DECISION

DEcompensated CIrrhoSIs: identification of new cOmbiNatorial therapies based on systems approaches

H2020 – 847949

D6.7 Checklist for participants to assure informed consent / other mechanisms for those unable to give a written consent

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Abbreviations

CIOMS	Council for International Organizations of Medical Sciences
WHO	World Health Organisation
UNESCO	United Nations Educational and Cultural Organization
GDPR	General Data Protection Regulation of the European Union
REC	Research ethics committee

Contributors

Contributor	Contribution	Estimate of person-months
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Table of Contents

1. Introduction

There are several ethical guidelines and international legal regulations on the requirements that should be respected in biomedical research. In the competitive calls for funding of both European and national biomedical research projects, compliance with certain ethical guidelines is binding, especially the Declaration of Helsinki (2013), of the World Medical Association and other regulatory references of legal nature.

We propose a checklist to delve into the ethical and legal bases that will determine the excellence of research projects beyond the mere fulfilment of the minimum established requirements. We also provide an overview of research ethics that is useful for the different agents involved in the research ecosystem, not for only researchers -and those who help carry out the proposals- but also for research ethics committees as reviewers and key actors of research. The recipients could also be potential participants who can be patients or healthy volunteers who must be informed before deciding about their participation in research projects that will revert to their benefit either directly or indirectly.

While it is true that the guides constitute a tool that allows proposing specific measures about the research ethics for each project that includes human beings, the guides are not automatically applied. It requires specialists in the topic for allowing the design and the implementation of the required research ethics-management tools. In this way, research will be performed in a way that it is consistent with the ethical standards.

Therefore, in the framework of the implementation of the DECISION project, we have developed a checklist, as an all-operative document whose purpose is to facilitate the identification, compliance, and verification of the key aspects related to research involving potential participants, the uses of human biological samples, and/or personal data. In sum, the proposal allows identifying ethical issues, but also methodological aspects, legal requirements and the societal impact of the research projects.

2. The cornerstones to developing the checklist

We have selected two ethical guides that we consider relevant in the fields of research ethics and bioethics understood as the analysis of not only the ethical aspects, but also legal and social aspects related to biomedicine and biotechnology: The Declaration of Helsinki (2013) of the World Medical Association and the CIOMS Guidelines for Biomedical Research Involving Human Subjects (2016) of The Council for International Organizations of Medical Sciences (CIOMS), an international, non-governmental, non-profit organization established jointly by WHO and UNESCO. The Helsinki Declaration influences this, due to the wide recognition and legitimacy that this declaration has, as well as the level of detail and problematization that it raises around the design and implementation of the informed consent process. In case of the CIOMS and WHO Guidelines, they have been issued by widely recognized international organizations in the field of health research. Furthermore, their structure, given through thematic guidelines, is useful for addressing the problems that arise in the matter giving rise to quite specific requirements and management tools for reviewing the methodological, ethical, legal, and societal aspects of each research project.

Likewise, the checklist includes some of the fundamental issues that must be verified for adequate compliance with the General Data Protection Regulation of the European Union, known as GDPR (2018) related to biomedical research.

3. To whom it is intended/ Recipients

The checklist is intended as a tool to facilitate the work of the diverse stakeholders who are part of the research ecosystem. In this regard, it provides the principal investigator and the research team with a tool for the design of the protocol, for the adequate implementation of the informed consent processes, and for the sake of research integrity. It could serve for monitoring and oversight of the research project in its inception and in case of possible amendments.

Furthermore, the members of the research ethics committees that should review the project are provided with a useful tool that, from a practical perspective moving from principles to procedures, could help to identify or to check key issues in biomedical research from the scope of ethics and human rights. At the same time, it allows them to verify directly the knowledge and expertise on this matter of the principal investigator, the members of the research team, and other agents involved in the preparation of the project and its research protocol and informed consent sheet.

Last but not least, it could also be useful for the potential participants, as it provides a kind of roadmap on how research works and the specific requirements that should be respected to promote research aligned with participants and society. At the same time, it could contribute to focusing research on participants and society and not only on the research itself and put them into the centre of the decision-making process.

Researchers, members of ethics committees, and participants interact throughout the research process. In this sense, it is important that each of these stakeholders also participates in the implementation of research ethics management based on this type of instrument designed considering the requirements of the research project.

4. Checklist

	Checklist	Yes	No	Comments
A.	**DECLARATION OF HELSINKI – ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS, WORLD MEDICAL ASSOCIATION (2013)**			
1.	The project has a section dedicated to a detailed description of the methodology and the need for the inclusion of human subjects.			
2.	Before the study begins, the research protocol must be submitted for consideration, comment, guidance, and approval to the entitled research ethics committee (REC) or committees of each local research site.			
3.	An assessment has been carried out to weigh the risks and benefits.			
4.	The minimum possible risk has been sought, and measures have been implemented to evaluate risks before and during the research project.			
5.	The project generates direct benefits for its participants.			
6.	The research project has been registered in a public database before the recruitment of the first participant.			
7.	**Informed Consent of the potential participants**			
7.1.	Potential participants able to provide informed consent			
	Each potential participant has been informed about the following:			
7.1.1.	Aims, methods, benefits, and potential risks of the study.			
7.1.2.	The right to refuse to participate in the study and to withdraw consent to participate at any time without any implications for their health or situation. Participation in biomedical research is always voluntary.			
7.1.3.	Any possible conflicts of interests, institutional affiliations of the researchers, and sources of funding.			
7.1.4.	The general outcome and results of the study.			
7.1.5.	Post-study provisions and any other relevant aspect of the study.			
7.2.	Potential participants who are physically or mentally incapable to provide informed consent			
7.2.1.	The legal representative must have been informed about the information included in paragraph 7.1.			

	Checklist	Yes	No	Comments
7.2.2.	The principal researcher has asked for informed consent from the legal representative.			
7.2.3.	The potential participant must have been informed about the information included in paragraph 6.1. Special attention should be paid to the specific needs of the participants as well as the methods used so that they truly understand the information provided to them and the implications of their participation.			
7.2.4.	If the potential participant expresses his disagreement, this must be respected. In that sense, he or she will not be included in the research project.			
7.2.5.	The potential participant who is not physically or mentally able to give his/her consent may only participate in that research in which the condition that prevents him from consenting is relevant for obtaining the results of the research.			
7.2.6.	The research project proves the need for these participants to be included.			
7.2.7.	The protocol shows the benefit of participation in the study: it must be specified if the benefit will be direct or if it benefits the group represented by the entitled potential participant.			
B.	**INTERNATIONAL ETHICAL GUIDELINES FOR HEALTH-RELATED RESEARCH INVOLVING HUMANS, CIOMS & WHO (2016)**			
1.	The scientific and societal value of the research project:			
1.1.	The project includes a specific section that describes the scientific and societal value expected from the project and its possible impact.			
1.2.	The research project is essential to the social value of health-related research and its design is scientifically sound. The information derived could not be obtained by other means.			
1.3.	The project aims to contribute to the formulation or evaluation of interventions, policies, or practices that promote and improve health.			

	Checklist	Yes	No	Comments
1.4	The principal researcher and its staff are qualified and trained properly and have the knowledge, skills, and expertise to conduct the proposed research. These conditions are expected to be proven. This includes research integrity and having received appropriate ethics education and training.			
2.	Equitable distribution of benefits and burdens in the selection of individuals and groups of participants in research			
2.1.	Groups, communities and individuals invited to participate in research must have been selected for scientific reasons and not because they are easy to recruit based on their social or economic situation.			
2.2.	The exclusion of groups that need special protection must be justified. The participation of vulnerable subjects has not been ruled out due to their condition as such.			
3.	Equitable distribution of potential individual benefits and risk in a research project			
3.1.	For research interventions or procedures that offer potential individual benefit to participants			
3.1.1.	Risks are acceptable if they are minimized and outweighed by the prospect of potential individual benefit.			
3.1.2.	The available evidence suggests that the intervention will be at least as advantageous, in the light of foreseeable risks and benefits, as any established effective alternative.			
3.2.	For research interventions or procedures that offer no potential individual benefits to participants			
3.2.1.	The risks must be minimized and weighed out with the social and scientific value of the knowledge to be gained (expected benefits to society from the generalizable knowledge).			
3.3.	Evaluation of individual research interventions and procedures of the research project			
3.3.1.	Researchers have evaluated the risks and potential individual benefits of each research intervention and procedure, and then evaluate the aggregated risks and potential individual benefits of the study as a whole.			
3.3.2.	The research protocol includes results from preclinical studies and, where applicable, early phase or exploratory trials of the proposed intervention in human beings.			
3.4.	Measures are taken to control and reduce the risks that could arise in the research			

	Checklist	Yes	No	Comments
3.4.1.	There is a plan to control and reduce the risks that could arise in the research. This plan includes:			
a.	Monitoring the study and providing mechanisms for responding to adverse events have been planned.			
b.	A Data Safety and Monitoring Committee (DSMC) to review and decide on data about harms and benefits has been established.			
c.	Clear criteria for stopping a study have been instituted.			
d.	Safeguards to protect the confidentiality of personal data have been installed.			
e.	Exemptions, when justified, from requirements to report information about illegal activities of study participants have been planned.			
3.4.2.	The risks that the members of the research team would face have been evaluated and have been minimized as much as possible.			
4.	Design and implementation of the informed consent process			
4.1.	General considerations			
4.1.1.	The research project shows that informed consent has been conceived as a process.			
4.1.2.	Informed consent has been requested after having provided the participants with relevant information.			
4.1.3.	Participants have been given sufficient opportunity and time to consider their participation and raised questions and doubts.			
4.2.	Written Information for participants in the informed consent process			
4.2.1.	A signed form evidencing their acceptance has been obtained from each participant. If this document has not been requested, the justification must have been included in the research project.			
4.2.2.	All potential participants have been provided with a written information leaflet that they may take with them. This written information has been reviewed and approved by the research ethics committee.			
4.2.3.	Aims, methods, sources of funding, possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-trial access, and any other relevant aspects of the study have been explained.			

	Checklist	Yes	No	Comments
4.2.4.	The informed consent form does not include any statement that leaves the impression that the participant waives any of his or her rights recognized by the applicable legal regulation.			
4.2.5.	The consent form does not include any language that appears to release the researcher, sponsor or research institution from liability for any negligence that may have occurred.			
4.3.	Research involving children and adolescents			
4.3.1.	The informed consent for the participation of the child or adolescent has been given by one of the parents or a legally authorized representative.			
4.3.2.	The agreement (assent) of the child or adolescent has been obtained in keeping with the child's or adolescent's capacity, after having been provided with adequate information about the research tailored to the child's or adolescent's level of maturity.			
4.3.3.	If children reach the legal age of maturity during the research, their consent to continued participation should be obtained.			
4.3.4.	The refusal of a child or adolescent to participate or continue in the research has been respected, unless, in exceptional circumstances, research participation is considered the best medical option for a child or adolescent.			
4.4.	Modifications and waivers of informed consent			
4.4.1.	Waivers to obtaining informed consent will only proceed if the research would not be feasible or practicable to carry out without the waiver or modification, it has important social value and it poses no more than minimal risks to participants.			
4.4.2.	The reasons that have generated the waiver have been described in detail in the research project.			
4.4.3.	A research ethics committee has approved a modification or waiver of informed consent to research.			
4.4.4.	No ethical review or waiver of consent was required because the activity is required by law.			

	Checklist	Yes	No	Comments
C.	**General Data Protection Regulation (GDPR), European Union (2018)**			
1.	The principles and rights set out in the GDPR regarding the processing of personal data have been reflected and included in the project.			
2.	The exercise of the above-mentioned rights is clear, and the persons responsible have been identified.			
3.	A Data Management Plan has been planned to explain the uses of personal data during the lifecycle of the project: from its inception to its end, including the reporting of results and further actions to be taken.			
4.	Data Controllers and Data Processors have been identified.			
5.	Data Protection Officer/s have been identified to provide an assessment.			
6.	Legal agreements regarding personal data treatments (i.e. Joint Controllership Agreement etc. have been prepared in due time.			
7.	A privacy policy has been designed at the inception of the project.			
8.	A Data Protection Impact Assessment has been planned and a methodology is available for use.			
9.	Technical and organizational measures have been designed to assure the protection of the personal data of potential participants and to identify and mitigate possible risks.			

5. Acknowledgement and Disclaimer

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