Identifying serious and complex ethics issues in EU-funded research

05 July 2021

Disclaimer:

This document has been drafted by a panel of experts at the request of the European Commission (DG Research and Innovation) and aims at raising awareness in the scientific community, and in particular with beneficiaries of EU research and innovation projects. It does not constitute official EU guidance. Neither the European Commission nor any person acting on their behalf can be made responsible for the use made of it.

Legal notice: This Guidance Note does not create any new obligations on the European Commission, Executive Agencies or researchers completing their Ethics Self-Assessment.

Acknowledgements:

This document was prepared by the Research Ethics and Integrity Sector, Directorate Research & Innovation, the European Commission with a collaboration with ethics experts under the supervision of Albena KUYUMDZHIEVA (DG R&I, currently EISMEA) and Ben HAYES.

The main contributors were experts: Ioannis BENEKOS, Vedran KATAVIĆ and Marjo RAUHALA and Siobhán O' SULLIVAN and the staff members of the Research Ethics and Integrity Sector, DG R&I: Lisa DIEPENDAELE, Yves DUMONT, Francesco DURANTI (currently HADEA) and Edyta SIKORSKA.

The document was consulted with the following ethics experts: Jacques DE KEYSER, Edward Stellwagen DOVE IV, Jan-Hendrik HEINRICHS, James A HOUGHTON, Vasiliki MOLLAKI and Doris SCHROEDER.

The Research Ethics and Integrity Sector, DG R&I would like to thank all those concerned.

European Commission
DG Research & Innovation
RTD.03.001- Research Ethics and Integrity Sector
E-mail: RTD-ETHICS-REVIEW-HELPDESK@ec.europa.eu
ORBN
B-1049 Brussels/Belgium

1. Introduction

EU-funded research must comply with ethical principles and relevant European, national and international legislation, including the EU's Charter of Fundamental Rights and the European Convention on Human Rights and its Supplementary Protocols.[1]

All research activities must respect:

- the principle of **proportionality**
- the right to **privacy**
- the right to the protection of **personal data**
- the right to **physical and mental integrity** of all persons
- the right to **equality and non-discrimination**
- high levels of protection of the **environment** and **human health**.[2]

All proposals, which successfully pass the scientific evaluation and are likely to be funded, shall be systematically screened to identify those activities raising complex or serious ethics issues. Such proposals shall be submitted to **an ethics assessment** by an independent ethics panel, pursuant to established procedures for Horizon Europe funded research.[3]

This Guidance note aims to guide those independent ethics experts with responsibility for screening proposals and **identifying whether serious and complex ethics issues are likely to arise in the execution of those projects**. This document is also designed to help applicants identify any such issues while preparing their proposals (and understand why their proposal may have been selected for an ethics assessment).

⚠ The seriousness and complexity of the ethics issues are **assessed on a proposal-by-proposal basis**. It is quite plausible that research proposals on very similar topics or involving similar techniques are assessed differently in terms of "seriousness" and/or "complexity", if they have different approaches, methodologies or potential outcomes.

⚠ Established fields of scientific research, such as medicine and clinical practice, are subject to legal regulation and well-established norms and principles through which serious and complex ethics issues can be identified and addressed, while this may not be the case with new technologies and applications, which may raise novel and challenging ethical concerns. **If the activities are standard practices, with a clear legal/ethics framework, the related ethics issues should not in the meaning of Horizon Europe be considered as serious or complex as they should be addressed by at local, regional and national level, should receive appropriate ethics approval/s and should not undergo an ethics assessment. In such cases of standard practices, there should be no need of ethics advisors or advisory boards.**

Please note that this Guidance Note **should be read in conjunction with wider European Commission (EC) Ethics rules and guidance notes**. For more information, please consult:

How to complete your ethics self-assessment

Online Manual on Funding & Tender Opportunities Portal

Ethics and Data Protection

Ethics in Social Science and Humanities

Other useful links are also available under the Ethics section of the Horizon Europe Program Guide

For research involving **human embryos** (hE) or **human embryonic stem cells** (hESC), an ethics assessment is always mandatory.[4] For all other projects, independent ethics experts will be determining which projects constitute serious and/or complex ethics issues and should be sent for ethics assessment.

[1] See Article 19 of the Horizon Europe Framework Programme and Rules for Participation Regulation (EU) 2021/695 (OJ L 170, 12.5.2021)
[2] Ibid.
[3] Ibid.
[4] See Article 19(3) of the Horizon Europe Framework Programme and Rules for Participation Regulation (EU) 2021/695 (OJ L 170, 12.5.2021)

2. Serious and/or complex ethics issues– general approach

Generally, ethics issues arise whenever research involves:

- humans participants, and/or their cells/tissues
- personal data
- animals
- methods, materials or experiments that could harm the environment, research staff or participants.

Or when research is conducted:

- in locations where the safety and security of researchers and participants may be jeopardised
- outside the EU, especially in countries that lack adequate regulation and/or have a limited capacity to enforce the relevant ethical standards and guidelines. Ethics issue may arise, for example, due to the situation in a particular area or due to the specificities of the local cultural context.

Ethics issues can also take the form of concerns about the potential misuse of new technologies, innovations, applications or research findings – even where research projects have benign intentions.

To **determine whether specific ethics issues are "serious" or "complex"** (or both), we use the general indicators and criteria, as set out below. Specific indicators and criteria that may assist in determining whether specific ethics issues may be deemed "serious" or "complex" (or both) follow in the subsequent sections.

Generally, ethics issues raised by research activities may be considered as "***serious***" when the proposed **research**, **method(s),** or **outcome(s)**:

- have the **potential to violate fundamental rights or freedoms** set out in the EU Charter of Fundamental Rights and European Convention on Human Rights, or undermine fundamental EU values such as human dignity, freedom, democracy, equality and the rule of law; or
- have the **potential to result in significant harm** to researchers, research participants, the public, animals or the environment; or
- in light of the European Code of Conduct for Research Integrity, fundamentally call into question the **integrity of the data and information included in the proposal or the integrity of the practices of the researchers**; or

Ethics issues raised by research activities may be considered as "***complex***" when the proposed **research, method(s)** or **outcome(s)**:

- involve the development or application of **particularly complicated methods or technologies that have not been sufficiently tested and give rise to uncertainty** as regards to the safety of participants and/or the impact of the expected results or outcomes on fundamental rights or research integrity; or
- **raise significant ethics issues 'at scale'** – for example, due to the number of research participants, controversial methods, high-risk technologies or jurisdictions involved; or
- **raise multiple or 'intersectional' ethics issues** – meaning that the ethics issues may compound one another to exacerbate the potential impact on a particular group (e.g. research into marginalised or vulnerable groups that exposes them to the risk of stigmatisation, exclusion, reprisals or increased marginalisation).

The ethics issues pertaining to a particular research proposal may also be considered as 'serious **and/or complex**' if:

- the area of research is the subject of **widespread debate among scientists and ethicists** *and* the specific methods or techniques involved get to the heart of those debates; or
- there are grave doubts about the **capacity of the researchers or participating institutions to effectively mitigate the risks** arising from the project's execution; or
- there is a high risk that the research **results/findings could be misused**, and adequate measures to mitigate or contain this risk cannot be identified or implemented; or
- there is an objective and serious **lack of awareness of key ethical issues in the proposal.**

3. Specific serious or/and complex cases

This section provides **examples** of indicators and criteria, that may help you determine whether the ethics issues raised by a particular project could be considered "serious" and/or "complex".

It is **not an exhaustive list**. Each research proposal has to be **assessed on its own merits** – if you identify substantial ethics concerns that are not covered in this section, you can still recommend a proposal for ethics assessment.

⚠ The following research activities **are not eligible for funding under Horizon Europe:**

- research activities directed at human cloning for reproductive purposes;
- research activity intended to modify the genetic make-up of human beings that could make such changes heritable (apart from research relating to cancer treatment of the gonads, which may be financed);
- research activities intended to create human embryos solely for the purpose of research or stem cell procurement, including the technique of somatic cell nuclear transfer;[5]
- research that leads to the destruction of human embryos;
- research that does not have exclusive focus on civil applications;

No funding shall be granted, neither within nor outside the EU, for research activities that are prohibited in all the Member States. No activity shall be funded in a Member State where such activity is forbidden.[6]

Research on **human stem cells** (both adult and embryonic) may be financed, depending both on the content of the scientific proposal and the laws of the Member States involved.

3.1 Human embryonic stem cells (hESCs), human embryos (hEs), human cells and tissues

For all research activities involving human embryos or human embryonic stem cells, an **ethics assessment is mandatory**, the provision of Statement by the Commission on ethics/stem cell research – Art. 19 apply, and the funding of hESC or hE proposals requires and must be approved by the Horizon Europe Programme Committee.[7]

The ethics issues pertaining to the use in research of other categories of human tissues/cells may be considered "serious and/or complex" if these are, for example:

- **collected** within the project **from vulnerable groups** (e.g. children, unconscious patients, or patients otherwise lacking capacity to consent, prison populations) or involve **foetal or embryonic tissue** (other than hESC) collected within the project or
- used in **organoid research concerned with neurological conditions** or applications; or involving human multi-organoid complexes or related to the development of **synthetic/artificial reproductive cells or organs** (e.g. development of ova, in vitro gametogenesis (IVG)), or involving gastruloids or embryoids.

3.2 Humans

Humans must be considered as 'research participants' whenever they are recruited, observed, actively engaged, or in any other way may be influenced, manipulated, or directed by the research. Regardless of the nature, methods, or topic of the proposed research activities (e.g. collecting biological samples, using personal data, medical interventions, interviews, observations, tracking etc.), ethical issues may arise in any research involving humans.

These issues may be considered as "serious and/or complex" when the proposed research, for example:

- has the **potential to result in significant harm** to the participants (or researchers), such as significant physical pain or bodily harm not related to simple routine medical procedures (e.g. taking a blood sample), psychological

[5] See Article 18(1) of the Horizon Europe Framework Programme and Rules for Participation Regulation (EU) 2021/695 (OJ L 170, 12.5.2021)
[6] See also Article 18(2) of the Horizon Europe Framework Programme and Rules for Participation Regulation (EU) 2021/695 (OJ L 170, 12.5.2021)
[7] See Article 11(4) of the Horizon Europe Specific Programme Decision 2021/764 (OJ L 167I)

harm, personal embarrassment or humiliation, or other harm that may adversely affect the participants in a significant way; or

- employs **covert methods or deception** that may cause harm to participants (or researchers), or entails participation in **unlawful activities** (e.g. following persons making irregular border crossings or supplying illegal goods or services), or is **unnecessary for the realisation of significant scientific, educational, or applied value of the research;** or
- includes **children/minors/people unable to give informed consent**, with no clear justification for their participation or benefit to them; or
- involves **highly vulnerable participants**, such as people exposed to or affected by multiple or intersecting vulnerabilities (e.g. refugees or migrants facing extreme poverty, gender-based stigmatisation, or violence), or methods that have the potential to significantly exacerbate the vulnerability of already vulnerable groups or individuals; or
- includes **vulnerable participants in first in-human or early-stage clinical studies** for new therapeutics (including new chemical entities, biologics, gene therapies), medical applications and procedures; or
- involves **'challenge trials'**, in which participants are **intentionally exposed to an infectious disease that may result in severe or chronic illness**, or when participants have underlying medical conditions that increase their risks for severe illness; or
- involves **clinical studies concerned with end-of-life or emergency care** and related clinical decision-making; or
- deploys **medical devices, particularly implanted devices**, that aim to or have the potential to bring about **involuntarily behaviour change or therapeutic 'adherence'**; or
- involves **potentially traumatising topics** (e.g. recounting of personal experiences of war, refugee flight, violence, assault, abuse, life-threatening illness or injury); or
- aims to **improve human performance** by interventions in or on the human body **(human enhancement[8]) –** in the form of implants, drugs, genetic enhancement or machines. This concerns especially interventions that are irreversible, internal to the body, have long term impacts (physical, psychological, social), have a limited timespan or require updates; or have implications for the privacy of groups and individuals; or
- involves untested forms of **human bio-engineering, human-machine integration or human-animal chimeras**; or
- suggests the potential **coercion of research participants** through excessive or inappropriate financial compensation, or because their relationship to the researchers suggests that their consent may be obtained under some form of duress or out of a sense of obligation; or
- **implies the circumvention of EU labour law** by 'crowdsourcing', 'micro tasking' or 'outsourcing' the research (e.g. research-related tasks undertaken by remotely located "crowd workers", who may be situated anywhere in the world, to perform discrete on-demand tasks); or
- uses **high-risk or inappropriate techniques and methods** that may expose participants to **unacceptable risk** (e.g. insecure online surveys addressing sensitive issues or processing sensitive/special category data, methods that encourage participation by vulnerable groups without regard to their vulnerability); or
- involves studies whose findings carry a **high risk of exposure or identification of individuals and/or stigmatisation of a minority or marginalised group** (e.g. on the basis of poverty, ethnicity, religion, gender/gender identity, disabilities, age, sexuality or perceived involvement in illegal activities); or

[8] Human enhancement is a modification aimed at improving human performance and brought about by science-based and/or technology-based interventions in or on the human body (Sean R. Jensen, Saskia Nagel, Philip Brey, Tanne Ditzel, Rowena Rodrigues, Stearns Broadhead, & David Wright. (2018). SIENNA D3.1: State-of-the-art Review: Human Enhancement (Version V1.1). Zenodo: https://zenodo.org/record/4066557#.YEo_-y2l1pQ)

- involves studies on **human sexuality** (e.g. research on assisted reproduction, fertility, pregnancy termination, gender reassignment and transgender issues).

3.3 Incidental or unexpected findings

Incidental or unexpected findings are traditionally associated with clinical research but may occur in human and social science research as well. Such findings fall outside of the scope of the principal research objectives but necessitate action on the part of the researchers.

The handling of incidental or unexpected findings may raise 'serious and/or complex' ethics issues as such findings can have a significant impact on research participants' wellbeing, cause psychological distress to researchers, raise safety or safeguarding issues, or require the researcher to disclose the information to appropriate or designated authorities.

Therefore, the ethics issues in a particular project may be considered as 'serious and/or complex' when the proposed research is likely to yield, for example:

- **medical or genetic** incidental findings that may have **life-changing consequences for research participants** due to their likely impact; or
- **social or behavioural unexpected or incidental findings that may require may require interventions to safeguard the well-being of research participants** (e.g. signs of physical abuse, self-harm, or drug dependency or neglect in minors); or
- findings that are **subject to positive disclosure obligations** under international or EU law, or the national laws of a country (EU or non-EU) in which the research takes place, requiring researchers to breach the confidence of research participants. Examples include criminal conduct such as war crimes, child sexual exploitation, human trafficking or terrorism.

3.4 Safety and security

The safety and security of everybody involved in research – whether as participants, investigators, interlocutors, communities or third parties impacted by the research – must be a priority in all research proposals.

The ethics issues raised by a particular project may be considered as 'serious and/or complex' if the proposed research, for example:

- involves considerable **health and safety risks** to researchers and/or participants; or
- **takes place in a situation of international or internal armed conflict, other situations of violence (including domestic violence) or humanitarian crises or emergencies**; or
- takes place in a **political climate that is hostile to the research topic or its objectives** and endangers researchers, research collaborators (including third party collaborators contracted to assist with the research activities in the relevant location, even if the research staff themselves remain in another location) and/or research participants; or
- involves the use of potentially **harmful substances, processes, technologies, organisms or materials** in a manner that raises significant concerns about individual security or safety or the protection of public health.

3.5 Animals and the environment

The EU has signed international conventions and adopted legislation regulating the use of animals in scientific experiments and protecting the natural environment, its flora, fauna and biodiversity.

In this respect, the ethics issues in a particular project may be deemed 'serious and/or complex' if the proposed research, for example:

- has the potential to result in **significant and irreversible harm to the environment, flora or fauna**; or
- involves **experimentation on animals that enjoy particular protection** (e.g. non-human primates, animals

living in the wild, endangered species) without clear benefit to their species or habitat; or

- involves untested forms of **animal bio-engineering, animal-machine integration or animal interspecies chimerism or synthetic biology**; or
- has the potential to result in **significant pain or distress to animals**, without a clear justification and/or sufficient measures to alleviate/prevent such suffering.

3.6 Research in non-EU countries

Conducting research activities, partially or wholly, in a non-EU country can raise numerous ethical issues, particularly in resource-limited settings. Special care must be taken to avoid any '*double standards in research and support equitable long-term research relationships between partners in lower-income and high-income settings, based on fairness, respect, care and honesty*'.[9]

In this respect, the ethics issues related to research activities conducted outside of the EU may be considered as 'serious and/or complex' if the proposed research, for example:

- appears to **take advantage of differences in standards or the absence of legislative protection** for research participants, local researchers and other local staff, data protection and privacy, animals, the environment or the public, particularly in lower-income settings; or
- seeks to **exploit scarce or protected local resources, without benefit-sharing community consent** (where practised and relevant) and/or appropriate **permission** from relevant local authorities; or
- takes place in a **setting where the subject matter or research methods are likely to be perceived as highly controversial** by a local community; or
- does not envisage **community assent, obtained through recognised local structures and/or local ethics approval** in the country where the research takes place; or
- involves risks of **stigmatisation or discrimination, or the possibility of self-incrimination**, for either the participants, investigators, interlocutors, communities or other stakeholders involved; or
- involves or impacts **indigenous people or vulnerable minority groups** without sufficiently taking into account the local context, vulnerabilities, core beliefs or value systems.

3.7 Data protection

Personal data refers to all information relating to an identified or identifiable natural person. All data controllers and processers, including researchers and service providers, must protect personal data in accordance with the EU General Data Protection Regulation (GDPR) and the respective national and sectorial legal framework.

An identifiable natural person is someone who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that person.[10]

Even if service providers and external collaborators are engaged in the research, the **obligation to safeguard data subject's rights and freedoms rests with the principal researchers** (e.g. the beneficiary and partners of a consortium). This obligation cannot be 'outsourced' or delegated (e.g., when surveys are conducted or data is processed or hosted by third parties or subcontractors). For more details, please consult the 'Ethics and Data Protection' guidance note.

The ethics issues related to the processing of personal data in a particular project may be considered as 'serious and/or complex' if the proposed research, for example:

[9] Global Code of conduct for research in resource-poor settings

[10] Article 2(a) EU General Data Protection Regulation (GDPR).

- envisages the **large-scale collection of special category data**[11] **and/or data related to criminal convictions and offences, if the intended processing poses a significant risk** to the rights and freedoms of the research participants; or
- involves the **covert observation or deception of research participants, to collect sensitive/special category data**; or
- uses **personal data that was not collected or otherwise provided by the data subjects** for research purposes, and for **which the data subjects may have a legitimate objection to** (e.g. data collected from 'closed' or private groups on social media platforms, covert activity trackers or sensors in connected devices, the processing of an identifiable individual's telecommunications traffic or geolocation data); or
- carries a **significant risk of breaching privacy or confidentiality** that is likely to result in threats to data subjects' physical safety, loss of business or employment opportunities, humiliation or damage to their reputation or relationships, or
- involves **profiling and/or systematic monitoring of individuals or group of individuals, and/or intrusive methods of data processing** (e.g. data-mining, web-crawling, social network analysis, geolocation tracking); or
- results in the **transfer of special category data to countries with inadequate data protection regimes**,[12] without the knowledge or explicit consent of the data subjects.

3.8 Development, deployment and use of Artificial Intelligence (AI) and other new and emerging technologies

Whereas established fields of scientific research, such as medicine and clinical practice, are subject to legal regulation and well-established norms and principles through which serious and complex ethics issues can be identified and addressed, this may not be the case with new technologies, which may raise novel and challenging ethical concerns.

The particular ethics issues raised by developing or deploying new technologies will depend on the context, use case or nature of the application. Specific caution is warranted for technologies that may pose a high risk of harm to people's health and safety or fundamental rights and freedom.

⚠ Examples of **high-risk areas and applications** that involve new and emerging technologies include:

- biometric identification systems;
- the administration of justice;
- law enforcement;
- migration, asylum and border control;
- democratic processes and institutions;
- the operation of essential critical infrastructure and services;
- access to education and vocational training;
- employment and worker management;
- access to public or private services and social welfare programmes.

When assessing the seriousness and/or complexity of the ethics issues involved in developing or deploying new technologies, you should take into consideration the type of research being proposed, the technological readiness level, as well as the severity and likelihood of the potential harm.

The ethics issues related to the use of new technologies in a particular project may be considered as 'serious and/or complex' if the proposed research involves the development, deployment or use of, for example:

[11] Special categories of personal data (formerly known as 'sensitive data') include personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, or trade union membership, and the processing of genetic data or biometric data for the purpose of uniquely identifying a natural person, data concerning health or data concerning a person's sex life or sexual orientation (Article 9(1) GDPR) EU General Data Protection Regulation (GDPR).

[12] How the EU determines if a non-EU country has an adequate level of data protection: https://ec.europa.eu/info/law/law-topic/data-protection/international-dimension-data-protection/adequacy-decisions_en

- **surveillance technology that is not necessary or proportionate in a democratic society** – for example due to the degree of intrusion, its blanket or indiscriminate effect, or lack of safeguards for affected individuals; or
- **societal scoring, automated behavioural or psychological profiling**, or the use of econometrics or artificial intelligence, to make probabilistic determinations about individuals and their behaviour, groups or entire populations that **could violate human dignity or lead to stigmatisation, or discrimination** against them; or
- systems/techniques that have the potential to lead to **significant negative social impacts** (e.g. on democracy, media, labour market, freedoms, educational choices, mass surveillance) **and/or significant negative environmental impacts** – either through intended applications or plausible alternative uses; or
- systems/technique aimed at **replacing or influencing human decision-making processes** in a way likely to adversely impact affected individuals (e.g. issues affecting human life, health, well-being or human rights, or economic, social or political decisions) or **have the potential to circumvent the autonomy** of those individuals; or
- systems/techniques/technology that can lead to **new manipulative, exploitative or social control practices**; or
- systems/techniques/technology with the potential to have harmful implications for **human rights, subordinate, deceive or manipulate people,** violate **bodily or mental integrity,** create **attachment or addiction**, or **hide the fact that people are interacting with AI**.

3.9 Misuse

The findings or outputs from research projects with benign intentions may have the potential to harm humans, animals or the environment if used for purposes other than those intended. While many research findings have the potential for misuse, the development or production of certain types of materials, methods, technologies or knowledge may pose a greater risk of unethical use than others may.

The ethics issues related to the potential misuse of findings or outputs or knowledge gained from a particular project may be considered as 'serious and/or complex' if the proposed research, for example, concerns the development of:

- **surveillance technologies** that – if deployed – are likely to have harmful implications **for human rights or unduly restrict civil liberties**; or
- **social, behavioural, medical or genetic profiling technologies** that could be used to stigmatise, discriminate against, harass or intimidate people, or to limit their autonomy; or
- materials, methods, technologies or knowledge that could tangibly result in **serious harm to humans, public health, animals or the environment** if they were released, modified or enhanced; or
- publicly available **tools that could expose exploitable flaws in the cyber- or physical security of critical sectors** (e.g. energy, transport, water, health, communications or finance).

References and further reading

- How to complete your ethics self-assessment
- Online Manual on Funding & Tender Opportunities Portal
- Horizon Europe Program Guide
- Horizon Europe Framework Programme and Rules for Participation Regulation (EU)
- Ethics and Data Protection
- Ethics in Social Science and Humanities
- European Code of Conduct for Research Integrity
- Statement by the Commission on ethics/stem cell research – Art. 19
- Commission Recommendation on internal compliance programmes for controls of research involving dual-use items
- Potential misuse of research results
- Research focusing exclusively on civil applications
- Global code of conduct for research in resource-poor settings
- SIENNA Ethical guidance for research with a potential for human enhancement
- Guidance note on research on refugees, asylum seekers and migrants