HYBRIDA

D5.2: Code of responsible conduct for the field of organoids and organoid-related technologies

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I. INTRODUCTION

I.1 Preambule

"Research integrity is generally understood to mean the performance of research according to the highest standards of professionalism and rigour, in an ethically robust manner[1]."

The Code of Responsible Conduct for Researchers on Organoids and Related Fields is the second document produced by the HYBRIDA project. This Code is a companion document to the HYBRIDA Operational Guidelines for Organoids and related fields (OGLs) for research on organoids and related fields. The focus of this Code is to develop and support research integrity within an ethical research ecosystem. While this framework must be operationalized locally and/or nationally in addition to the EU level, this document offers recommendations for institutions to consider for fostering a culture of research integrity.

Within the HYBRIDA project, this Code provides guidance and standards to support researchers working on organoid and related technologies and research organizations that home such research. Consequently, the HYBRIDA Code should support the work of research ethics committees, of associated integrity bodies, of research organizations and of the general public that address concerns and challenges related to the organoid research studies and practice.

In order to align with EU requirements, formats and recent documentation, the HYBRIDA Code is built upon the ALLEA European Code of Conduct for Research Integrity (ECoC) structure, addressing and exploring the specificities of the organoid research field, thus we will use the acronym ORF-ECoC, ORF standing for Organoids and Related Fields. Just as the ALLEA ECoC, ORF-ECoC is conceived as a self-regulation document intended to bring an ethical, research-integrity mindset in the research field, individually, collectively or/and institutionally.

It is essential to take into consideration that responsible conduct and integrity are not only a matter of individual behavior but also embedded collective practices, reason for which a systemic view involving research institutions and organizations is needed. Ethics, responsible conduct and integrity need to be part of the project from the planning stages to the end, both for researchers and their institutions, funding agencies and publishers.

As already mentioned, the HYBRIDA Code has to be considered fully linked to the HYBRIDA Operational Guidelines for Organoids and related fields (OGLs), thus we ask readers to refer to HYBRIDA OGLs to find

[1] Definition from the SiS.net is the international network of National Contact Points (NCPs) for Science with and for Society (SwafS) funded by the EU Framework Programme for Research and Innovation Horizon 2020. Information leaflet: https://ec.europa.eu/research/participants/documents/downloadPublic?documentIds=080166e5bf5c08aa&appId=PP GMS

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what is the HYBRIDA project for, what is the methodology adopted to elaborate OGLs and ORF-ECoC, the ethical framework used including an analysis of what should mean "ethical-by-design" for researchers on organoids and related fields, a specific section of the specificities and the questions raised by research on organoids for the informed consent, a discussion of three open questions on models of embryo, complex organoids of the nervous system and intellectual property, a glossary and several tools to improve research on organoids and related fields such as 1° the Minimum Information About an Organoid and its Use ORF standing for Organoids and Related Fields (MIAOU); 2° Evaluator checklist for organoid experimental studies (ECHOES); 3° the Research Ethics Committee/ Research Integrity Office check list (RICOCheck) and the 4° Donors of organoids TRUSTED list (Tissue Research Under Secure Transparent Ethical Donation) . These four questionnaires, that will be implemented soon on a European registry, and the respect of OGLs are fundamental parts of research integrity for researchers in the field and their organizations.

The ORF-ECoC is not an exhaustive document. It is conceived as an ethical landscape and self-regulating framework to guide researchers, who are supported to search further clarification and support with the relevant offices and ethical bodies (including Members of RECs and RIOs, RFOs, Research managers, Associations of industries, Citizen Science associations, Members of HTA bodies, Research Policy makers, Legal experts, Science journalists, Biobank officials, Patient organizations, Civil society organizations, etc.) when confronted with uncertainties of this new research field. In the EU, stem cell research and research on embryos are regulated by law, although there are several differences among member states in their national legislations (see the D3.2 HYBRIDA for details). Some countries adopt a very restrictive line prohibiting any kind of stem cell research or research on embryos while some others provide specific preconditions for stem cell research. In spite of the heterogeneity in legislation of the Member States, the European Union seems to play an important role in the rule of law at an international level, and also with regard to raising ethical concerns. Current international regulatory frameworks, as e.g. the Oviedo Convention, the Universal Declaration on Bioethics and Human Rights and European legislation, emphasize several safeguards and rights that demand "absolute protection" when applying health innovations. But in spite of this, there are still several discrepancies in national legislations that allow for different approaches since health issues, as well as public health and bioethics related issues, remain to be regulated by countries.

Taking into consideration the novelty of the organoid research field, such recommendations should be updated every 4 or 5 years. The objective of this Code is to guide researchers and support institutions and organizations to foster the development of a shared culture of ethical and responsible research in order to improve accountability, Transparency, reproducibility and professional commitment. We will come back to these aspects.

The current Code is also sensitive to the public reactions and expectations. According to the study conducted by HYBRIDA WP 4, the public has complex attitudes, from acceptance to hope (involving notions such as treatment, increase the life expectancy) to rejection or fear (particularly regarding the brain organoids, the consent, the donation of biological material). It has to be emphasized that organoid research is not perceived per se, but in relation to related technological fields:

> The attitudes of the participants towards organoids are is formed through analogies with other technologies (organ donation, blood donation, IVF). Participants used their prior knowledge of related to organoid research technologies and procedures for the purpose of forming their

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attitudes. Also, specific experiences of participants set the context of discussion about how they feel towards organoids. At this point of deliberation, fears and worries emerged, but expectations and hopes were, also, expressed. Worries, fears, expectations and hopes were expressed though personal experiences and facts that had happened in the context of other technologies and procedures. Worries and fears concerned the storage and the management of the biological material and the consequent use or misuse of personal data, access to potential benefits from the development of organoid research (access to therapies) and the consequent broadening of social inequalities, commercialization in science (for example with stem cells) and the absence of a regulatory and legal framework for organoid research[2].

In this context, several questions arose during HYBRIDA's co-creation workshops: how can the reputation (of researchers, of patients, of institutions, etc.) be constantly respected? What about the Indicators of Compromise (IoC) factors? How can an ethical Code become more efficient in guiding current public and research opinions and practices? Taken altogether, soft law as well as hard law should be mobilized to build trust between the public and the scientists. To do so, it is essential that scientists work within institutions that both promote research integrity, in example having a RIO (Research Integrity Office) as the organizational entity responsible for the implementation of it at each institution level - advice and prevention being prioritized-, and help them to behave so, in example through the development of materials for education and training (including mentorship) on research integrity, ethical behaviour, and good research practices in the organoid field.

[2] *Public attitudes, understandings and perspectives on organoid research*. WP4 Deliverable 4.3. Hybrida Project.

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II. METHODOLOGY

2.1 From the European to the global landscape

According to the 2018 Bonn PRINTEGER Statement[3], there is a constant need for guidance on how institutions and organizations can tackle with issues related to research integrity and research misconduct. In response to this open question, the European Code of Conduct for Research Integrity[6] drafted by All European Academies (ALLEA)[4] places at its core four main principles:

- **Reliability** in ensuring the quality of research, reflected in the design, the methodology, the analysis and the use of resources.
- **Honesty** in developing, undertaking, reviewing, reporting and communicating research in a transparent, fair, full and unbiased way.
- **Respect** for colleagues, research participants, society, ecosystems, cultural heritage and the environment.
- **Accountability** for the research from idea to publication, for its management and organization, for training, supervision and mentoring, and for its wider impacts.

2.2 Methodological Steps for Responsible Research

The aim of HYBRIDA's ORF-ECoC is to develop and support research integrity within an ethical research ecosystem. Our comments and recommendations within given items of the ALLEA ECoC are based on some basic principles. As previously mentioned, research institutions should create an environment promoting and supporting research integrity, including internal RIO and training opportunities for scientists. In line with public concerns reported by Hybrida 4.1 and 4.2 documents, a RIO should also develop criteria to evaluate its impact, such as Indicators of Compromise (IoC) factors. The ORF-ECoC builds on ALLEA recommendations for a better implementation of research integrity. Also, conclusions of the European project Standard Operating Procedures for Research Integrity (SOPs4RI), that describe three areas and nine topics for actions[5], were considered:

Area	Topic	Action (See in annex 2 the Table S1 for full descriptions.)
Support	Research environment	Ensure fair assessment procedures and prevent hypercompetition and excessive publication pressure.
Support	Supervision and mentoring	Create clear guidelines for PhD supervision (such as on meeting frequency); set up skills training and mentoring.

[3] https://printeger.eu/the-bonn-printeger-statement/.
[4] https://allea.org/wp-content/uploads/2023/06/European-Code-of-Conduct-Revised-Edition-2023.pdf
[5] Standard Operating Procedures and Guidelines that Research Performing and Funding Organizations. https://sops4ri.eu.

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Support	Integrity training	Establish training and confidential counselling for all researchers.
Organization	Ethics structures	Establish review procedures that accommodate different types of research and disciplines.
Organization	Integrity breaches	Formalize procedures that protect both whistle-blowers and those accused of misconduct.
Organization	Data practices and management	Provide training, incentives and infrastructure to curate and share data according to FAIR principles.
Communication	Research collaboration	Establish sound rules for transparent working with industry and international partners.
Communication	Declaration of interests	State conflicts (financial and personal) in research, review and other professional activities.
Communication	Publication and communication	Respect guidelines for authorship and ensure openness and clarity in public engagement.

While organoids might prove essential in innovating the personalized medicine filed, no overpromises should be made at the current moment: 'hope based on unfounded hype can create unrealistic expectations among patients and can negatively affect science and medicine when promises are not realized'[6]. Communication from the research community to the wide public should take this into account.

[6] *Personalized* Medicine in the Making, Human Perspectives in Health Sciences and Technology 3, "Patient-Derived Organoids in Precision Oncology – Towards a Science of and for the Individual?", p 141. Accessible at: https://doi.org/10.1007/978- 3- 030- 74804-3_7

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III. Good Research Practices

The ALLEA Code describes good research practices in the following contexts, that we adapted to the HYBRIDA Code of Responsible Conduct for Researchers in the Organoid field:

- Research Environment
- Training, Supervision and Mentoring
- Research Procedures
- Safeguards
- Data Practices and Management
- Collaborative Working
- Publication and Dissemination
- Reviewing, Evaluating and Editing

We took in consideration the latest up-date published by ALLEA: "The 2023 edition also takes account of changes in data management practices, the General Data Protection Regulation (GDPR), and recent developments in Open Science and research assessment. The 2023 edition of the European Code of Conduct also reflects a new awareness of the importance of research culture in enabling research integrity and implementing good research practices."

To give concrete expression to the above values, this document sets out a multi-part framework, structured around the research cycle, to guide researchers and institutions in the pursuit of integrity and ethical behavior. The purpose of this framework is to encourage discussion and debate about ethical research practice and not merely to provide a set of rules that must be adhered to without reflection. In the following sections, ALLEA Recommendations are written in italic and bold followed by specific implementation for organoids and related research.

Considering the specific applications of ECoC to organoids and related fields, some topics appeared missing or not clear enough in how they may apply to organoid related field, and consequently some specific additions to the European Code of Conduct for organoid research should be considered:

1. Sensitive domains of research integrity more specific to organoid research

- **Ethical Procurement and Use of Biological Materials**: Guidelines on the ethical procurement of human tissues and cells for creating organoids, emphasizing informed consent and respect for donor rights.
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- **Transparency and Public Engagement**: Initiatives to enhance public understanding of organoid research, including its potential benefits and ethical considerations, fostering an informed dialogue between researchers and the public.

2. Good Research Practices in Organoid Research

- **Data Practices and Management**: Special emphasis on the confidentiality and privacy concerns related to genetic information derived from organoids, aligning with GDPR and other relevant data protection frameworks.

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3. Violations of Research Integrity Specific to Organoid Research

- **Misuse of Organoids in Research and Therapy**: Addressing potential misapplications of organoid technology, such as creating organoids with sentient potential or for purposes not aligned with ethical guidelines and societal values.

- **Inequitable Access to Benefits**: Recognizing and mitigating risks related to the commercialization of organoids, ensuring equitable access to advancements in organoid-based therapies and diagnostics.

4. Engagement with Stakeholders

- **Inclusion of Patient Advocacy Groups and Ethical Committees**: Engaging with patient and donors advocacy groups and ethical committees in the research design and review process, ensuring that organoid research addresses patient needs and ethical considerations.

- **Regulatory and Legal Frameworks**: Collaborating with regulatory bodies to develop specific guidelines for organoid research, considering the rapid technological advancements and their societal implications.

This led us to propose some amendments that are presented and argued in Hybrida 5.3 document.

3.1 Research Environment

- ***Research institutions and organizations promote awareness and resource incentives to ensure a culture of research integrity.***

HYBRIDA Operational Guideline for organoids and related research was designed to support a culture of research integrity. Research institutions should promote awareness of HYBRIDA OGL and support training to use it. This should start from the very beginning of the research (origin of tissue/cell donation, informed consent), through the ethical issues according to the type of organoids produced (see our categories 1a, 1b and 2) and up to the very end (field of application among the four described: fundamental research, production of derived products, preclinical or clinical). Research institutions and organizations will include organoids and related field in their promotion of awareness and their culture of research integrity. In some jurisdictions this might just be a compliance to existing regulations. For example, in France, after two regulations in 2016 and 2021 on scientific integrity, it is mandatory to include a teaching credit dealing with scientific integrity, ethics in research and deontology in each biology training program[7], and soon a scientific oath will be pronounced by PhDs[8]. One or more pedagogical elements focusing on organoids has to be included in these training courses general dealing with scientific integrity. For young researchers but also all along the scientific life for any researcher, teachers/lecturers, the institutions should systematically develop an integrity, ethics and deontology training in the thematic schools and workshops dealing with organoids.

- ***Research institutions and organizations create an environment of mutual respect and promote values***

[7] On December 2021, the French Ministry of Higher Education and research issued a Decree on scientific integrity. This decree changes the conservation and availability of data and source codes, the implementation of DMPs and the publication of negative results for the French public research institutions. Accessible at: https://www.openaire.eu/blogs/france-new-decree-on-science-integrity-to-boost-support-for-open-science.

[8] https://www.science.org/content/article/france-will-require-ph-d-s-take-research-ethics-oath

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such as equity, diversity, and inclusion.

Research institutions and organizations foresee the creation of a RIO in charge of proposing policies, procedures and regulations in relation to the responsible conduct of research, as well as the detection, investigation, and prevention of research misconduct in the field of organoids and related technologies.

HYBRIDA Operational Guidelines describes the procedures on good research practice for organoids, namely the Minimal Information about Organoid and its Use for Researchers and scientific evaluators (MIAOU/ECHOES) and the equivalent (RICOCheck) for ethical reviewers. The institutions encourage the use of MIAOU/ECHOES and RICOCheck in all *Calls for projects* involving the use of organoids, including in Research related committees and in salary award committees. They refer to MIAOU/ECHOES and RICOCheck in their charter of ethics for the research profession.

Of note, since organoids are derived from tissues and stem cells, the values of diversity and inclusion should also apply to donors. The large development of Chapter 6 of OGLs on the specific aspects of informed consent for research on organoids is intended to increase the mutual respect between researchers and donors. Instruments such as the TRUSTED list should be implemented in such purpose.

- ***Research institutions and organizations create an environment free from undue pressures on researchers that allows them to work independently and according to the principles of good research practice.*** There are here no specific issues related to organoids.

- ***Research institutions and organizations demonstrate leadership in clear policies and procedures on good research practice and the transparent and proper handling of suspected research misconduct and violations of research integrity.***

A proper survey should ensure that any research conducted with human material is ethically grounded, and a particular attention should be given to a clear and proper handling of donors' informed consent. Misnaming of organoids is among research misconduct and violation of research integrity. Organoids are not organs and should never be named "mini-XX". We also recommend a proper ethical review when research deals with models of human embryos, directly or even indirectly when non-human primates are used, since such research is usually conducted as a step toward human application.

- ***Research institutions and organizations actively support researchers who receive threats and protect bona fide whistle- blowers, taking into account that early career and short-term employed researchers may be particularly vulnerable.***
- There are here no specific issues related to organoids.

- ***Research institutions and organizations support proper infrastructure for the management and protection of data and research materials in all their forms (encompassing qualitative and quantitative data, protocols, processes, other research artefacts and associated metadata) that are necessary for reproducibility, traceability and accountability.***

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Robustness of the research results depends on thorough research execution, systematic documentation, and data quality. This is why the HYBRIDA Consortium developed an Operational Guidelines for the field of organoids and organoid-related technologies which mentions how and why the careful collection of data is necessary not only for ensuring the quality of the results but also for maintaining records of collection methodology. These records are essential for judging data quality and for ensuring that future researchers can replicate the results. For further details, please refer to the Minimal Information about Organoid and its Use for Researchers (MIAOU/ECHOES) section in the HYBRIDA Guidelines.

The institutions should set up the conditions for secure data storage and ensure that the associated metadata are consistent with MIAOU/ECHOES. They also facilitate the open publication of data and protocols and, if possible, the use of electronic laboratory notebooks in emerging fields such as organoids.

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3.2 Training, Supervision and Mentoring

- ***Research institutions and organizations ensure that researchers receive rigorous training in research design, methodology, analysis, dissemination, and communication.***

In the institutions' training offer, the teaching units on methodology for carrying out good research should include the MIAOU/ECHOES prerequisites. Organoid trainings and educational formats (such as case studies) are proposed to the organoid research community. Training in communication should prevent misconduct such as misnaming.

- ***Research institutions and organizations develop appropriate and adequate training in ethics and research integrity to ensure that all concerned are made aware of the relevant codes and regulations and develop the necessary skills to apply these to their research.***

In the training offer of the institutions, the teaching units deal with scientific integrity, research ethics and deontology, it is suggested to include the prerequisites of MIAOU/ECHOES and the RICOCheck for organoid field. The informed consent is of particular importance for any research involving human patients/tissues/cells and the corresponding section of the Operational Guidelines for the field of organoids and organoid-related technologies develops an arborescence to guide researchers in this specific field. Research institutions and organizations will develop adequate training based on these proposals.

- ***Senior researchers, research leaders, and supervisors mentor their team members, lead by example, and offer specific guidance and training to properly develop and structure their research activities.***

There are here no specific issues related to organoids.

- ***Researchers across the entire career path, from junior to the most senior level, undertake training in ethics and research integrity.***

The ethics and integrity of science should be an integral part of the education and training of all scientists. A positive attitude towards reflection, anticipation and deliberation of responsible conduct in research is essential for the organoid field (RAD process). In this sense, researchers using organoids should undertake: integrated learning organoid paths to support PhD researchers in their development, 'mind the gap' online training for junior and senior organoid researchers, masterclasses for organoid senior professors and doctoral supervisors[9]. Dedicated sessions for training in ethics and research integrity should be included in each scientific meeting reporting on progress in organoids research and related fields. Master class and summer schools dedicated to organoid science should include dedicated training in ethics and research integrity. A follow-up of the evolution of MIAOU/ECHOES in specific field of organoid research should be promoted.

[9] Inspired by the design proposed within the KU Leuven *Research Integrity*. Accessible at: https://www.kuleuven.be/english/research/integrity/training.

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• ***Senior researchers, research leaders and supervisors mentor their team members and offer specific guidance and training to properly develop, design and structure their research activity and to foster a culture of research integrity.***

Components (laboratories) of universities and research institutions provide in-house training in scientific integrity, research ethics and deontology, to ensure, in particular, respectful behavior when supervising students and interacting with colleagues, and knowledge and implementation of the MIAOU/ECHOES and RICOCheck standards.

3.3 Research Procedures

• ***Researchers take into account the state-of-the-art in relevant fields when developing research ideas.*** There are here no specific issues related to organoids.

• ***Researchers design, carry out, analyze and document research in a careful and well-considered manner.***

Robustness of the research results on organoids depends on thorough research execution, systematic documentation, and data quality. Careful collection of data is necessary not only for ensuring the quality of the results but also for maintaining records of collection methodology. These records are essential for judging data quality and for ensuring that future researchers can replicate the results.

Responsible conduct of research on/with organoids starts with the planning stage. The choice of research questions and rationale is a critical starting point. The creation of new knowledge and translation are important outcomes of research. While translation of research comes at a later stage, researchers should proactively think about the downstream impact.

Although the outcomes of research cannot be planned or perceived in advance, it is possible to have a well-documented plan in place outlining the objectives, roles, and responsibilities. Researchers must have appropriate data management systems in place with detailed and easily traceable records for outcomes and milestones, systematic and rigorous analysis, any ethical and regulatory approvals, keeping in mind that they might need updating as conditions change in the future. All appropriate licenses, participant consents, and requisite permissions should be secured before starting the research. Researchers should ensure they are abreast of all the relevant regulatory and governance requirements. They should also consider the novel documents recommended in HYBRIDA's OGL such as MIAOU, ECHOES, RICOCheck and even more the Tissue Research Under Secure Transparent Ethical Donation (TRUSTED). Research organizations should support researchers with an appropriate research governance system[10] within a sound research and project management framework.

[10] Standard Operating Procedures for Research Integrity (SOPs4RI) Report and Website, https://sops4ri.eu.

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- ***Research protocols take account of, and are sensitive to, relevant differences among research participants, such as age, gender, sex, culture, religion, worldview, ethnicity, geographical location, and social class.***

The implementation of the informed consent process as detailed in Chapter 6 of the Operational Guidelines (***OGL***s) merits particular emphasis. It's crucial that both oral and written information provided to participants is tailored to their individual understanding, and the clarity of consent forms should be actively verified. The Tissue Research Under Secure Transparent Ethical Donation (**TRUSTED**) aims to mitigate uncertainties regarding the potential future reuse of donated cells or tissues and the scope of donor-approved uses. Further collaborative efforts are required to establish optimal conditions that honor donor intentions while fostering research progress. Moreover, the issue of withdrawing consent presents significant challenges in the context of using highly engineered cells for organoid development. Therefore, HYBRIDA advocates for the establishment of a dedicated EU taskforce to develop uniform guidelines for researchers and their institutions in this area.

- ***Researchers make proper and conscientious use of research funds.***

There are here no specific issues related to organoids.

- ***Researchers share their results in an open, honest, transparent, and accurate manner, and respect confidentiality of data or findings when legitimately required to do so.***

Research findings are truly impactful only when publicly shared and communicated. Moreover, researchers earn their property rights by giving away their findings in the form of publications. Researchers must present all results, including favorable, unfavorable, and null findings. The honest reporting of all findings is essential as a matter of record and to save time for future researchers, who need not redo the work that has already been done.

For the organoid field, the donor and/or the patient informed-consent and the anonymization of data has to be applied. The FAIR EU project, conceived to facilitate and promote 'the application of FAIR principles in health research data, derived from the publicly funded health research initiatives to make them Findable, Accessible, Interoperable, and Reusable (FAIR)'[11].

- ***Researchers report their results and methods, including the use of external services or AI and automated tools, in a way that is compatible with the accepted norms of the discipline and facilitates verification or replication, where applicable.***

Researchers on organoids should publish in only recognized peer-reviewed journals that adhered to international declaration on research integrity such as DORA[12].

[11] Accessible at: https://www.fair4health.eu/en/news/fair4health-key-outputs-for-the-scientific-community.

[12] The Declaration on Research Assessment (DORA). Accessible at: https://sfdora.org/

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3.4 Safeguards

- ***Researchers, research institutions, and organizations comply with relevant codes, guidelines, and regulations.***

The Operational Guidelines and the current Code are the first European recommendations that directly concern the organoid field. More generally, the European Research Area and Innovation Committee (ERAC) proposed, in June 2021, six principles that promote Open Science and gender equality: Foster the diversity of open research ecosystems; Promote inclusiveness and collective involvement in the design of Open Science and research evaluation policies; Encourage a responsible attitude in research evaluation; Foster transparency in research evaluation and trustworthiness in the added value of Open Science and gender equality; Provide the right incentives through evaluation; Create a virtuous circle between training and evaluation[13].

- ***Researchers handle research participants and subjects (be they human, animal, cultural, biological, environmental, or physical) and related data with respect and care, and in accordance with legal provisions and ethical principles.***

The RICOCheck questionnaire has been elaborated based on the ethical European self assessment form in order to take organoid specificities into account

- ***Researchers have due regard for the health, safety and welfare of the community, of collaborators and others connected with their research.***

Information concerning the cells or organoids must contain the virological status, while preserving the donor's anonymity. (see MIAOU/ECHOES). In addition, as with any long-term culture, a regular assessment of possible mycoplasma contamination must be set up, and the data must be easily accessible to other researchers.

- ***Research protocols take account of, and are sensitive to, relevant differences in age, gender, culture, religion, ethnic origin and social class.***

It is crucial to ensure equitable access to therapies emerging from organoid research. Considerations must also be made for the biological diversity represented in constructed organoids. A significant ethical consideration is the potential creation of vulnerable populations through the use of organoids in preclinical or clinical research. For example, if organoids developed from the cells of a specific ethnic group are used to test a new drug, but the findings are then generalized without validating efficacy across a broader range of ethnicities, this could inadvertently lead to treatments that are less effective for those not represented in

[13] ERAC 'Triangle Task Force' Guideline Paper on 'Research evaluation in a context of Open Science and gender equality', https://data.consilium.europa.eu/doc/document/ST-1201-2021-INIT/en/pdf.

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the initial research group, thus creating a new vulnerable population. This underscores the need for inclusive research practices that reflect the diversity of the global population to prevent such ethical oversights.

The MIAOU/ECHOES checklist has been established to allow easy assessment and follow-up in these matters. However, if the researchers on organoids and related fields are fully called to fight any form of bias and/or discrimination, it is hardly difficult to imagine that culture, religion, ethnic origin or social class might have any significance in our field with the exception of the informed consent that may have to be adapted using a variety of media (film, comics…) to be fully understood by every donor.

- ***Researchers recognize and weigh potential harms and risks relating to their research and its applications and mitigate possible negative impacts.***

Based on the Ethics-by-design and RAD approaches described in the Hybrida Operational Guidelines for research on organoids and related fields, any recommended or legally requested ethical review and approval should be anticipated and performed before the starting of the research. The organoid research makes appeal to the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity, an international agreement which "aims at sharing the benefits arising from the utilization of genetic resources in a fair and equitable way"[14].

There is a potential danger associated with organoids misuse and dual use. Misuse refers to the application of organoid technology in ways that are ethically or legally questionable, while dual use denotes the use of organoid research for both beneficial purposes and harmful applications, such as bioweapons development.

Example: Creation of Bioweapons

One alarming example of the potential for dual use involves the creation of bioweapons. Organoids could theoretically be engineered to produce pathogens or toxins under conditions that mimic human organs more closely than traditional cell cultures. This could facilitate the development of biological weapons that are more effective, harder to detect, and more resistant to existing medical treatments. For instance, lung organoids could be misused to study the progression of airborne pathogens or to engineer viruses with enhanced transmissibility and virulence, posing a significant threat to global health security.

To mitigate these risks, the scientific community, regulatory bodies, and international organizations must collaborate to establish robust ethical guidelines and oversight mechanisms. This includes:

- **Comprehensive Risk Assessments**: Evaluating the potential for misuse and dual use of organoid research at the project proposal stage, including a consideration of the intended and unintended consequences.
- **International Collaboration and Transparency**: Fostering a culture of openness and collaboration across borders to ensure that research advances are shared responsibly, with a focus on preventing the dissemination of knowledge that could be misused.

[14] Regulation (EU) No 511/2014 of the European Parliament and of the Council on compliance measures for users from the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization in the Union was adopted on 16 April 2014. Implementing the mandatory elements of the Nagoya Protocol in the European Union, it entered into force on 9 June 2014 and applies from the date the Nagoya Protocol itself entered into force for the Union, i.e. 12 October 2014. Accessible at: https://ec.europa.eu/environment/nature/biodiversity/international/abs/legislation_en.htm.

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- **Ethical and Regulatory agreements**: Developing and enforcing international agreements and national regulations that specifically address the dual-use potential of organoid technology, including restrictions on certain types of research and export controls on sensitive materials and information.
- **Public Engagement and Education**: Engaging with the public to raise awareness about the ethical implications of organoid research and to build trust in the scientific community's commitment to responsible research practices.

By addressing the potential for misuse and dual use proactively, the scientific community can harness the full potential of organoid research while safeguarding against ethical pitfalls and ensuring that this innovative technology serves the greater good.

- ***Researchers overseeing projects that cross professional boundaries, such as citizen science or participatory research, take responsibility for ensuring research integrity standards, oversight, training, and safeguards.*** No specificity for research on organoids.

3.5 Data Practices and Management

- ***Researchers, research institutions and organizations ensure appropriate stewardship and curation of all data and research materials, including unpublished ones, with secure preservation of all data, metadata, protocols, code, software, and other research materials for a reasonable and clearly stated period.***

For organoids and related fields this section should be entitled "Biological sample practice and management" to take into consideration essential elements concerning the conditions of harvesting, storing and making available the biological samples allowing the production of organoids. Data on organoids research and related files need to be stored securely during all phases of the organoid research process. Researchers, research institutions and organizations need to ensure:

a. Clear data ownership and accountability (please see the section Informed Consent).
b. Access restrictions with appropriate protocols to ensure safety and privacy.
c. Data integrity by giving access to the original data.
d. Cautious and reliable data collection, storage, and retrieval.
e. Data integrity and security through periodic back-ups and redundant storage in multiple media.
f. Requirements from funders and other stakeholders with respect to data storage and sharing.

More details are provided in HYBRIDA OGLs and partnership with a European registry will allow preservation and accessibility of the generated data.

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- ***Researchers, research institutions and organizations ensure access to data is as open as possible, as closed as necessary, and where appropriate in line with the FAIR Principles (Findable, Accessible, Interoperable and Re-usable) for data management.***

In order to support and strengthen the FAIR Principles, HYBRIDA Consortium suggests the creation of a Research Integrity Office as an integral and permanent unit within the research infrastructure of the institution. The Office should play a dual role of coach/adviser and enforcer. As a coach/adviser, the RIO encourages and enables a culture of research integrity and provides training. As enforcer of the application of legislation, it monitors research activities for possible malpractice, and acts swiftly, fairly and tactfully when cases of research misconduct are brought to its attention. There are resources, governance structures, models, and guidance available for establishing an RIO.

Each RIO would also have to develop its own guidelines regarding processes and procedures for dealing with allegations of research misconduct. For further inspiration, please check the *ENRIO Handbook Recommendations for the Investigation of Research Misconduct*[15].

- ***Researchers, research institutions, and organizations are transparent about how to access and gain permission to use data, metadata, protocols, code, software, and other research materials.***

Considering the specificity of research on organoids, particularly the length of time to produce and analyze them, appropriate rules for data archiving, storage and retrieval, including the data retention period. Data that cannot be easily reproduced should probably be retained indefinitely.

- ***Researchers inform research participants about how their data will be used, reused, accessed, stored, and deleted, in compliance with GDPR.***

The EU publications within the SIS network[20] emphasizes as well on the necessity to keep records of the data and to have a quality management for all file records:

Failure to keep records	Good scientific record keeping is necessary for data analysis, publication, collaboration, peer review, and other research activities. Record keeping is necessary to support intellectual property claims, it can help to defend against a false allegation of research misconduct and is important in the care of human subjects. The requirement is to maintain proper records that are complete, accurate and understandable to others.

[15] ENRIO Handbook. *Recommendations for the Investigation of Research Misconduct;* accessible at: RIO

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Data mismanagement	As the type of research differs very much between the various scientific fields, general statements regarding the quality of research data management are not possible. Nevertheless, good data management practices that are already established within a number of scientific fields can be introduced in other fields. Responsible research data management includes correctness in data collection, consistency, analysis, processing, ownership, control, storage, protection, retention and sharing[21].

- ***Researchers, research institutions, and organizations acknowledge data, meta- data, protocols, code, software, and other research materials as legitimate and citable products of research.***

A sound, systematic, and rigorous research practice depends upon the underlying ontological, epistemological, and methodological assumptions. Careful data collection, the systematic use of rigorous methods, including precisely adapted statistical methods, and the proper interpretation of the findings are essential aspects of research integrity. In this regard, the MIAOU questionnaire of Hybrida OGLs is intended to collect these elements or to help generating them based upon the information provided.

- ***Researchers, research institutions, and organizations ensure that any contracts or agreements relating to research results include equitable and fair provisions for the management of their use, ownership, and protection under intellectual property rights.***

3.6 Collaborative Working

- ***All partners in research collaborations take responsibility for the integrity of the research and its results.***

Research is increasingly a collaborative enterprise, with interdisciplinary profiles and complex team interactions, skills and competencies. Collaborations, however, add another layer of complexity to research that is not usually present when a researcher is working alone. Once again for organoids this means a continuous process from the oral information given to the patient and then the patient's informed consent related to the cells and/or tissue of origin donation to proper handling of the results.

- ***All partners in research collaborations formally agree at the outset, and monitor and adapt as necessary, the goals of the research and the process for communicating their research as transparently and openly as possible.*** There are here no specific issues related to organoids.

- ***All partners in research collaborations formally agree at the outset, and monitor and adapt as necessary, the expectations and standards concerning research integrity, the laws and regulations that will apply, protection of the intellectual property of collaborators, and procedures for handling conflicts and possible cases of misconduct.*** There are here no specific issues related to organoids.

- ***All partners in research collaborations are consulted and formally agree on submissions for publication of research results and other forms of dissemination or exploitation of the results.*** There are here no specific issues related to organoids.

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3.7 Publication and Dissemination

- ***Authors formally agree on the sequence of authorship, acknowledging that author- ship itself is based on: (1) a significant contribution to the design of the research, relevant data collection, its analysis, and/ or interpretation; (2) drafting and/or critical reviewing the publication; (3) approval of the final publication; and (4) agreeing to be responsible for the content of the publication, unless specified otherwise in the publication.***

Concerning authorship, the EU publications within the SIS network emphasize on these already mentioned aspects:

Ghost or guest authorship	Ghost authorship occurs when a significant contribution is made to a manuscript without that contribution being acknowledged. On the contrary, guest (or gift) authorship occurs when someone who did not contribute in any way to the research and its write-up is included in the author list because they give extra credibility to the article. Both ghost and guest authorship undermine the credibility of scientific reporting.

Artificial Intelligence (AI) is increasingly becoming an integral part of organoid research, from the initial stages of development to publication. In the laboratory, AI algorithms assist researchers in analyzing complex biological data, optimizing organoid growth conditions, and predicting organoid behavior in response to various stimuli. This application of AI not only accelerates the research process but also enhances the precision and reliability of experimental outcomes. Furthermore, AI plays a crucial role in the interpretation of results, identifying patterns and insights that may not be immediately apparent to human researchers. As the research progresses towards publication, AI tools can assist in drafting manuscripts, ensuring that data is presented clearly and concisely, improving the English fluency for non-english native speakers, and even suggesting suitable journals for submission. Throughout the organoid research lifecycle, AI acts as a powerful tool that enriches understanding, fosters innovation, and streamlines the path from discovery to dissemination. However, AI may also content biases or be misused. It should be thus mandatory to mention the use of AI tools during the research project.

- ***Authors include an 'Author Contribution Statement' in the final publication, where possible, to describe each author's responsibilities and contributions.***
  There are here no specific issues related to organoids.
- ***Authors acknowledge important work and contributions of those who do not meet the criteria for authorship, including collaborators, assistants, and funders who have enabled the research.***
  There are here no specific issues related to organoids.
- ***Authors disclose any financial and non- financial conflicts of interest as well as sources of support for the research or the publication.***
  There are here no specific issues related to organoids.
- ***Authors and publishers promptly issue corrections or retract publications, if necessary, the retraction processes are clear and the reasons stated, and authors are given credit for issuing corrections post-***

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publication.
There are here no specific issues related to organoids.

- ***Authors, research institutions, publishers, funders, and the research community acknowledge that negative results can be as relevant as positive findings for publication and dissemination.***
  There are here no specific issues related to organoids.
- ***Authors are accurate and honest in their communication to colleagues, policy- makers, and society at large.***
  There are here no specific issues related to organoids.
- ***Authors are transparent in their communication, outreach, and public engagement about assumptions and values influencing their research as well as the robustness of the evidence, including remaining uncertainties and knowledge gaps.***
  There are here no specific issues related to organoids.

- ***Authors adhere to the same criteria as those detailed above whether they publish in a subscription journal, an open access journal, or in any other publication form, including preprint servers.***

Any publication on organoids constructed from human cells requires an opinion from a Research Ethics Committee. There are no other specificities concerning the publication on organoids, and ALLEA general rules apply.

3.8 Reviewing, Evaluating and Editing

- ***Researchers take seriously their commitment and responsibility to the research community through refereeing, reviewing, and assessment, and this work is recognized and rewarded by researchers, research institutions, and organizations.***
- ***Researchers, research institutions, and organizations review and assess submissions for publication, funding, appointment, promotion, or reward in a transparent and justifiable manner, and disclose the use of AI and automated tools.***
  There are here no specific issues related to organoids.
- ***Reviewers and editors declare any actual or perceived conflicts of interest and, when necessary, withdraw from involvement in discussion and decisions on publication, funding, appointment, promotion, or reward***
  There are here no specific issues related to organoids.
- ***Reviewers maintain confidentiality unless there is prior approval for disclosure.***
  There are here no specific issues related to organoids.
- ***Reviewers and editors respect the rights of authors and applicants, and seek permission to make use of the ideas, data, or interpretations presented***
  There are here no specific issues related to organoids.
- ***Researchers, research institutions, and organizations adopt assessment practices that are based on principles of quality, knowledge advancement, and impact that go beyond quantitative indictors and take into account diversity, inclusiveness, openness, and collaboration where relevant.***

ALLEA recommendations for *Reviewing, Evaluating and Editing* entirely apply to organoid research and researchers. There are no specificities concerning the reviewing, evaluating and editing on organoid, ALLEA general recommendations orient the general context.

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IV. Violations of Research Integrity

4.1 Research Misconduct and other Unacceptable Practices

Research misconduct is traditionally defined as fabrication, falsification, or plagiarism (the so-called FFP categorization) in proposing, performing, or reviewing research, or in reporting research results:

- ***Fabrication is making up results and recording them as if they were real.***
  There are here no specific issues related to organoids.

- ***Falsification is manipulating research materials, equipment or processes or changing, omitting or suppressing data or results without justification.***
  There are here no specific issues related to organoids.

- ***Plagiarism is using other people's work and ideas without giving proper credit to the original source, thus violating the rights of the original author(s) to their intellectual outputs.***

There are here no specific issues related to organoids.

There are further violations of good research practice that distort the research record or damage the integrity of the research process or of researchers. In addition to violations of the good research practices set out in this European Code of Conduct, examples of other unacceptable practices include, but are not confined to:

- ***Allowing funders, sponsors, or others to jeopardise independence and impartiality in the research process or unbiased reporting of the results.***
  There are here no specific issues related to organoids.

- ***Misusing seniority to encourage violations of research integrity or to advance one's own career.***
  There are here no specific issues related to organoids.

- ***Delaying or inappropriately hampering the work of other researchers.***
  There are here no specific issues related to organoids.

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- ***Misusing statistics, for example to inappropriately suggest statistical significance.***
  There are here no specific issues related to organoids.

- ***Hiding the use of AI or automated tools in the creation of content or drafting of publications.***
  There are here no specific issues related to organoids.

- ***Withholding research data or results without justification.***
  There are here no specific issues related to organoids.

- ***Chopping up research results with the specific aim of increasing the number of research publications ('salami publications').***
  There are here no specific issues related to organoids.

- ***Citing selectively or inaccurately.***
  There are here no specific issues related to organoids.

- ***Expanding unnecessarily the bibliography of a study to please editors, reviewers, or colleagues, or to manipulate bibliographic data.***
  There are here no specific issues related to organoids.

- ***Manipulating authorship or denigrating the role of other researchers in publications.***
  There are here no specific issues related to organoids.

- ***Re-publishing substantive parts of one's own earlier publications, including translations, without duly acknowledging or citing the original ('self-plagiarism').***
- There are here no specific issues related to organoids.

- ***Establishing, supporting, or deliberately using journals, publishers, events, or services that undermine the quality of research ('predatory' journals or conferences and paper mills).***
  There are here no specific issues related to organoids

- ***Participating in cartels of reviewers and authors colluding to review each other's publications.***
  There are here no specific issues related to organoids.

- ***Misrepresenting research achievements, data, involvement, or interests.***
  There are here no specific issues related to organoids.

- ***Accusing a researcher of misconduct or other violations in a malicious way.***
  There are here no specific issues related to organoids.

- ***Ignoring putative violations of research integrity by others or covering up inappropriate responses to misconduct or other violations by institutions.***
  There are here no specific issues related to organoids.

In their most serious forms, unacceptable practices are sanctionable, but at the very least every effort

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must be made to prevent, discourage and stop them through training, supervision and mentoring and through the development of a positive and supportive research environment.

There is no uniform European definition of research misconduct or unacceptable practices. Research misconduct does not include inadvertent errors or differences of opinion; however, generally accepted standards play a major role in describing significant departures from accepted practices. "Knowingly, intentionally, or recklessly" departing from standard practice can be grounds for allegations of misconduct". According to the ENRIO Handbook, issues regarding 'research integrity, misconduct or other misbehaviors should primarily be handled within the research community and/or institutional bodies set up specifically for the scientific community'[16], as these problems might be self-regulating within the community.

Recommendation for the organoid field: if papers contain verifiable fabrication, it seems important that papers are marked and retracted quickly.

4.2 Dealing with Violations and Allegations of Misconduct

National and institutional guidelines differ as to how violations of good research practice and allegations of misconduct are handled. However, it is always in the interest of society and the research community that violations are handled in a fair, consistent, and transparent fashion. The following principles need to be incorporated into any investigation process:

- ***Anyone accused of research misconduct is presumed innocent until proven otherwise.***
  There are here no specific issues related to organoids.

- ***Investigations are fair, comprehensive, and conducted expediently, without compromising accuracy, objectivity, or thoroughness.***
  There are here no specific issues related to organoids.

- ***The parties involved in the investigation declare any conflict of interest that may arise during the investigation.***
  There are here no specific issues related to organoids.

- ***Measures are taken to ensure that investigations are carried through to a conclusion.***
  There are here no specific issues related to organoids.

- ***Investigations are conducted confidentially in order to protect those involved.***
  There are here no specific issues related to organoids.

- ***Institutions protect the rights of bona fide whistle-blowers during investigations and ensure that their career prospects are not endangered.***

[16] For further information on these terms, please check *ENRIO Handbook. Recommendations for the Investigation of Research Misconduct*, p.3, Available at: http://www.enrio.eu/wp-content/uploads/2019/03/INV- Handbook_ENRIO_web_final.pdf.

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- There are here no specific issues related to organoids.

- ***General procedures for dealing with violations of good research practice are publicly available and accessible to ensure their* Transparency *and uniformity.***
  There are here no specific issues related to organoids.

- ***Persons accused of research misconduct are given full details of the allegation(s) and are allowed a fair process for responding to allegations and presenting evidence.***
  There are here no specific issues related to organoids.

- ***Investigations into research misconduct consider the role of both individuals and institutions contributing to the breach of good research practice.***
  There are here no specific issues related to organoids.

- ***Action is taken against persons for whom an allegation of misconduct is upheld, which is proportionate to the severity of the violation.***
  There are here no specific issues related to organoids.

- ***Appropriate restorative action is taken when researchers are exonerated of an allegation of misconduct.***
  There are here no specific issues related to organoids.

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Open Conclusions

- **Codes of Conduct (CoCs):** CoCs are practical guides that must be collaboratively discussed within the relevant group to foster a vigilant mindset towards ethical issues in Research Integrity (RI). This requires an iterative approach to ensure deep understanding and application.

- **Ethical Training:** Detailed engagement with checklists is a fundamental part of ethical training. Implementing COC principles in specific contexts necessitates continuous attention to Research Integrity issues throughout the research process and collective problem-solving. A key question to ask is: "What does this mean in my/our situation?"

- **Data Management and Rights**: Effective data management involves addressing the rights, acknowledgments, and rewards associated with data use, ensuring equitable and respectful handling of data. The COPE (committee of publication ethics) forum exemplifies how to construct a European forum aimed at addressing these open questions, providing a model for fostering dialogue and solutions in data management practices.

- **Quality and Integrity** in participative science: Ensuring quality and integrity in citizen science projects, requires careful consideration. This includes addressing how the results of citizen science can be utilized while maintaining scientific standards.

- **Collaboration vs. Commercial Interests:** There may be a need to introduce principles that govern cooperation between the academic and private sectors, especially when commercial interests could potentially conflict with the principles of open science. Individuals and groups must be vigilant and proactive in identifying and understanding potential conflicts of interest, even when they are not immediately apparent.

- **Institutional Responsibilities:** Institutions should support researchers by promoting responsible RI practices and defending them from threats, notably those arising from sensitive or controversial research topics and social media backlash.
  Advocating for research freedom and favoring collaborative efforts over competitive ones are crucial. Shifting focus from publication quantity to recognizing the quality of research and diverse qualitative indicators aligns with recent trends in research assessment.
  Building trust in science is a critical institutional role, achieved through open collaboration and transparent communication, avoiding sensationalism and openly acknowledging uncertainties.
  The purpose of publications and communications is to spread validated knowledge, not to seek fame or notoriety.

- **Publications**: The aim of publications and communications is to inform and to diffuse validated

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knowledge not to impress or to gain notoriety.

- **Funding agencies** must support a broad spectrum of research, including both basic and exploratory studies, using fair and appropriate assessment criteria and accepting the inherent uncertainties in research.

- **Government-Level Responsibilities**: Governments should reconsider success criteria for research, moving away from immediate gains to recognize research's broader value and impact. Observing DORA principles is essential to support the shift towards a qualitative paradigm in research assessment, encouraging multidisciplinary research and equitable assessment methods that treat all disciplines fairly.

Conflict of Interest

- **Addressing Perceptions**: Conflicts of interest exist not only in clear regulatory scenarios but also when perceived as potential issues within the community or environment. Individuals and groups must be vigilant and proactive in identifying and understanding potential conflicts of interest, even when they are not immediately apparent.

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II. ANNEXES

Annex 1 Topics to address in organizational research integrity promotion plans[17]

Nine topics that Research Performing Organizations (RPOs) must address in their Research Integrity Promotion Plan (RIPP)	
Prioritizing people and enhancing capabilities	
Research environment	To foster research integrity and minimize research misconduct and questionable research practices, RPOs need to nurture a supportive environment. Hyper-competition, harmful publication pressure, detrimental power imbalances, and conflicts should be explicitly addressed and adequately handled. Fair, transparent, and responsible policies for assessing, appointing, and promoting researchers must be in place. Diversity and inclusion must be actively promoted. Collegiality, openness, reflection, and shared responsibility are vital elements of a working environment where the risk of major and minor breaches of research integrity is minimized.
Supervision and mentoring	Competent supervision and mentoring must be offered to researchers at all stages of their career development. The RIPP should specify procedures and criteria for qualifying as a supervisor or mentor and should include guidelines for supervision and mentoring of researchers at different career stages, with due attention to responsible research practices.
Research integrity training	Adequate training in research integrity must be provided to researchers at all career stages by qualified trainers. Specific training and opportunities for exchanging experiences should be offered to staff handling research integrity issues and to those teaching research integrity courses. The **RPO** should also ensure that researchers have access to adequate online information about research integrity and responsible research practices.
Building research integrity into organizational structure	
Research ethics structures	To ensure that researchers in the organization can adhere to research ethics requirements, **RPO** s must develop and maintain suitable supportive mechanisms. Research ethics structures should include dedicated and

[17] *Guideline for Promoting Research Integrity in Research Performing Organizations*, Standard Operating Procedures for Research Integrity' (SOPs4RI). Accessible at: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/guideline-for-promoting-research-integrity-in-research-performing-organizations_horizon_en.pdf.

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	adequately trained research ethics committees reflecting the character of research activities within the organization. The RIPP should include procedures for ethics reviews relevant to the various research areas and disciplines within the organization.
Dealing with breaches of research integrity	Even in environments with a strong research integrity culture, breaches of responsible research practices occur. **RPO**s must set up transparent procedures to receive, detect, handle, and sanction research integrity breaches. Procedures to ensure that researchers can consult research integrity officers or councilors in confidence should be part of the RIPP. To ensure that whistle-blowers as well as those accused of research misconduct are protected and that allegations are investigated fairly, **RPO**s should establish research integrity bodies and standardized procedures within the organization or draw on national arrangements. The RIPP should also outline remedies following detection of breaches of research integrity, such as correction or retraction of papers, sanctioning of researchers who engaged in misconduct, and appropriate steps towards prevention in the future.
Data practices and management	**RPO**s must provide guidance, training, and adequate infrastructures related to data management and ensure that practices are compliant with legislation and applicable codes of conduct. Specific policies and procedures included in the RIPP must address legitimate concerns such as data protection, privacy, and Intellectual Property Rights, and ensure compliance with national and international regulations such as the General Data Protection Regulation (GDPR) of the European Union. The organization must provide adequate infrastructures for secure data collection, storage, retention, archiving, and sharing. Moreover, **RPO**s must facilitate data management and curation procedures aligned with FAIR principles with a view to making data findable, accessible, interoperable, and reusable.
Ensuring clarity and Transparency	
Research collaboration	Collaboration across disciplines, sectors and countries is an integral part of research. **RPO**s must have policies and procedures for ensuring that research collaboration can be done responsibly in situations that demand specific attention, e.g. when researchers from different disciplines or with different professional backgrounds collaborate, when EU-based researchers collaborate with researchers from countries not covered by the GDPR and the European Code of Conduct for Research Integrity, or when **RPO**s collaborate across sectors.
Declaration of interests	It is important that **RPO**s enable researchers to provide transparent declarations of interests and ensure that conflicts of interests are handled adequately. Researchers must be supported by policies and procedures in the RIPP that specify the organization's approach to declaring interests and handling conflicts of interests in relation to research conduct, funding, peer review, evaluation, assessment, promotions, and collaboration across different sectors. In relation to commissioned research and consultancy work,

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	the RIPP must outline the steps that the organization takes to be transparent and clear about potential conflicts of interests.
Publication and communication	**RPO**s must specify their expectations about procedures related to the publication and communication of research results. Specific policies and procedures to be included in the RIPP should address the use of preregistration, preprints, and online repositories, guidelines for the attribution of authorship, procedures for handling authorship disputes, the organizational approach to open access, FAIR data curation, expectations about the use of reporting guidelines, procedures for avoiding predatory journals, strategies for responsible peer review practices, and mechanisms to support and acknowledge public communication of research findings.

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III. ANNEXES: GLOSSARY

ALLEA: All European Academies: European Federation of Academies of Sciences and Humanities, representing more than 50 academies from about 40 EU and non-EU countries.

Accountability: Anticipation of the positive and negative impacts of research or evaluation work, extending to all roles within a research or institutional context.

Biobanks: Large collections of biological specimens linked to relevant personal and health information (health records, family history, lifestyle, genetic information) that are held predominantly for use in health and medical research.

Biological Samples: Any material that is derived from a human, animal or microbial source, such as blood, tissue, cells, DNA, RNA or proteins, and which are used for laboratory experiments and analysis.

Clinical Research: Clinical research corresponds to scientific studies carried out on human beings with a view to developing biological or medical knowledge. This is prospective research, involving the follow-up of patients or healthy volunteers. Such research is essential to better understand and treat diseases, and to identify potential risk factors.

Clinical trial: A clinical trial is an experimental situation in which a therapeutic hypothesis is tested in humans. A clinical trial on a drug, for example, aims to assess the efficacy and safety of the new molecule.

Consent: The provision of clear, accurate, and comprehensive information about a research study means that consent can be given voluntarily and can be withdrawn at any time without negative consequences.

DORA: The Declaration on Research Assessment. This term refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It primarily focuses on the direct, intended consequences of technologies as well as their indirect, unintended consequences.

ECoC: European code of conduct

EChOES: Evaluator Checklist for organoid experimental studies

FAIR: Findable, accessible, interoperable, reusable

Fundamental Research: Research carried out to improve our understanding of fundamental principles. It is not necessarily directed towards any specific practical aim or application.

Honesty: Accurate and complete presentation of project details, acknowledging potential biases, conflicts of interest and uncertainties.

HTA: Health technology assessment. This term refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It primarily focuses on the direct, intended consequences of technologies as well as their indirect, unintended consequences.

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IOC: Indicators of compromise. When applied to the realm of research integrity, the concept of IoCs represents factors or evidence that can indicate issues or breaches in the ethical conduct of research. This can encompass a range of behaviors and outcomes, such as Publication Pressure, Data Manipulation, Ethical Breaches or Conflict of Interest.

IVF: In vitro fertilization

MIAOU: Minimum information about organoids and their use

Norm: A norm is a proposition that expresses what must or must not be done.
E.g. you shall not kill!

OGL: Operational guidelines

OIP: Organoid integrity platform

Openness: *Institution to institution*: a commitment to open science (open access, open data -FAIR- open methodologies and protocols) the promotion of interdisciplinarity, multidisciplinarity and cross-disciplinarity, and the promotion of collective efforts.

ORF-ECoc: Organoid research field ECoC

Organoid: A three-dimensional structure grown from stem cells that mimics an organ and can be used in biological and medical research.

Personalized medicine: A medical practice that uses information about a person's own genes or proteins to prevent, diagnose, or treat disease.

Precision medicine: Precision medicine looks at the genetics, environment and lifestyle of a person in order to select the treatment that could work best for them.

RAD: Reflexivity, anticipation, deliberation

REC: Research Ethics Committee

Reliability: Robustness and reproducibility of research work and the assurance of objective, transparent evaluations based on sound methodologies.

Reproducibility in research: Ability to reproduce figures and a discussion of results and conclusions based on access to raw data and a description of the materials and methods used.

Respect: Acceptance of protocols, decisions and counter-arguments and the acknowledgment of contributions, achievements and feedback.

Responsibility: Diligent and impartial conduct of evaluation that considers the potential impacts and

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implications of the evaluation.

RFO: Research funding organization

RIC: Research integrity committee

RIO: Research integrity office

RICOCheck: Research integrity committee organoid checklist

RIPP: Research integrity promotion plan

RPO: Research performing organization

SWAF: Science with and for society

Transparency: Open sharing of, and access to, raw data, methodologies, evaluation procedures, and rules of governance.

TRUSTED: Tissue research under secure transparent ethical donation
This acronym, TRUSTED, highlights the critical elements of the donation process: Tissue Research: Specifies the type of research, emphasizing the scientific focus on tissues and cells. Under Secure Transparent Ethical Donation: Reflects the core values of security, transparency, and ethics in the donation process. It assures donors that their wishes will be respected, and their contributions will be used responsibly and with integrity.

Values: *Universal value*: A value is a universal value if it has the same value or worth for all, or almost all, people. Spheres of human value encompass morality, aesthetic preference, traits, human endeavour and social order.
Contextual value: as opposed to universal values, contextual values actually depend on the context in which they are looked at and modified.

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