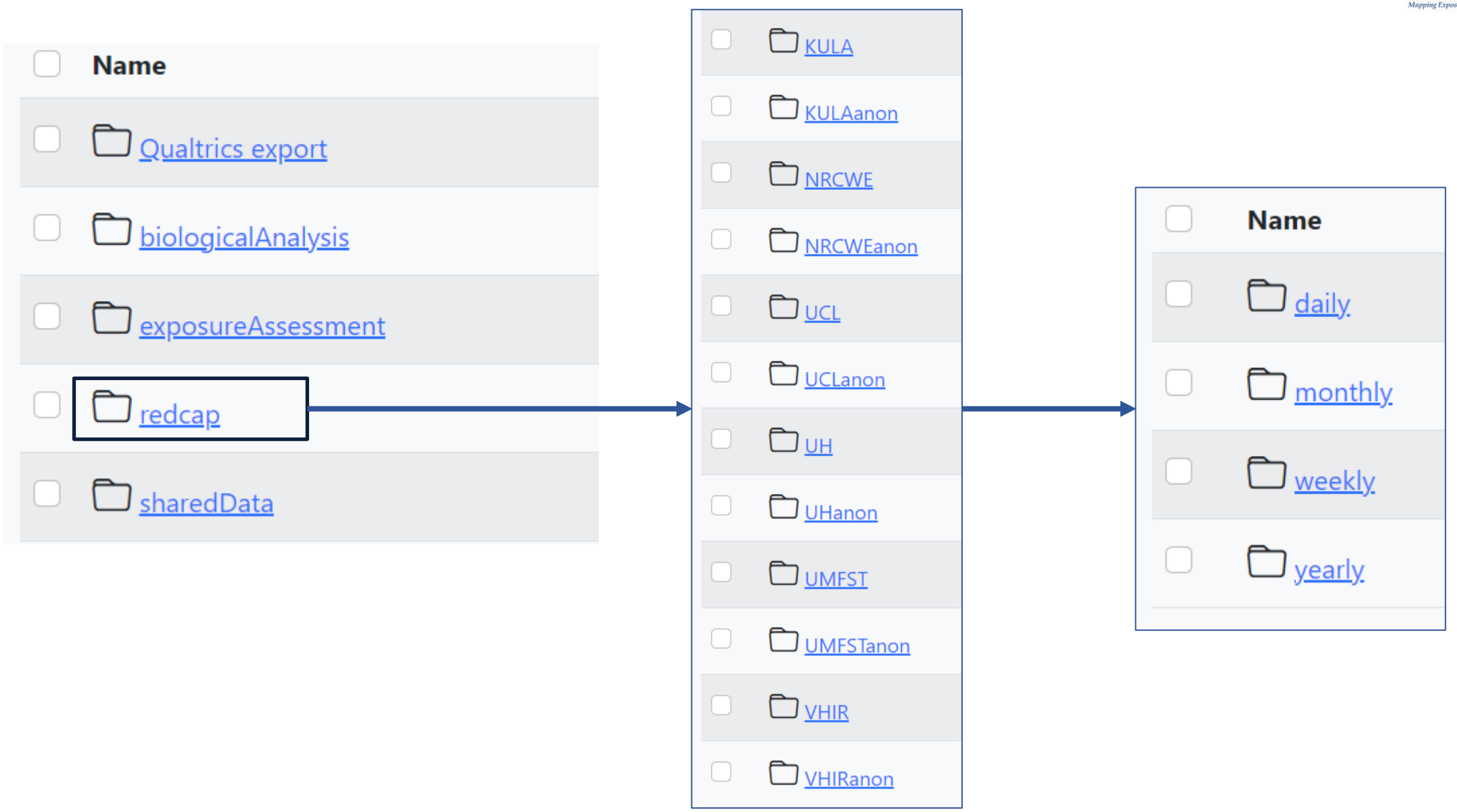
Data collection workflow

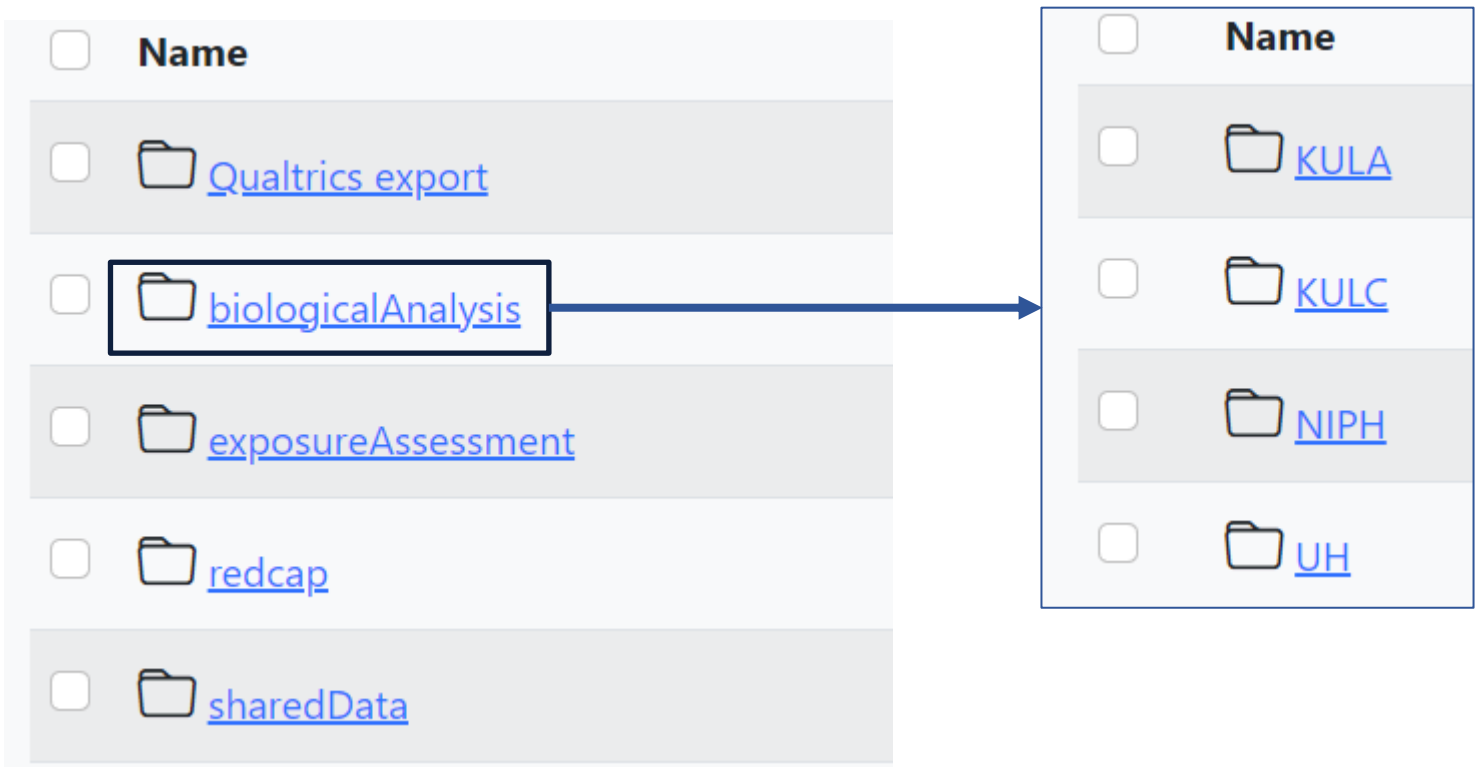


Data collection workflow



How does it look in ManGO?




Name
Qualtrics export
biologicalAnalysis
exposureAssessment
redcap
sharedData
Name
KULA
KULC
NIPH
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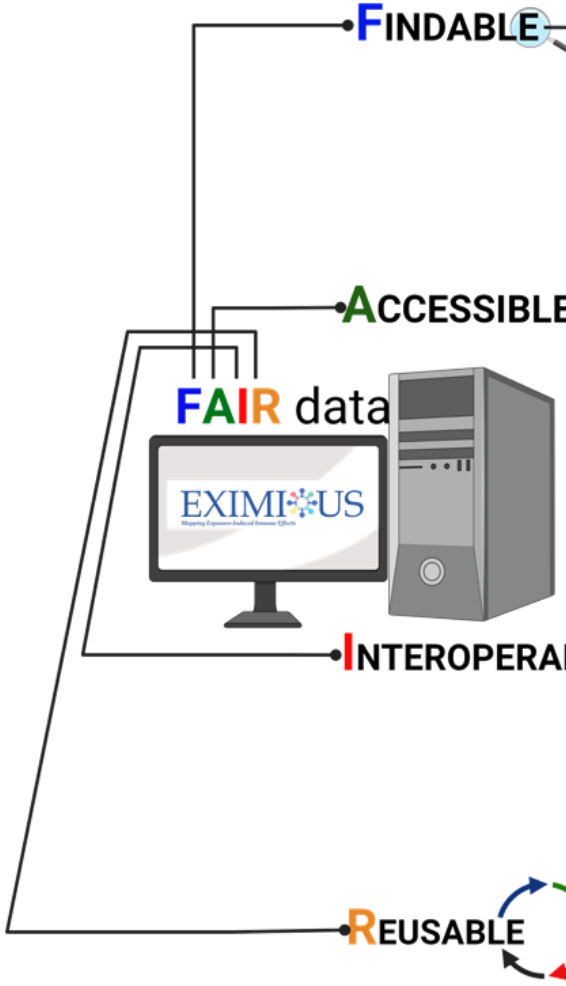
Making the data FAIR



FAIR checklist	How EXIMIOUS makes data FAIR?
F1. (meta)data are assigned a globally unique and persistent identifier **F2.** data are described with rich metadata (defined by R1 below) **F3.** metadata clearly and explicitly include the identifier of the data it describes **F4.** (meta)data are registered or indexed in a searchable resource	1. Persistent identifier assigned to ensure traceability of data, from collection, to transport and sharing and processing 2. Each data type generated in the project is described with rich metadata, metadata searchable in Data repository of EXIMIOUS (iRODS-Metalnx)
A1. (meta)data are retrievable by their identifier using a standardized communications protocol **A1.1** the protocol is open, free, and universally implementable **A1.2** the protocol allows for an authentication and authorization procedure, where necessary **A2.** metadata are accessible, even when the data are no longer available	1. IRODS (Metalnx) used for EXIMIOUS data repository 2. README file outlining process of data upload, download, addition of metadata, managing permission, search option 3. Access requires authorization, data access audited 4. Agreement for code of conduct for Data managers 5. Secure folder with restricted access, Shared folder for open data (within the project) 6. Different access rights created to make data "as open as possible and as closed as necessary"
I1. (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation. **I2.** (meta)data use vocabularies that follow FAIR principles **I3.** (meta)data include qualified references to other (meta)data	1. Readme file with description of file and resources to understand content 2. Rich metadata, with information of source of data, sample volume, sample preparation, analysis method, quality control, related publications (DOI) 3. Information on associated data 4. Data analysis script/ protocol
R1. meta(data) are richly described with a plurality of accurate and relevant attributes **R1.1.** (meta)data are released with a clear and accessible data usage license **R1.2.** (meta)data are associated with detailed provenance **R1.3.** (meta)data meet domain-relevant community standards	1. Project-level documentation (Study design, hypothesis, protocol, methodology, instrumentation) 2. File level documentation (explaining how datasets are linked, data dictionary explaining meaning of variables) 3. Metadata includes information of level of data, sampling and analysis method, version control 4. Data with restricted access- Data licensing to be decided on a case basis

EXIMIOUS
Mapping Exposure-Induced Immune Effects

DMP-CHECK

EXIMIOUS DMP-CHECK	Task	Means to achieve task (EXIMIOUS examples)	EXIMIOUS timeline (months)	Resources (Uploaded version of the documents might be available in course of time)	Check list
Project pre-award					
Defining data collection objective	Defining how all of the data is relevant and limited to the purposes of the project ('data minimization' principle)	Define clearly the research objectives, objectives of data collection, collection of personal information and defining how it is directly relevant and necessary to accomplish a specified task/ objective. (*Additional data minimization steps in EXIMIOUS are described in the manuscript*)	Pre-application	https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R1725	☐
Ethics and Integrity	Identify ethical considerations	Consult the EC self-assessment and the local ethics office of the applicant's institute	Pre-application		☐
	Complete the ethics self-assessment	Consult the EC self-assessment and the local ethics office of the applicant's institute	Pre-application	Adobe Acrobat Document https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/common/guidance/how-to-complete-your-ethics-self-assessment_en.pdf	☐
	Describe the clinical study (*For calls that involve clinical studies, participants might be required to add additional document to the application as annex to the proposal*)	Consult the EC self-assessment and the local ethics office of the applicant's institute	Pre-application	Adobe Acrobat Document https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/temp-form/af/information-on-clinical-studies_he_en.docx	☐
	Prepare a brief outline describing data management and personal data protection as requested by the funding agency	Consult the Research Data Management Helpdesk at applicants host institute	Pre-application	Adobe Acrobat Document https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/programme-guide_horizon_en.pdf	☐
Project Post-Award					
Contracts and agreements / Ethics review, Grant signature	Ethics review by funder	Reviewed by ethics officer (funding agency) multiple 'ethics requirements' become contractual obligations and are implemented in the grant agreement before the agreement could be signed. Ethics requirements due after project start are included in the grant agreement in the form of 'ethics deliverables' and are submitted to the EC.	0	Adobe Acrobat Document https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/programme-guide_horizon_en.pdf	☐
SOP		processing and storage; the order of sample collection; instructions for sample handling; time allowed from collection to processing and storage among others. At every step of the process, feedback was collected from cohort owners, lab technicians about ease and practicality of sampling and the protocol was updated for clarity.			
Ethics	Submit application(s) for ethical approval or amendments (as might be applicable) for each included study population	Based on the DMP V1 and SOP V1, cohort owners submitted their application to their respective institutional ethical committee for ethical approval keeping both National and EU regulations in mind.	8	https://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/ethics_en.htm	☐
Data management platforms	Select suitable data management platforms and define security measures	Consult the data management helpdesk at the coordinating institute and reach consensus among partners. Some of the selected platforms include: SharePoint- web-based collaborative platform; REDCap-Research Electronic Data Capture; Qualtrics- web-based survey tool; MetaInx - web application designed to work alongside iRODS	Continuous		☐
FINDABLE data provisions	F1. (Meta)data are assigned a globally unique and persistent identifier	1. Persistent identifier assigned to ensure traceability of data, from collection, to transport and sharing and processing 2. Each data type generated in the project is described with rich metadata, metadata searchable in data repository of EXIMIOUS (iRODS-MetaInx) (*Additional provisions are described in the manuscript*)	Continuous	Adobe Acrobat Document https://doi.org/10.1038/sdata.2016.18 https://force11.org/info/the-fair-data-principles/ https://force11.org/info/guiding-principles-for-findable-accessible-interoperable-and-re-usable-data-publishing-version-b1-0/	☐
	F2. Data are described with rich metadata (defined by R1 below)				☐
	F3. Metadata clearly and explicitly include the identifier of the data it describes				☐
	F4. (Meta)data are registered or indexed in a searchable resource				☐
ACCESSIBLE data provisions	A1. (Meta)data are retrievable by their identifier using a standardized communications protocol	1. IRODS (MetaInx) used for EXIMIOUS data repository 2. README file outlining process of data upload, download, addition of metadata, managing permission, search option	Continuous	Adobe Acrobat Document	☐
	A1.1 The protocol is open, free, and universally implementable				☐

ELSEVIER

Environmental Research

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It is not scientific enough… but it is important!

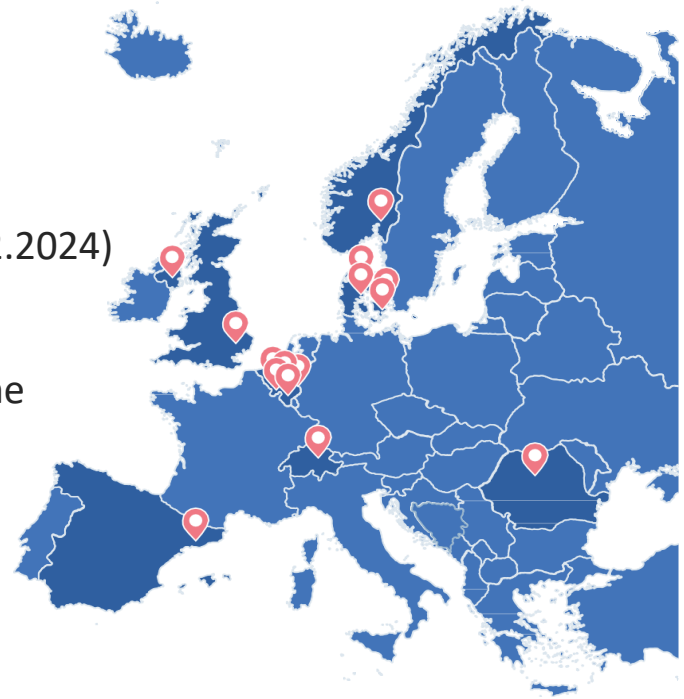
15 partners

7 countries across Europe

5 years (01.01.2020 - 31.12.2024)

1 of 9 projects within the European Human Exposome Network (EHEN)

MEMBER OF THE European Human Exposome NETWORK



EXIMIOUS_H2020

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