TABLE FOR COMMENTS

COMMENTS ON WHO WORKING DOCUMENT: WORKING DOCUMENT REC TOOL REV. 1
TITLE OF THE DOCUMENT: WHO TOOL, BENCHMARKING ETHICS OVERSIGHT OF HEALTH-RELATED RESEARCH WITH HUMAN PARTICIPANTS: INDICATORS AND FACTSHEETS, FINAL DRAFT – 26 NOVEMBER 2021

Name: The Mason Institute (a collective response from legal and bioethics scholars)

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*Kindly complete the table **without modifying the format** of the document - thank you.*

General comment(s) if any :	**Originator of the comments**
This response is submitted by members of the Mason Institute, based in the School of Law at the University of Edinburgh, Scotland. The Mason Institute is an interdisciplinary network aimed at investigating the ethical, legal, social and political issues at the interface between medicine, life sciences and the law. More information about the Mason Institute can be found here: https://www.law.ed.ac.uk/research/research-centres-and-networks/mason-institute A recently completed project under the auspices of the Mason Institute – the Liminal Spaces project – examined multiple dimensions of health research regulation, including robust ethical oversight, the role of ethics committees, the pursuit of social value, stakeholder engagement, regulatory stewardship, the use of best practices and the important issue of public trust. This project resulted in many publications, policy briefs and other resources that are all **freely available** on the project website here: https://www.law.ed.ac.uk/research/research-projects/liminal-spaces These resources will be useful for WHO Member States in "evaluating their existing capacity to provide appropriate ethical oversight of health-related research with humans by identifying strengths and limitations in their laws and in the organizational structures, policies, and 39 practices of the bodies responsible for research ethics oversight." As to the Working Document, we have three high level points to make that apply to the draft as a whole:	All comments in the document come from members of the Mason Institute (MI)

1. **Law:** the team submitting this response is composed of a majority of lawyers, but we are struck by how much 'faith' the working document seems to place in law as the optimal basis for securing certain key features of good practice in ethical oversight, and that the absence of legal provisions defining the mandates, roles and authority of RECs to oversee ethical issues in health-related research with humans is seen as less than optimal. It is our experience of working with colleagues in many countries around the globe that ethics review and guidance has often grown up piecemeal and in a responsive mode as human health research has gathered pace over the last half century. It is certainly not the norm internationally that most countries have legislated for ethics review or the role of RECs in ethical oversight of health research. Indeed, to take Europe as one regional example, few if any countries in this region have legislated for ethics review outside the relatively narrow context of clinical trials involving medicinal products. Various forms of governing the ethics of health-related research therefore remain *outside* the remit of law; instead, it falls to policy and other forms of 'soft' law to regulate the work of those tasked with assessing the ethics issues associated with health-realted research, be they researchers, sponsors, research ethics committees, or other actors. And yet, despite the absence of hard law outside the confines of clinical trials, it is generally accepted that research ethics governance processes in many regions are functioning relatively well. To suggest that many countries in Europe are operating sub-optimally due to the absence of law, outside of clinical trials for health-related research, strikes us as a rather radical claim, and it is unlikely that many governments will take up the cause to put research ethics review of all forms of health-related research on a statutory footing any time soon. Our research indicates that law itself is not a driver of optimal performance of research ethics oversight, nor a necessary and sufficient condition to govern (and govern successfully) the form and function of research ethics committees. Given this, we would be concerned if the final WHO tool gave the impression that a legislative basis for sound ethical oversight was necessary or even an optimal way to proceed. There is a related concern that law is often backed legal sanction; we are concerned about the effects additional laws governing RECs, and in turn individual members, would have on current and future retainment and recruitment of REC members, as well as the collateral effect it would create for health research and innovation across the globe. Many countries, for example, have established a National Regulatory Authority (NRA) under who auspices RECs operate, or alternatively, institutional RECs operate according to governance frameworks, policies, and standard operating procedures endorsed by their institutions. Such NRAs and institutions might have a legal basis but the same is not necessarily true of all of the functions of a REC covered in the Working Document, particularly for RECs in countries that do not have an NRA and otherwise operate solely as "local RECs" within disparate institutions. We suggest then, as an alternative, that the section on "Using these Indicators" make it clear that the work of a REC under an NRA or institutional framework or policy that complies with the provisions of EC01 would also be sufficient and equivalent to having "legal provisions".

2. **Right to Vote:** There seems to be an assumption in the document that RECs necessarily and always work based on a voting system (and by implication that decisions are carried by a majority). Again, in our experience, this is not always the case and this kind of wording might be unduly restrictive and/or exclusionary. Our research on research ethics committes in the UK, including both within universities (for health-related research not involving the National Health Service) and for research ethics committees operating within the National Health Service, makes clear that *consensus* is the operating system in place to come to decisions concerning the ethics issues involved in research projects, and how they ought to be addressed. Our discussions with colleagues in

other countries also indicate that voting rarely, if ever, takes place in REC deliberations. Suggesting that non-members should not have 'the right to vote' therefore may give the false impression that voting is standard practice, and may also be taken as a signal to silence the voices of non-members, when in practice REC deliberation is about full and open deliberation among all people who have been invited to participate in the deliberation of a research project, be they standing committee members or *ad hoc* or invited experts. 3. **Terminology:** At various junctures, terminology is used that is question-begging. For example, what is meant by "research" and is this to include clinical audit? Such questions are not merely academic, as what constitutes research and what constitutes clinical audit may well determine what is subject to review by a REC, be it under policy, law, or other normative instrument. Setting out in the final WHO tool what is considered research will be crucial for RECs in determining under what circumstances they ought to consider becoming involved in providing appropriate ethical oversight of health-related research with humans. In EC01.01, how are "low risk studies" defined for the purposes of the exemption? What is meant by "responsible research institutions" in EC07? Other specific examples are given below, but as a general recommendation for clarity and helpfulness, we suggest that it would be helpful to include a brief "Definitions" section in the final WHO tool.	

Section	Line	Comment/rationale	Proposed change/suggested text	Classification L= low, M= medium, H= high	Originator of the comments (for WHO use)
01	69	This provision begins: "As required by internationally accepted ethical standards,…" It strikes us as strange that ethical documents seek to proscribe a legal basis. As a minimum, we would check this claim. If at all suspect, we suggest it be removed.	Remove source of "international ethical standards" to justify the need for a legal basis for REC action	M	MI
01	89-96	This section talks about independence. However, independence seems to be solely concerned with conflict of interest. This is not the only measure of independence.	Consider including other measures of independence, such as freedom of thought and decision-making, avoidance of undue influence by any vested interest and having the ability to 'stand apart' from inappropriate influences in taking an "uncontaminated decision".	H	MI

Section	Line	Comment/rationale	Proposed change/suggested text	Classification L= low, M= medium, H= high	Originator of the comments (for WHO use)
01	89-96	We note it is stated here that it is not possible to overrule RECs disapproval - what about an appeal to a superior National Regulatory Authority, another REC (such as an appeal from a departmental REC within a university to a central university REC, or to another REC within the health service), or judicial review? Such a facility does not undermine independence of a REC, it is concerned with fair process for investigators.	Consider including recognition of the possibility of appeals to a NRA, other RECs, or the eventuality of judicial review of REC decisions in a court of law	H	MI
01	115-116	There is an unjustified presumption that association of ethical standards with legal requirement is optimal in verifying whether RECs in their reviews satisfy “the ethical standards articulated in WHO guidance or its equivalent”.	Remove this sub-indicator or the explicit association between a legal requirement and ethical standards. Instead, it should be assessed via this indicator whether the governing instrument, be it any of law, policy, regulation, framework or so on sets out commonly accepted standards by which RECs should review health-related research.	H	MI
01	115-125	We are surprised not to see mention here of ‘social value’, especially since this is the subject of Guideline 1 of CIOMS and the Working Document refers to “WHO guidance or equivalent”	Include mention of social value whenever there is discussion of the range of considerations for a REC. For more on social value, see here: https://www.law.ed.ac.uk/sites/default/files/2021-03/Social%20value%20policy%20brief_1.pdf	H	MI

Section	Line	Comment/rationale	Proposed change/suggested text	Classification L= low, M= medium, H= high	Originator of the comments (for WHO use)
01	143-152	The provision here requires RECs to conduct review of ongoing research without specifying the need, nature and proportionality of such a review – this has serious resource implications, it is not a common current practice, and when it is done it might not be done by RECs themselves. What about requiring reporting rather than review in the event of material change from the approved protocol? Furthermore, making this a legal requirement is very onerous - with which sanctions if it is not done?	Remove the requirement for continuing review of ongoing research, unless this is defined as involving light touch and based on reporting from investigators when there is a material change from the approved protocol	H	MI
01	168-174	RECs can suspend/terminate research – is there not a better role here for funders? We are not aware of RECs holding this authority in many countries, as distinct from other regulatory actors. Why is this the role of a REC and nor a National Regulatory Authority? What about a right of appeal? Suspension and then what? Will there be review of the decision? On what time frame?	More thought should be given to this function, who should carry it out, with what consequences, with or without an appeal, and on what time frame.	H	MI
01	239-247	Suspend or revoke REC authority for "serious noncompliance" strikes us as question-begging. What are examples of this kind of noncompliance? What of transparency of procedures?	Specify more clearly what is meant by this phrase.	H	MI

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02	405-412	This section on removal of REC members could be more complete	Removal of REC members can also be done relative to the terms of reference and conditions of appointment	M	MI
02	466-472	This section talks about sufficiently competent staff – there are major implications for regular review process required above; also, this is not just about human resources, also economic resources - link to EC03.05	Consider the implications of requiring REC review on an on-going basis	H	MI
02		This section talks about staff training, but that training is not just about ethics but also regulatory and procedural requirements surrounding a range of types of research applications. Consider, for example, research protocols that involve multiple field of regulation – such as straddling clinical trials, tissue banking, data protection, stem cells etc – staff need to be trained to guide and navigate researchers through the regulatory landscapes. We have argued elsewhere for the need for **REGULATORY STEWARDSHIP** for such complex cases and other challenges in regulation.	Training should also extend to "regulatory stewardship" for dealing with complex cases and helping investigators navigate multiple regulatory environments. For more on regulatory stewardship, see here: https://www.law.ed.ac.uk/sites/default/files/2021-03/Regulatory%20stewardship%20concept%20note.pdf	H	MI
03	559-563	The section speaks of the "actual cost of review", is this to include cost of regular re-review as research is on-going? How is this to be calculated? Should it be covered upfront? This could serve as a serious potential	Consider costs of follow-up review.	H	MI

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		disincentive to research or as between countries. It might lead to a race to countries where review has the lightest touch.			
04	592-605	There is also a role for stewardship in this section, e.g. in rapidly identifying exempt or expedited review but also complex cases!	See above of regulatory stewardship	H	MI
04	633-642	Another example of where there is no mention of social value, but see CIOMS	Include 'social value'	H	MI
04	689-701	There is a lost opportunity here to foster productive relationships between RECs and investigators. Often a PI can be invited to attend and this can expedite review and foster trust on both sides in the research ethics review process and better mutual understanding.	Consider including facility to invite PI to attend	M	MI
04	722-729	The urgency to act during a PHE should not come at the expense of robust testing of the ethical and public acceptability of any research to be conducted. Rapid response testing of such requirements is also needed.	Ensure that the development of any rapid review mechanism, procedures or review template is attuned to the needs of the context and involves meaningful community engagement.	H	MI
04	748-752	Consider the role of precedent - what about publishing anonymised summaries and commitment to transparency? This is mentioned later, but should also appear here,	Mention role for publishing anonymous summaries and being fully transparent.	M	MI

Section	Line	Comment/rationale	Proposed change/suggested text	Classification L= low, M= medium, H= high	Originator of the comments (for WHO use)
04	771-777	Further mention of commitment for on-going review. See above concerns.	See above.	H	MI
04	804-806	No mention of data protection, which is related to but also quite different from confidentiality.	Add “data protection”	H	MI
04	851-859	How do you ensure efficient coordination between RECs? A role for a NRA? This is another example of where there is a role for regulatory stewardship.	Add regulatory stewardship, as per suggestion above.	M	MI
05	911-914	How do RECs own their decisions, even in summary? Also linked to EC 05.06 – this is good practice outlined here. Link to this section and also comments above at 748-752.	Ensure that the commitment to transparency and summaries is repeated throughout the Working Document.	H	MI
05	1029-1042	This section talks about participants being able to ask about studies they have been involved in – but how will they trace to a particular REC? Arguably there is a need for metadata in a country to allow for searchability - who is responsible? There is also scope here to add reference to appeals by PIs for any complaints they might have.	More thought and detail is required on the logistics of this right of participants; also consider a right of appeal by investigators for any complaints.	H	MI

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06	1130-1140	This is about REC process for research participants complaints – but the REC is judge and jury in its own cause. This raises serious concerns of justice and conflicts of interest both for research participants and investigators alike.	Review terms of this process.	H	MI
06	1173-1180	As above for investigators, no appeal	Review terms of this process	H	MI
06	1206-1215	It is very good to get feedback but who oversees the overseers? Same for internal audits at 06.05	Review terms of this process	M	MI
07		Definition of "research institutions? Do audits count as research?	See suggestion above about the need for a Definitions section	H	MI