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1. Introduction

This deliverable represents the starting point for the ELSI (Ethics, Legal and Societal Implication) guidelines that will be adopted for the Research Infrastructure for EnvIRonmental Exposure assessmeNt in Europe (EIRENE RI).

EIRENE RI, which was prioritised in the 2021 Update of the ESFRI Roadmap, fills the gap in the European infrastructural landscape and pioneers the first EU infrastructure on the human exposome (environmental determinants of health). The EIRENE PPP (Preparatory Phase Project) was launched to prepare the implementation of the EIRENE RI as a consolidated European research infrastructure, enabling the development of advanced technologies and complementary services, for the characterization of complex environmental exposures and their impact on the European population.

The ELSI guidelines will have to ensure that personal data (defined in the General Data Protection Regulation (see below) as any information relating to an identified or identifiable natural person (the 'data subject')), sensitive data and human biological samples are collected, stored, handled, transferred, and analysed following legal rules and ethical guidelines, and that the rights of the data subjects are protected and guaranteed.

These guidelines will ensure that the processing of data complies with all national and EU level ethical and legal considerations, in particular, the General Data Protection Regulation (GDPR) (Regulation (EU) 2016/679) and the Clinical Trials on Medicinal Products for Human Use Regulation (CTMP) (Regulation (EU) No 536/2014), the latter to be considered as a reference despite the fact that EIRENE RI will not carry out clinical trials. The aim of the GDPR is to protect the personal data (defined in GDPR as 'any information relating to an identified or identifiable natural person' (the 'data subject')) of individuals in the EU and the EEA, and to harmonise data protection rules across the EU member states. GDPR regulates the rights and controls that data subjects have over their personal data, such as the right to access, erase, port, or object to the processing of their data. GDPR also imposes obligations and responsibilities on data controllers and processors, such as the duty to inform, secure, report, and comply with the data protection principles.

The guidelines will also ensure that the storage and use of human biological samples complies with all national and EU-level ethical and legal considerations. In particular, Directive 2004/23/EC on quality and safety in the therapeutic use and transplantation of tissues (European Council, 2004), the European Convention on Human Rights and Biomedicine (Council of Europe, 1997) and the Recommendation (Rec(2006)420) on research with human biological materials (Council of Europe, 2006).

A separate Data Management Plan deliverable (D3.1) will be provided based on the current deliverable.

The EIRENE RI ELSI 'living' guidelines will take advantage of former or ongoing EU initiatives (e.g., HBM4EU (the European Human Biomonitoring project under H2020), the European research infrastructure for biobanking (BBMRI-ERIC), and the Partnership for the Assessment of Risk of chemicals (PARC)) in which sensitive personal data and human biological sample management have been or are among the core activities. The guidelines will ensure that the EIRENE RI consortium fulfils its legal and ethical obligations.

2. Difference between Law and Ethics

Both Law and Ethics establish rules and principles, which are implemented and followed to ensure personal safety, social order, and adherence to social mores. The main difference between law and ethics is that a law defines binding rules to be applied at the local or national levels (generally speaking international treaties, conventions, recommendations require national ratification) while ethics define guidelines.

According to common understanding the major differences include meaning, objective, obligation, etc. (Table 1).

Table 1 - Differences between law and ethics
(*modified after: https://keydifferences.com/difference-between-law-and-ethics.html*)

Basis for Comparison	Law	Ethics
Definition (https://dictionary .cambridge.org)	System of binding rules of a particular country, group, or area of activity that governs the whole society and the actions of its individual members	Set of moral principles that guides people concerning basic human moral conduct
Objective	Pursue personal safety and social order	Act according a set of beliefs about what is morally right and wrong
Governed by	Government	Individual, Legal and Professional norms
Expression	Expressed and published in writing	In general, they are abstract but can be written
In case of breach	Subject to monetary fine or criminal persecution	Behaviour widely deprecated and disciplined according to internal rules
Binding	Law has a legal binding	Ethics do not have a binding nature

In recent years, the massive mainly digital collection of personal data from individuals has led to an increased attention on the protection of the rights of data subjects. This coincides with the growth of research on human health and the increase of data collection alongside the open access principles of research data. Ethical guidelines were used as the basis for legislation such as the GDPR (EC, 2016) and CTMP (EC, 2014). In addition to the GDPR, national legislation or related EU measures will also apply to research in EIRENE.

3. Ethical and Bioethical Principles in EIRENE RI

EIRENE RI will offer a new approach to the assessment of human environmental exposures to pollutants and their impacts through the "*holistic exposome concept [*that] *shifts focus from the individual determinants of health to the interdisciplinary assessment of a wide range of factors including indoor and outdoor environment, socioeconomics, lifestyle, and the individual's ability to cope with various stressors such as infection or stress*".

This population-based research will assess, among other things, chemical exposures and their downstream biological effects through harmonised cohort studies based on *in-vitro*, *ex-vivo,* and *in-silico* studies that can help to identify causal exposure-response relationships.

As cohort studies will serve as research platforms that provide access to personal data and biological samples to researchers over many years, ELSI guidelines will be key in handling this data. Such sensitive personal information needs appropriate protection regarding: "*recruitment, especially parental authority to include a child in research; initial parental consent and subsequent assent and/or consent from the maturing child; withdrawal by data subject; confidentiality and sample/data protection; handling personal sensitive information; and disclosure of results*", for example (Ries et al., 2010).

Population-based (cohort) research entails collection, handling and analysis of personal data. Some of these personal data are sensitive data as defined in the GDPR, including genetic data and data concerning health[1]. The difference between personal data and sensitive personal data is that the GDPR prohibits processing sensitive personal data with some specific exemptions. . Therefore, specific consent should be expressed for processing cohort data. Among the list of exemptions, the ones reported below should be considered:

- You have obtained explicit consent from the individual, unless prohibited by law.
- There are reasons of substantial public interest.
- There are public health reasons for the processing (i.e., the prevention of epidemics).
- For scientific, archival, historic, research or statistic purposes (pseudonymized).

As such GDPR does not specify any additional protective measures to be taken for sensitive data, but in practice making a distinction may be sensible as the (ethical and legal) consequences of non-compliance may be higher for sensitive data.

All EEA countries (EU members and Norway, Liechtenstein and Iceland) have adopted GDPR in their national legislation. However, some countries may have additional (more stringent and based on the so-called 'opening clauses') privacy protection regulation. Therefore, regulatory compliance must always be verified at the national level. For non-EEA countries the EU can determine whether a country outside the EU offers an adequate level of data protection, and adopt an adequacy decision for this country. Such adequacy decision allows that personal data can flow from EEA countries to this third country.

Handling of personal data, be they sensitive or not, relies on three basic cornerstones (Art. 25 Reg (EU) 2016/679):

- informed consent to be given by the data subject;
- data minimisation;
- appropriate technical and organisational data protection measures to be taken by all parties handling the data along the data lifecycle, such as pseudonymization.

Although pseudonymisation is good practice for working with personal data, pseudonymised data is still personal data and hence subject to GDPR.

[1] Including all elements related to health, namely health status, including morbidity and disability, the determinants having an effect on that health status, healthcare needs, resources allocated to healthcare, the provision of, and universal access to, health care as well as healthcare expenditure and financing, and the causes of mortality (GDPR Article 9.1).

Data will need to be treated and curated while fully respecting bioethical considerations, international and national laws, and continuously paying attention to changes in the regulations for storing, sharing, and handling data that may occur during the lifetime of the RI.

4. Open Science and FAIR data

EIRENE RI and RIs in general, embody Open Science, as they integrate previously scattered capacities into an efficient network. including access rules, security policies, and strategies on archiving, curation, and long-term preservation of data. Open science is premised upon broad access to scientific knowledge, tools, data, and publications. It promotes accurate verification of scientific results, reduces duplicities, and increases efficiency, productivity, cost effectiveness, collaboration, innovation, and trust in science.

Data management in EIRENE RI will follow the FAIR (Findable, Accessible, Interoperable, Reusable) principles. The FAIR principles are a prerequisite for efficient reuse of data within and across research domains. However, they do not imply open access to data. EIRENE RI adopts the principle 'as open as possible, as closed as necessary'. The latter is particularly important for the (re)use of personal data. Findability and reusability of data will be guaranteed through the open publication of rich metadata. Interoperability will be enhanced through the use of harmonised standards for (meta)data and semantic annotations. Actual access to the data will be granted in line with the ELSI guidelines. Access conditions and procedures will be made explicit in the metadata.

Before defining these guidelines, it must be clarified how the available samples and data as well as the samples and data expected to be collected at national and European level in the future will be managed in EIRENE RI at national or/and centralised EIRENE RI level.

5. Data in EIRENE RI

Within the EIRENE RI, existing and newly generated data will be used to further understanding the links, or lack thereof, between exposure and health effects and outcomes.

Existing Data

Reuse of existing personal data may be constrained especially by the initial informed consent signed by the data subject, e.g., by including a narrowly defined purpose for processing the data, statements on the period of data storage, and statements that limit data exchange to third parties. Additionally, the data owner/custodian may not be an EIRENE partner, which may complicate dialogue on data access and procedures for data exchange and use.

Newly Generated Data

When collecting new data, EIRENE RI will be able to set its own standards and provide templates, e.g., for consent including purpose definition. Due attention will be given to the formulation of informed consent forms in such a way that they allow reuse of the data after being used for the original study, while respecting all rights of the data subjects. In PARC a harmonised informed consent template has been developed for use in human biomonitoring studies. This template can serve as a starting point for other types of studies in the EIRENE RI that generate and handle personal data.

EIRENE will establish its own Data Centre, which will provide core services, and also link to a distributed network of national hubs where data is generated and managed. It will require oversight to ensure compliance with international and national legislation while at the same time ensuring that FAIR principles are applied to the fullest extent possible (. Personal data can be stored in hubs that will manage the data and data access. Only the metadata will be accessible through the central Data

Centre. Set-ups for distributed analysis, performed by trusted entities, or federated analysis will be explored.

Figure 1 provides the envisaged set up that was presented in the EIRENE RI Design Study. It will be updated when drafting the details of the EIRENE RI DMP.

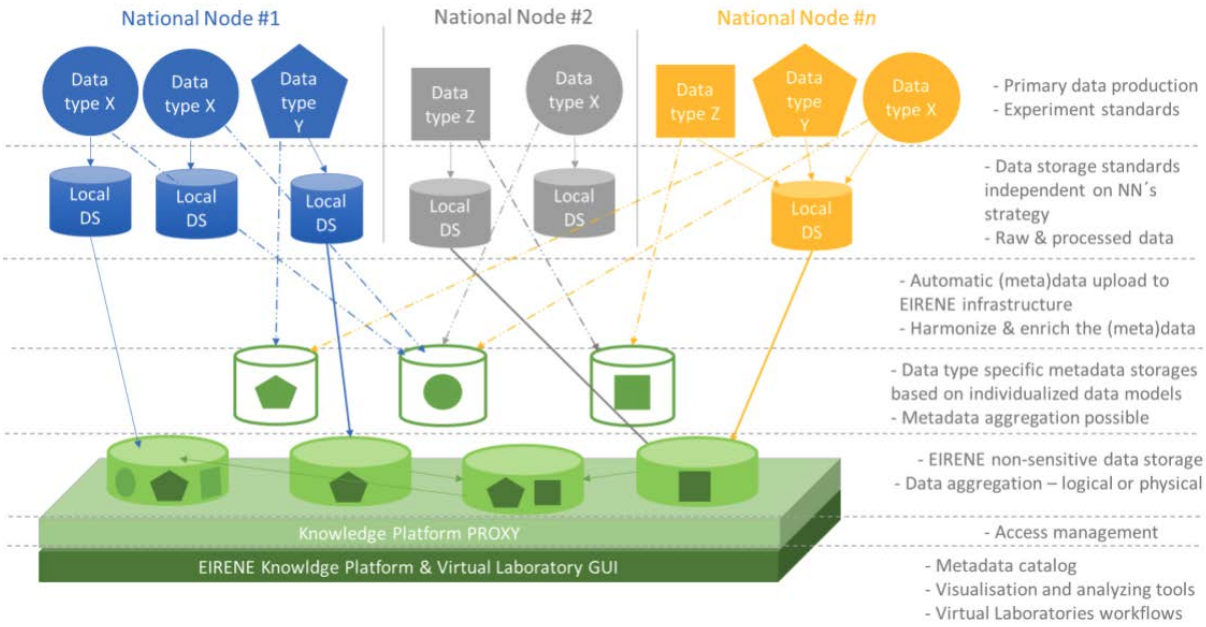

Figure 1: Provisional illustration of layers of exposome data and metadata production, storage, harmonisation, sharing, access management and user interface (EIRENE RI Design Study, Final Report)

The data within EIRENE can be classified in two major categories (see section "Data types" for details):

a. **Environmental:** monitoring data on chemical and physical parameters from measurement sites/campaigns. Data acquisition should be carefully and extensively documented, according to the FAIR principles. This data is not expected to be sensitive, but the data owner/provider must be clearly identifiable.
b. **Population studies:** data on population studies, including human bio-monitoring data, lifestyle data, socio-economic data, health data, for example. Such categories can also include data from questionnaires.

Data access can be via national nodes or the EIRENE Data Centre that can store tools for dealing with bioinformation, quality assurance, metadata verification and compliance with FAIR principles.
It is expected that national nodes will contribute to more than one, if not all data categories. This is where it is important that the national data managers ensure that data that is made accessible on the hubs complies with national legislation, whilst still being as FAIR as possible (Figure 2). The interactive online tools that give access to data, processing algorithms and models, intended for scientists to share resources and create a research environment will be the EIRENE Virtual Laboratory.

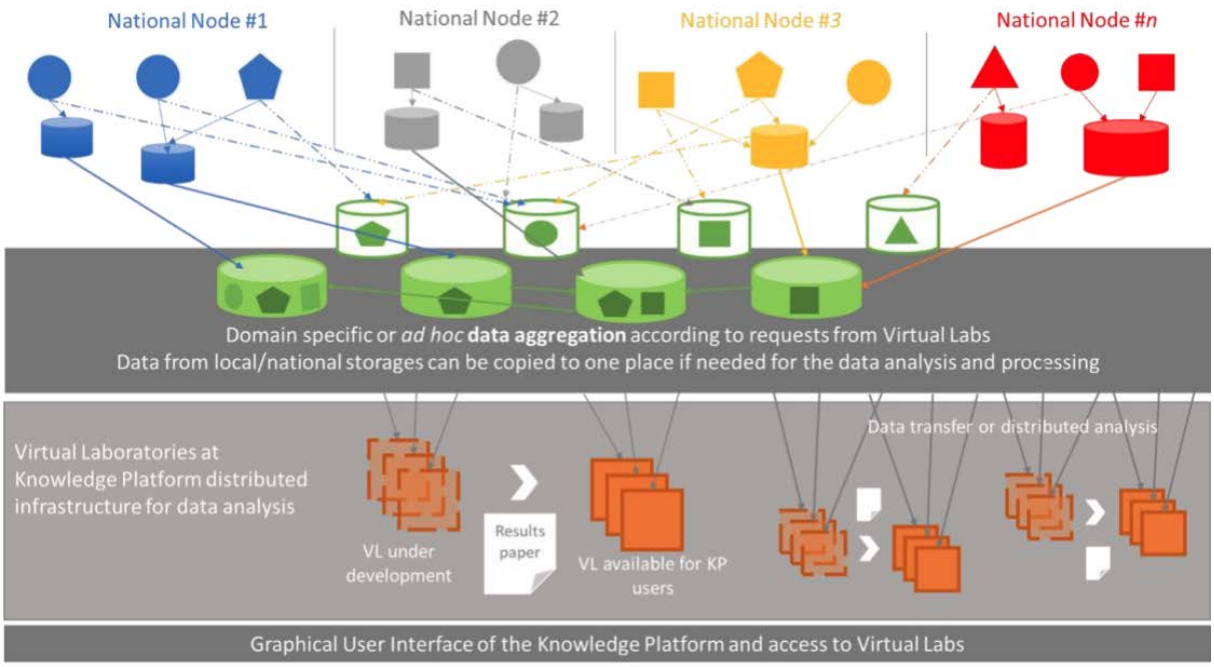

Figure 2: Data and metadata exploitation by Virtual Laboratories (VL) within the Knowledge Platform (KP). Upper part of the figure follows the data and metadata flows described in Figure 1. The lower part of this figure shows the VL lifecycle. Users can develop their own data analysis pipelines on EIRENE data sets. Once the results of such a pipeline are published, the pipeline is open for use by other users. VL can be run on different cloud infrastructures and maintained independently by several National Nodes/Institutions (after: EIRENE RI Design Study, Final Report)

Data Types

Possible data types generated or collected in EIRENE where ethical and legal considerations may be applicable, include environmental, social, economic and health disciplines (Table 2).

Table 2 – Possible personal data types generated or collected in EIRENE.

Data Type	Notes
Nucleotide sequence-based	Including genomics, epigenomics, metagenomics and transcriptomics. Examples: genome, gene and transcript sequences
Biological and biochemical markers	Includes nucleic acid–based biomarkers. Examples: gene mutations or polymorphisms and quantitative gene expression analysis, peptides, proteins, lipids, metabolites, microbiome
Chemical exposure markers	Chemicals or their metabolites detected and/or measured in human biological samples (including mycotoxins)
Health and medical data	Derived from medical records, medical examinations or self-reported health (through questionnaires) Including psychological and stress data, human morphometry, etc.

Personal environment	Personal geolocation data, time-activity patterns, personal exposure data extracted from geospatial data, questionnaire data
Socio-economic data	Personal socio-economic data collected through questionnaires or geospatial collections and analyses
Nutrition & lifestyle	Including personal data on lifestyle and nutrition collected through questionnaires, wearables, trackers, apps, etc.

6. EIRENE RI data users and possible scenarios

Before establishing ELSI guidelines, an overview of possible actors and scenarios relevant to the EIRENE RI can illustrate the framework to which such guidelines might be applied. Actors and scenarios can be updated when identified during the implementation of EIRENE RI virtual laboratories. The following table (Table 3) gives an overview of the four main figures involved with data handling.

Table 3 - Non exhaustive list of actors and scenarios to which ELSI guidelines can be applied.

Actor	Description	Objective	Possible data access procedure
Data provider	The data provider is a single researcher, a group or an infrastructure that provides data.	The data provider shares the dataset and gives adequate information on data types and possible concerns on ethics rules that might be applied	Has access to the provided data
Data custodian	The data custodian is responsible for preserving the data and granting proper access to different data types.	The custodian manages the technical environment where data resides. They ensure safe custody and storage of data, and provide access to requested data.	The data custodian has access to data for carrying out his role. They provide metadata and data access to data users respecting ELSI guidelines.
Researcher (data user)	A researcher is the data user who can execute algorithms for analyses remotely (on the same server where the data resides) or locally (on the researcher's pc).	A researcher requests access to use an EIRENE RI virtual laboratory for data analysis	A researcher requests access to use data and guarantees full respect of ELSI guidelines.
Member of the Ethics Advisory Board	A member of the Ethics Advisory Board is an expert on ethics related to exposomics research and/or an expert in ethics on data and information	To ensure the implementation of data ethics in digital applications	Not necessary.

	technologies.		
Member of the Data Protection Boards	A member of the Data Protection Board is a Data Protection Officer with expertise in exposome research	To ensure the implementation of legal data protection aspects in EIRENE RI	Not necessary

7. Guidelines for EIRENE RI

To define and adopt concrete guidelines EIRENE will benefit from the experience of the European Human Exposome Network, HBM4EU (https://www.hbm4eu.eu), PARC, and existing infrastructures such as BBMRI-ERIC (https://www.bbmri-eric.eu/), ELIXIR (https://elixir-europe.org/), and GA4GH (https://www.ga4gh.org/). All these projects and infrastructures deal with human samples and sensitive personal data. EIRENE RI will build further on the templates, guidelines and best practices that they have developed or are developing. EIRENE RI will investigate their fitness for purpose for its own use cases and services. This experience will be extremely valuable for preparing Data Management Plans within EIRENE. Furthermore, it will place the onus on EIRENE participants to ensure that their sample and data handling practices are aligned with those of existing infrastructures.

EIRENE RI will evaluate external sources for their usefulness, specificity and comprehensiveness for EIRENE RI. Where necessary existing guidelines will be revised and adapted, or additional guidelines will be drafted. A specific resource (developed by BBMRI) which may be of high value to EIRENE RI and which will be evaluated, is the GDPR Code of Conduct for Health Research (https://code-of-conduct-for-health-research.eu/).

EIRENE RI will adopt a similar approach to that developed and implemented by BBMRI-ERIC (https://www.bbmri-eric.eu) to assure compliance with ELSI guidelines.

BBMRI-ERIC has established ELSI services to facilitate "*compliance with regulatory requirements and best practice standards*". The services include the ELSI Helpdesk, ELSI Knowledge Base, and Ethics Check. To provide broad and accessible support to the community they have also established events, dialogues, and podcast services.

The development of EIRENE RI services will be overseen by an Ethics Advisory Board (EAB) which will consist of data ethics and IT experts to ensure the implementation of data ethics in digital applications. The EAB will be part of the EIRENE RI governance.

EIRENE RI ELSI Knowledge Base

The EIRENE RI Knowledge Base will be an open-access resource platform containing information on ELSI-related matters relevant to the human exposome. The service will include sections on Regulations, Laws, Best practices, a selection of the most relevant articles, as well as Code of conduct, Data policy, Recommendations for data preservation and custody, templates for compliance with Regulations (see example in Annex 1, derived from Regulation (EU) No 536/2014, Article 7.1 (h) and adapted to the context of the EIRENE RI) and best practices.

EIRENE RI ELSI Helpdesk

The EIRENE RI Helpdesk will act as a central service, to effectively address questions on legal and ethical aspects of data collection, processing, and management. The information generated from this service will feed the Knowledge Base. The service will be available to researchers and EIRENE RI National Nodes, as well as any research infrastructures working in the human exposome field. A specific

helpdesk email address will be established and its management will be decided in the framework of the EIRENE RI Governance structure.

EIRENE RI Ethics Check

The EIRENE RI Ethics Check will assist with the compulsory ethics self-assessment component of data collection and management, to support national nodes and individual researchers with ethical, legal, and societal issues that may arise from their activities in accordance with regulatory frameworks and ethical standards.

The EU Guidance on How to complete an ethics self-assessment (EC DG R&I, 2019) will be considered as a tool to drive data collection and management.

8. Conclusions

This deliverable highlights major ethical and bioethical principles that will have to be considered in the various stages of data generation, sharing and utilization. Data that will be dealt with in EIRENE RI are of various types that are part of environmental and socio-economic data categories. These two broad categories of data types include several subcategories such as health data, human bio-monitoring data, personal and lifestyle data, among others. One of the major goals of EIRENE is to establish a Data Centre aimed to provide core services which will be linked to national hubs national data platforms where data will be generated and managed. The EIRENE Data Centre will require oversight to ensure compliance with international and national legislations while at the same time will have to ensure that FAIR principles are applied at any stage of data processing and utilization. These data sets will be used to elaborate mitigation strategies for reducing the risks associated to human exposure to major environmental stressors (i.e., toxic compounds, climate change) for various socio-economic scenarios. Among the services that EIRENE will provide to general public, stakeholders and policy makers, interoperable multi-media modelling linking the environmental and socio-economic pressure factors to human exposure and derive (elaborate) optimal mitigation strategies to lower the risk factors for human health. The elaboration of the ELSI guidelines for EIRENE will be necessarily a continuous process through the end of the Preparatory Phase of EIRENE RI in order to consider all different needs of data providers, data users and legislation to ensure global equity and data compliance with ethical principles, in particular, the General Data Protection Regulation (GDPR) and the Clinical Trials on Medicinal Products for Human Use Regulation (CTMP), the latter to be considered as a reference despite the fact that EIRENE RI will not carry out clinical trials. In conclusion this report is a first draft presenting major aspects to be considered in the data value chain and services that EIRENE RI members and national hubs will provide to a wide range of end users.

9. References

- BBMRI-ERIC, 2023. European research infrastructure for biobanking. Available at: https://www.bbmri-eric.eu/
- Council of Europe, 1997. Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine. (Oviedo Convention) ETS 164.
- Council of Europe, 2006. Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin and its Explanatory Memorandum
- ELIXIR, 2023. European life sciences infrastructure. Available at: https://elixir-europe.org/
- European Council, 2004. Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells
- European Council, 2014. Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC Text with EEA relevance
- European Council, 2016. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)
- GA4GH, 2023. Global Alliance for Genomics and Health. Available at: https://www.ga4gh.org/
- HBM4EU, 2023. Human Biomonitoring for Europe project. Available at: https://www.hbm4eu.eu
- Klánová J., 2020. EIRENE RI Design Study. Final Report.
- Ries N.M., LeGrandeur J., Caulfield T., 2010. Handling ethical, legal and social issues in birth cohort studies involving genetic research: responses from studies in six countries. BMC Medical Ethics, 11(4).

Annex 1

Examples of compliance with EIRENE RI applicable rules for the collection, storage, and future use of human biological samples (following (Regulation (EU) No 536/2014, Article 7.1 (h)))

Full title of the research activity	**EIRENE RI number**
Responsible entity for the samples (legally):	

How to use this document

This form may be used by researchers to provide information about "compliance with the applicable rules for the collection, storage and future use of biological samples from clinical trial subjects" (Regulation (EU) No 536/2014, Article 7.1 (h)). This is not a mandatory form and different national arrangements may be in place, which should be confirmed prior to submission.

The original template has been developed by the EU Clinical Trials Expert Group to comply with Regulation (EU) No 536/2014 Clinical Trials on Medicinal Products for Human Use.

I – Description of the biological samples involved in the research
Section 1 - Does this research involve new sampling of the subjects (newly collected samples)? **□ Yes, please fill in the requested information in section 1** **□ No, not applicable. Please continue with section 2** **Note: The sponsor needs to fill in *at least one* of the sections 1 or 2**
1.1 What type(s) of samples will be collected from the subject? *State the original material that is collected from the patient e.g. blood, tissue (state type of tissue), urine, saliva etc. Do not include information on the preparation of the sample.*
1.2 Total number of samples, fragments (e.g. aliquots, tissue blocks, sections) and the total volume (if applicable) per individual subject:
1.3 The maximum number of samples and maximum volume (if applicable) on one single occasion:
1.4 Will the samples be collected as part of routine health care?

Section 2 - Does this research involve the collection of existing archive samples (e.g. archived diagnostic material or other biobank material)?

□ Yes, please fill in the requested information in section 2
□ No, not applicable. Please continue with section 3

Note: The sponsor needs to fill in at least one of the sections 1 or 2

2.1 What type(s) of archived material/samples will be used?

2.2 Provide the total number of samples, fragments (e.g. aliquots, tissue blocks, sections) and total volume (if applicable) that the Sponsor needs access to from each individual subject.

Example: 20 sections per biopsy from each individual subject is needed

2.3 Will new consent be obtained for the use of the archive samples in the research (if in line with national legislation)? If not, explain.

(if applicable, add the text of the original consent)

II – Use, storage, and transfer of biological samples

Section 3 – Use of samples for a purpose within the objective of this research (i.e. for use described in the protocol)

Note: This section must be filled in for both newly collected and existing archive samples

3.1 Where will the samples be analysed?

i.e. within the clinical laboratory, within/outside the researcher's organisation, within/outside the Member State where collected or within/outside EU/EEA.

3.2 If the samples will be sent to another organisation for analyses (as part of the trial), how will they be managed after the analyses have been carried out?
i.e. destroyed, returned to the responsible entity for the samples (legally), stored at the site where analysed, anonymised etc.

Note: An agreement (Material Transfer Agreement or equivalent) that regulates how the sample are to be handled shall be established with the recipient

3.3 Where will the samples be stored?
i.e. within/outside the researchers organisation, within/outside the Member State where collected or within/outside EU/EEA

3.4 How long will the samples be stored?

3.5 What type of connection is available between samples and individual subjects?

- ☐ Direct connection *(samples marked with e.g. initials, date of birth)*
- ☐ Pseudonymised connection *(samples marked with code)*
- ☐ No connection, samples are anonymised *(i.e. samples can neither directly nor indirectly, with reasonably means according to recital 26 of the General Data Protection Regulation (EU) 2016/679, be linked to the sample donor)*

3.6 Who will have access to the samples?

3.7 Who will have access to the sample code list (if applicable)?

Section 4 - Will newly collected samples or existing archive samples be stored for future use?
For other use than described in the protocol. Note that some purposes (secondary use of samples) may require additional approval, in Most Member States by an ethics committee

☐ Yes, please fill in the requested information in this section
☐ No, samples will be destroyed, please continue with section 5

4.1 What is the purpose of the future use?

4.2 How long will the samples be stored?

4.3 Where will the samples be stored?

4.4 What type of connection is available between samples and individual subjects?

- ☐ Direct connection *(samples marked with e.g. initials, date of birth)*
- ☐ Pseudonymised connection *(samples marked with code)*
- ☐ No connection, samples are anonymised *(i.e. samples can neither directly nor indirectly, with reasonably means according to recital 26 of the General Data Protection Regulation (EU) 2016/679, be linked to the sample donor)*

4.5 Who will have access to the samples?

4.6 Who will have access to the sample code list (if applicable)?

4.7 Will the donor be re-contacted to give new consent to the use of the samples in future research? If not, explain.

4.8 If secondary future use of the samples will be in question, will an ethics committee or biobank committee be reviewing whether the purpose of the new study is within the scope of the original provided consent (if applicable according to national legislation)?

4.9 Who will be able to make use of the samples?
4.10 How will unsolicited findings be handled?
III – Additional information
Section 5 - Additional information that is required by the current Member States national arrangements and regulations. The sponsor should confirm this prior to submission **Note: This section will only be filled in if applicable**
5.1 Provide any information (not described above) that is of relevance to the Member State applicable rules on collection, storage, transport and future use of the samples, e.g. on specific national arrangements and regulations regarding the use of human biological samples.