EIRENE PPP

Horizon Europe

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D2.2 – Roadmap for the development of EIRENE RI services

WP 2 – Development of services

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Abstract

EIRENE RI (Research Infrastructure for EnvIRonmental Exposure assessmeNt in Europe) fills the gap in the European infrastructural landscape and pioneers the first EU infrastructure on human exposome (environmental determinants of health). EIRENE PPP aims to prepare the implementation of EIRENE RI as a consolidated European research infrastructure enabling the development of advanced technologies and complementary services on the characterization of complex environmental exposures and their impact on the European population.

This deliverable describes the roadmap for developing EIRENE RI services. The roadmap builds further on the inventory of services (Deliverable 2.1) that has been submitted previously. Based on the inventory of services, synergies, and gaps in relation to other research infrastructures were identified. Also, a proposal is made on developing quality management schemes and harmonization criteria.

EIRENE, as a new research infrastructure, will promote European excellence in Environmental & Health research by providing European researchers with transnational and/or virtual access to harmonized capacities, unique services, and comprehensive data addressing the current and future needs of public authorities. The current deliverable contributes to this ultimate goal.

Introduction

WP2 Overview and Objectives

Work package two (WP2) of EIRENE PPP focuses on developing specific services. This WP is structured in three main tasks according to the grant agreement: (i) the core services to be provided by the EIRENE RI will be identified, considering services already provided in other ESFRI RI to avoid duplicities. The identified services are structured in the pillar structure defined in WP1; (ii) the capacity and readiness to offer these services to the user community is assessed; (iii) rules and procedures for a user's access to such services will be elaborated.

WP2 Deliverables

D2.1 - List of EIRENE Core services according to the pillar structure (submitted M18).
D2.2 - Roadmap for the development of EIRENE RI services (due M24)
D2.3 - EIRENE RI Service Access rules & Procedures (due M30)

Deliverable 2.1- Recap

The core services of EIRENE were determined in the second year of the PPP project (M18), and reported in Deliverable D2.1. The list of core services was based on

- research needs identified in the EIRENE research strategy in WP1
- proposed EIRENE structure of six pillars developed in WP1 and described in D1.2 (EIRENE RI Architecture)
- reports of National Nodes (D1.1) and
- additional survey mapping capacities, needs, and already existing services in more detail across the EIRENE partners/national nodes.

Deliverable 2.1 was submitted in M18 and described 10 services (Table 1). A more detailed description of the services can be found in Annex 1. These services were categorized according to a pillar structure (Table 2). Most of the countries indicated that the list of services they provided is complete. Furthermore, most countries indicated that their services are unique for the country. However, many could not judge whether their service is unique on a European level, i.e., whether it is not already provided by other research infrastructures. This topic will require additional work (Roadmap point 1: gaps and synergies). Also, many countries did not yet discuss the list with their stakeholders. This will be done in 2025. Annex 2 shows the status per country.

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Table 1 Description of core services in the field of Exposure Research Europe.

Nr	Service description
1	Collecting and providing samples (including bio, environmental, and specimen banks) to determine exogenous substances
2	Access to cohort study or survey data on an individual level
3	Measurements of exogenous substances including target and nontargeted measurements of chemical mixtures (or other pollutants) as well as parent and transformation exposure markers in humans and the environment
4	Omics-based analysis of markers of biological response (separate: metabolomics, lipidomics, adductomics, (epi)genomics, metagenomics/microbiomics, transcriptomics, proteomics, phenomics)
5	Quantification/determination of toxicity (human- and ecological), pathways and modes of action (in-vivo, ex-vivo, in-vitro, in-silico)
6	Biostatistical and/or bioinformatics tools and platforms to investigate the exposome and human health interactions
7	Databases and exposure maps on environmental factors (e.g. pollutants, temperature, noise, socio-economic, lifestyle)
8	FAIR cataloging of exposome data (e.g. cohorts, algorithms)
9	Training offerings in the field of exposome research and Training needs*
10	Additional service(s) **

* These outcomes are not part of this deliverable but will be reported under WP6.In the overviews below, these are omitted.

** Services that were not listed could be added here.

Table 2 *Pillar structure of the EIRENE core services and their corresponding domains.*[1]

Pillars	Access mode			Domain	EIRENE services classification
	Physical	Remote	Virtual		
A Chemical profiling	✓	✓		Laboratory capacities for chemical profiling (selective / non-selective data acquisition)	(Target/non-target) measurement of exogenous substances (parent compound and transformation products) and their mixtures in the environment and human biofluids and tissues
B Toxicological profiling	✓	✓		Laboratory capacities for hazard assessment (non-animal toxicological models to test toxicity of chemicals, their mixtures & environmental samples	Quantification/determination of toxicity (human and eco-adverse outcome pathways and modes of action in-vivo, ex-vivo, in-vitro, in-silico)
C Biological Profiling	✓	✓		Laboratory capacities for biological profiling (elucidating the impact of toxic exposures on health)	Omics-based markers of biological response (both MS-based and sequencing technologies), e.g., (epi)genomics, transcriptomics, metagenomics/microbiomics, proteomics, metabolomics, lipidomics, adductomics
D Environmental data & samples		✓	✓	Data from large-scale longitudinal environmental (air, indoor, soil, food, consumer products – on-site, remote, satellite) monitoring for assessing the external exposome	Databases and portals presenting environmental (pollutants, temperature, noise), exposure maps, and other tools that can be further combined with socioeconomic and/or lifestyle data Biobanked samples enabling delivery of such data Access to monitoring networks enabling collection of such data/samples
E Human data & samples		✓	✓	Data from longitudinal population cohorts covering various groups, cross-sectional studies, health surveys, and clinical studies as an information source on population exposure and health	Databases and portals presenting human environmental (chemical biomonitoring, temperature, noise) and socioeconomic exposure, behaviour, lifestyle, and health data Biobanked samples enabling delivery of such data Access to population studies enabling collection of such data/samples
F Tools		✓	✓	Data management, processing, federated analysis, modeling, and presentation tools and platforms, computational capacities and virtual laboratories	Fair cataloguing of exposome data (e.g., cohorts, algorithms) Biostatistical and/or bioinformatics tools and platforms for investigating exposome-human health interactions

[1] Page 4 of the document *Deliverable D2.1 – List of EIRENE core services, WP – Development of services, WP Leader UU, submitted March 2024*

ROADMAP

Figure 1 shows the timeline of the Preparatory phase (2022-2025), the Implementation phase (2026-2030), and the Operation phase (2031-). The roadmap for the development of EIRENE services is described in this deliverable.

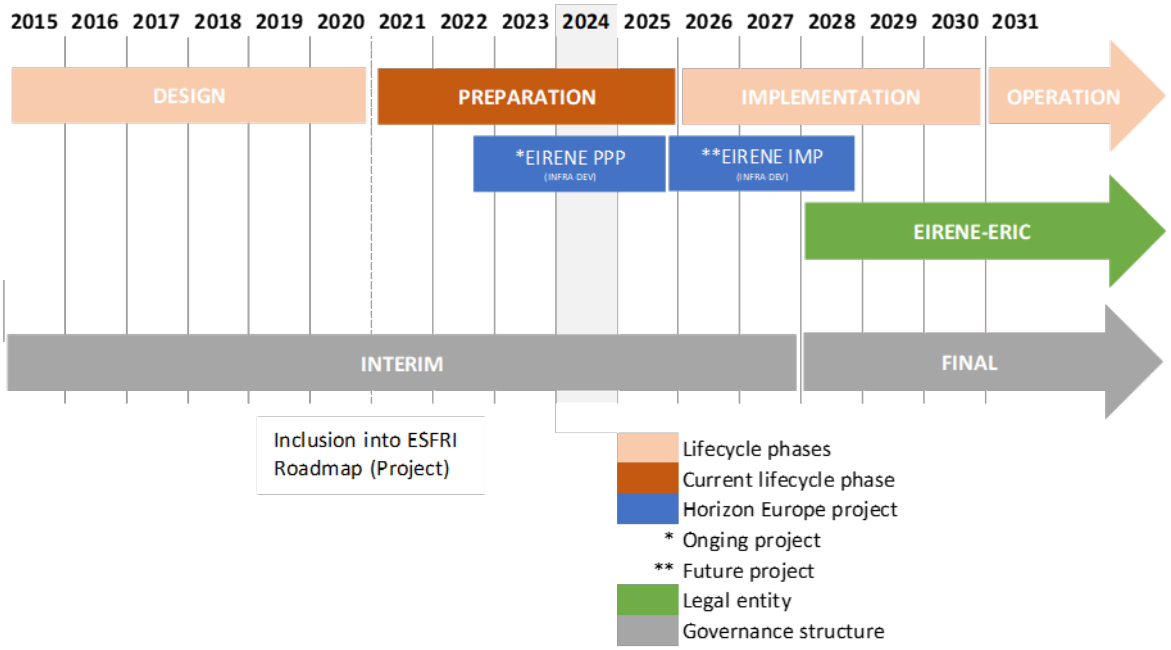

Figure 1. Timeline of EIRENE Preparatory, Implementation, and Operation Phases.

Selection of services (2024)

Based on the inventory of available services, a selection has to be made of which services will take part in the EIRENE infrastructure. Multiple criteria are used to make this decision. First, service providers must be willing to act as service providers to the user community. The facility has to have sufficient capacity for the demand and has to fit the EIRENE pillar structure. The services inventory will be presented in the EIRENE/IHEN (International Human Exposome Network) meeting in October 2024. IHEN is an international network of exposome researchers and stakeholders that are future users of the infrastructure. Therefore, this meeting will be instrumental in discussing the service inventory with partners, potential users and other stakeholders. Based on the outcomes, a first selection of services will be made of services that will be available via an online request procedure. A good balance over the pillar structure will be aimed for.

Evaluation of the level of commitment and readiness (2025)

The service providers of the selected services will be asked for their level of commitment and readiness. Ascertaining whether a service provider is committed requires consideration of costs and capacity. In a pilot done in the Netherlands we asked the previously identified service providers to complete the EIRENE cost sheet (see Annex 3), to estimate the costs of the service and to estimate the capacity. From this pilot it became clear that 75% of the facilities that filled in the questionnaire filled in this cost sheets. The other 25% decided not to continue as they considered themselves ineligible or not yet ready to act as a service provider. Crucial

for this were discussions within their organizations about work to be done to be a service provider and the uniqueness of their service to the exposome field, among other things. Therefore, cost sheet inventory will be rolled out over all European potential EIRENE service providers in 2025 for 2 reasons: i) to obtain information about total costs and service unit costs and ii) to get the available capacity clear. Furthermore, that survey round will enable to obtain further confirmation that there is synergy but no redundancy with other ESFRIs.

Identify pilot service providers (2024)

In the survey of D2.1, the inventory of services, the institutes indicated whether they would like to participate in a pilot. Within Deliverables 4.1 and 4.2, the pilots are described and worked out. A selection of services is made based on the readiness to already developed access procedures.

Perform Pilots (2025)

Pilots are performed in a selection of service providers across the pillars, for .. services in total to test all procedures (from applicant request until provision of results). Deliverables 4.1 and 4.2 describe in detail how this will be performed.

Open Access System (2025)

At the end of 2025, the first version of the Open Access System will be available to users for requests for the use of EIRENE services. The system is currently being developed and tested.

In order for a service applicant to gain access to a service, an online platform needs to be put in place, including a catalogue, login functionalities, a tracking system to log the applications, etcetera. Furthermore, user support and helpdesk should be developed.

Consolidate way of working (2025-2026)

The way of working in the future infrastructure will need discussions around several themes to come to a consolidated plan. The themes are:

- Central Coordination Units EIRENE is a distributed research infrastructure offering a wide range of services (see Table 2). Therefore, specific institutes may serve as Central Coordination Units for a specific pillar because of their expertise in this service field. They will be in charge of judging application requests.
- Political landscape. National financial support for the RI depends on the political climate in the member states. National nodes may have to work smartly together with their national research infrastructures to be as lean and effective as possible. This may have implications for the way the ERIC is set up. This needs continuous monitoring.
- Evaluation of proposals/requests. Scientific quality and capacity will be key. The pilot will simulate various scenarios. A first check of the technical feasibility may be needed before the scientific committee judges the scientific excellence. Other points to decide on are routine/excellence, time/timings of the evaluation period, and committee composition.
- QA/QC and Certification. Services will require a certain level of quality. To meet the desired quality, QA/QC procedures must be implemented. Certification of specific services (e.g. laboratories) may be needed. Per pillar, this has to be worked out, and proposals to be made to discuss and consolidate. Expert groups will be in the lead to deliver this.

- Amount of service providers. From the survey, it appears that there are many service providers per pillar, probably even after the criteria check. The optimal number of service providers per pillar and deciding who takes up a certain task should be decided.
- Synergies and complementarity with other ESFRIs. When other ESFRIs are better at specific tasks and services than EIRENE, this should be acknowledged and acted upon. For instance, if an RI other than EIRENE has capacity and know-how that is needed for EIRENE, this should be explored. An example is the capacity of raw data storage of untargeted metabolomics data at EMBL.
- Communication module. This will be located at the Head Office. The architecture needs to be developed.
- Data sharing. Data-sharing procedures using material transfer agreements (MDTA) must be explored. Option 1) make an ERIC specific (M)DTA to transfer materials and data with the requester. Option 2) use existing (M)DTAs from the service provider and applicant. In the latter case, a check by the ERIC on minimal requirements of what to arrange might be needed. Typical items to define are how and for what are the data used, who is the data owner, what terms are involved, how acknowledgements are arranged, GDPR, liability, publication rights, and IP, among other items.
- Open access. The data should become as open as possible and as closed as (legally) needed.

These discussions will result in key documents for implementation and operation phase:

  - documents defining the relationship, responsibilities, and duties of all the EIRENE RI actors and participants
  - procedures for accepting new members, guidance on the development of national hubs,
  - operational documents for user's access, material and data transfer agreements, liability and IPR rules, etc.

Implementation phase (2026-2030)

Key documents for the implementation phase are finalized and put into action.

The services that have been selected and comply with the EIRENE criteria will be offered to users via a central portal.

In time, multiple other access procedures of selected services that were not yet tested will be tested and added to the list of services.

Training is the responsibility of the facility and should be arranged for the applicant. This is especially needed in the case of transnational physical access.

Evaluation and monitoring should be in place at the national and European levels.

Operational phase (2030-)

Exposome Research Infrastructure is well established infrastructure in the Food, Health and Environment Infrastructure landscape.

Sustainable financial planning has been implemented to maintain and develop the infrastructure

KPIs are put in place to monitor performance

Critical selection of (new) services by the board will prevent overlap with other infrastructures and lead to maximal synergy and uniqueness.

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ANNEXES

Annex 1 Description of Services

Service 1 Collecting and providing samples (including bio, environmental, and specimen banks) to determine exogenous substances

Explanation Presence of biobanks, environmental banks and specimen banks as well as services for sample collection.

Describe the services your institution currently offers regarding service 1. The collection and provision of samples (including bio, environmental, and specimen banks) to determine exogenous substances.

Service 2 Access to human health and/or exposure data

The following questions are regarding the institute's access to cohort study or survey data on an individual level. It concerns the available cohort studies (either individual cohorts or existing cohort infrastructures) that are enriched with exposure data available at your institute.

Service 3 Measurements of exogenous substances including targeted- and non-targeted measurements of chemical mixtures (or other pollutants) as well as parent and transformation exposure markers in humans and the environment

Explanation For each service offered, please specify whether environmental samples, biological specimens, or both can be handled and in which matrices.

Information that was requested in the survey:
Type exogenous substance: Non-targeted/Suspect screening of xenobiotics (include list of xenobiotics, this can be at group level, e.g. food additives, drugs)
Type of measurement: LC-HRMS with semi-quantitative results.
Biological specimens/matrices: urine, serum, plasma, breast milk, placenta.

Service 4 Omics-based analysis of markers of biological response (separate: metabolomics, lipidomics, adductomics, (epi)genomics, metagenomics/microbiomics, transcriptomics, proteomics, phenomics).

Explanation For each service offered, please describe the type of matrices employed as well as the "omics" applied.

Information that was requested in the survey:

Type of omics: LC-MS/MS proteomics
Matrices: plasma, in vitro samples
Markers: both targeted as untargeted proteins (specify if possible)
Other info: e.g. qualitative and quantitative, type of equipment

Service 5 Quantification/determination of toxicity (human- and ecological), pathways and modes of action (in-vivo, ex-vivo, in-vitro, in-silico)

Explanation for each service offered, please include if it is in vivo, ex-vivo, in vitro, or in silico.

Information that was requested in the survey:

In vitro assessment - Safety and preclinical testing
Type of models: in vitro organ specific cell models, 2D/3D organoids of liver/hepatotoxicity, gut and skin epithelia, kidney, reprotoxicity - testicular models.
Type of samples: chemicals, mixtures, matrices (please specify further)
Mechanistic endpoints: nuclear receptor reporter gene assays, cell proliferation, tumor promotion and

progression.
Other info: e.g. certifications, specific and/or unique equipment.

Service 6 Biostatistical and/or bioinformatics tools and platforms to investigate the exposome and human health interactions

Information that was requested in the survey:

Include description of biostatistical- and bioinformatic pipelines available, including type of data (e.g. epigenetics, transcriptomics, metabolomics), type of analysis, type of methodology, type of tools and platforms.

Service 7 Databases and exposure maps on environmental factors (e.g. pollutants, temperature, noise, socio-economic, life style)

Explanation For each database and/or exposure maps indicate the geographic area (e.g. region, country, EU wide etc) for which this is provided, type of environmental factor.

Information that was requested in the survey:

Include type of environmental factor available, type of maps (incl geographical area (e.g. region, country, EU wide, etc)), type of platforms used.

Service 8 FAIR cataloging of exposome data (e.g. cohorts, algorithms)
Explanation Services that aim to make exposome data FAIR: findable, accessible, interoperable and reusable.

Information that was requested in the survey:

Describe processes, systems and/or tools that makes your data FAIR (findable, accessible, interoperable and reusable).

Service 9 Training offerings *part of WP 6, not part of WP2*

Explanation Training offerings are training/education modules that you can offer to the EIRENE Infrastructure. These are focused on, or highly related to, the services you filled in this survey thus far. Also, they can be diverse e.g., academic courses and programmes, summer schools, tailored trainings, workshops.

Service 10

Additional service(s)

Information that was requested in the survey:

Describe any additional service(s) currently offered at your institute that have not yet been mentioned in sections 1-9

Annex 2

Outcome of D2.1 the survey on the comparison of the offered services in relation to 1) completeness, 2) uniqueness in own country, 3) uniqueness in Europe and 4) stakeholder engagement. Green=yes, orange=partially, red=no, yellow is unknown/unsure.

	1	2	3	4
	Is the list of services complete for your country?	Are the services for EIRENE in your country unique for your country (and not provided by another ESFRI in your country)	Are the services for EIRENE in your country unique for Europe and not provided by another ESFRI in Europe	Were stakeholders consulted to discuss the service list?
Austria				
Belgium				
Cyprus				
Czech Republic				
Denmark				
Finland				
France				
Germany				
Greece				
Italy				
Luxembourg				
Netherlands				
Norway				
Slovakia				
Slovenia				
Sweden				

Annex 3

Dear EIRENE-NL partner, please fill in this cost sheet for each service you intend to provide to the EIRENE Research Infrastructure as indicated in the EIRENE survey you participated in. You can fill out the worksheet per service you provide. You find 5 copies of the sheets. If you have more than 5 services you provide, you can add worksheet copies yourself. At the right you find explanation of the fields, and at the end of the sheet there is room for feedback. Thanks so much for your participation! The EIRENE-NL coordination team.

Country				
University/Institution				
Department & Unit				
Contact Person Name				
EIRENE Service Category				
Service Name				
Access Mode				
Unit of Access				
Explain/Describe the Unit of Access				
Reference Period	From:	2022	To:	2023

A. Type of Direct Cost (choose from dropdown list)	Comments	Direct Costs (€)
Total A		**0,00**

B. Category of staff [4]	FTE	Comments	Personnel Costs (€)
Total B			**0,00**

C. Indirect eligible costs: 25% x (A+B)	0,00
D. Total access costs = A+B+C	0,00
E. Total quantity of access provided to all users (i.e. both internal and external)	0
F. Unit cost =D/E	**#DIV/0!**
H. Total available quantity of access (i.e., capacity)	**0**
I. Utilization of capacity (E/H*100)	#DIV/0!
J. How much of H: "total available quantity of access " can you provide to EIRENE	0
K. Utilization of capacity for EIRENE (J/H*100)	#DIV/0!

Explain how you estimated (H) the capacity	
Any other remarks, questions, unclarities	