November 2014

Global Forum on Bioethics in Research: The Future

The GFBR Satellite and Relaunch Meeting in Mexico City in June 2104 provided an exciting opportunity for the Interim Steering Committee of the GFBR to take stock of where the GFBR fits in with current initiatives and debates in international research ethics and to ensure that in future, the revised GFBR provides the best platform for international dialogue, consensus building and resolution of key ethical issues in international health research.

It was agreed that the GFBR has a unique opportunity to widen the scope of interests and issues of global significance for the bioethics, research ethics and health research communities, allowing voices and perspectives from many different countries and continents to be heard and acted upon. (Importantly, there were people from around 25 countries and 6 continents at the Mexico meeting, primarily constituted of representatives from low and middle income countries.) Uniquely, it can provide a genuine environment for dialogue, allow the sharing of theory and evidence-based research and open opportunities for equal partnership between research groups from different institutions, countries and regions. Critically, the GFBR should stay focused on where it can make a difference to research practice around the world.

Discussions in Mexico also highlighted that in moving forward, the Interim Steering Committee should consider how to integrate the following into the GFBR model:

1. **Substantive issues**: Given that research is becoming more global in scope, it may be beneficial for the GFBR to engage with substantive ethical issues such as fairness, justice and global inequalities (not just procedural aspects of running RECs), as there are real contributions to be made by and for the GFBR that will affect and influence research practice.
2. **Agenda setting**: Informing debate about the setting of priorities in global research ethics is critical for the GFBR. A number of established issues, debated and driven largely by researchers and funders from high income countries, dominate the field and it is important that countries are able to determine their own research ethics priorities or be supported to establish what these should be. The GFBR could provide a platform for different voices and perspectives to set research ethics priorities and agendas for the international research community.
3. **Applied focus**: It is important that the outputs that the GFBR produces are meaningful, practically useful and create genuine engagement that leads to progress. One key challenge is in embedding the work, discussions and findings of the GFBR into policies and into practice.
4. **Network Building**: Previous GFBR meetings have served to promote collaborations and informal networks but in working towards a goal of translating GFBR discussions into practice, it would be advantageous to establish a mechanism to pilot models of short-term collaborative initiatives between participants of GFBR meetings.

The Interim Steering Committee of the GFBR is committed to building on the discussion and the representativeness of the Mexico meeting in planning for 10th GFBR meeting to be held at Fondation Méxieux Les Pensières conference center in early November 2015.

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Global Forum on Bioethics in Research: Meeting report from satellite meeting at the International Association of Bioethics World Congress, Mexico City 24 June 2014

The theme of the one-day meeting was "The ethics of international collaborative research". Over the course of the day, several key themes emerged in the presentations and subsequent discussions:

Research Ethics Committee (REC)[1] review

- The role of REC within a wider research ethics and governance context

A substantial number of challenges faced in research and research governance concern the functioning, efficacy and efficiency of research ethics committees. Any efforts to understand these challenges need to situate the REC within a broader context of research ethics and governance, as the REC is only one element in the ethical governance of research. Although the primary task of the REC is to ascertain whether or not a research protocol has reached a threshold for constituting ethical research, the processes and functions of the REC are frequently burdened with the weight of resolving other problems. REC approval is neither a necessary nor sufficient condition for the conduct of ethical research, but the strong emphasis on REC processes and functions often entails that the other elements of the research system are overlooked for critical examination.

RECs also frequently perform duties beyond ethical review and the protection of research participants, for example, being required to provide legal oversight, administrative authority or to ensure research is complaint with particular requirements in the interests of the institution, funding body or government body. Members representing these interests, but with little or no ethics expertise, are often placed onto RECs. Additionally, it is often clear that one committee does not have the expertise to conduct ethical review on different types of protocol.

In terms of suggestions for improving ethics review, it is worth considering that the functioning of RECs is not the only important element: the satisfaction of participants that they have been protected from harm and their rights respected is a crucial function of the research ethics system. Furthermore, on-going reviews of research should also be considered as a key role for RECs: ethics reviews are prospective and there is often little awareness of how the research will happen in practice. Finally, it is important that ethics review systems should not be chosen as top down or bottom up at the outset of developing research infrastructure but should be responsive to the particular context in which research is being undertaken: multi-site, international studies may require different levels and types of review in different contexts.

- Lack of standards, regulation, oversight and accountability

Several central and related problems in research ethics systems across the world are a lack of standards of review, poor or variable capacity for assessing ethical issues, and a lack of

[1] A range of names are used, each of which might have slightly different responsibilities. Research Ethics Committee (REC) here is used as a catch-all term to describe Research Ethics Committees; Ethical Review Committees; Institutional Review Boards and other bodies set up to provide ethical review of research protocols.

consistent regulation and oversight. There is frequently little transparency over who is ultimately responsible for ethics decisions, who has oversight and whether or not the processes of ethics review are robust. However, the current review process for the CIOMS[2] guidelines highlights that it should not be assumed that difficulties with RECs are confined to LMICS: many developed countries have poorly functioning research ethics systems and we cannot assume that the processes that have developed in these countries are better or could be transferred to other contexts.

A number of factors present challenges for creating standards and consistency in approach. Firstly, it is not clear how standards could be developed: it is difficult to establish what counts as having done a good job of ethics review, as a range of 'reasonable' decisions needs to be allowed to be made and variations in capacity will substantially affect what efficiency would look like in different circumstances. Secondly, the lack of normative and regulatory frameworks in some countries means that multiple strategies for handling research ethics need to be developed, but there is often limited scope for evaluating the systems that do evolve.

Thirdly, the development of standards faces a paradoxical situation: on the one hand a lack of standards means there is little trust or faith in the ability of research ethics systems to properly scrutinise protocols and this leads to duplication of review, often unnecessarily. On the other hand, if sets of standards are 'imported' from other countries or institutions, they may be seen as alien and insensitive to local needs or considerations. This makes the creation of standards that can apply across sites and countries more complex.

Finally, RECs face a challenge in judging the appropriateness of practical solutions to ethical issues given the complicated governance context of collaborative research. Different jurisdictions between countries and institutions mean that even if ethical principles are accepted universally, the specific circumstances in which projects are undertaken mean those principles are implemented differently in practice. Good practice may vary substantially in diverse settings. This creates a substantive ethical issue over whether some ethical concepts are culturally relative: for example, is it acceptable to agree to disagree on certain issues such as what constitutes informed consent?

These issues would benefit from the availability of global and regional fora for discussing ethical review, providing a consultation service and allowing a platform for catalysing ethics research, for example through piloting proposals to move towards better systems. It is hoped that standards could be developed that are applicable across the continents whilst being sensitive to local needs. Some accepted standards can be firmly established, for example, that REC members need training in ethics review and to be independent. It is plausible that empirical ethics research could lead to the development of metrics to assess the quality of ethics review, if it can in practice be agreed as to what counts as success or good performance.

- Multiple layers of REC review

Proposals often have to go through a number of different layers of ethics review in order to be approved at every level, from the local to the international, from a hospital or institution to a funder or government. There may be benefits to multiple review in some instances but there is a general consensus that these can be excessive and not beneficial either to the

[2] See for an outline: http://www.cioms.ch/images/stories/CIOMS/Bhan_CIOMSwg_2014Mexico.pdf

quality of research or to participant protection. Other problems in the wider system of research ethics are sometimes compensated for through tightening or adding layers of ethical review. Multiple layers of review may also have the consequence that each part of the system assumes that somebody else has oversight over specific issues, which can result in errors and poor practice. The mistaking of good procedure for good practice is at the root of much of the political rationale for increasing bureaucracy and in the absence of trusted relationships, there is a tendency to create more layers for ethical review.

A useful way to consider whether multiple reviews are beneficial or obstructive is to determine if they create a 'value-added' process. Sometimes there is value in conducting more than one ethical review so that they can be sensitive to different contexts. There may be good ways to help integrate different levels of review through collaboration, rather than repetition, to improve efficiency. Collaborative reviews are intended to solve problems of time (multiple reviews take longer to complete, especially across different time zones); redundancy (multiple reviews may add little value in practice); and lack of appropriate expertise (different RECs may be better qualified than others on particular issues or with regard to different participant populations).

- Active on-going research to improve ethics review

Empirical research into the differences within and between research ethics systems will be needed if improvements to existing systems can be made, both procedurally and substantively. Several interesting examples of empirical ethics research exist, for example the collaborative ethics review system being developed between the University of Indiana and Kenya's Moi University[3]. Here, the administrative structure for joint ethics review is being put in place, with co-chairs, procedural roles and regular teleconferences. Evaluation metrics for the ethical review process are also being considered. The initiative is looking to develop the concept of 'equivalent protection' as a way of reducing the need for multiple, inefficient reviews.

In Peru, the independent initiative REDCEI is aiming to help RECs fulfil their function of being able to conduct ethically rigorous review of research proposals, where many universities have no RECs at all. In addition, the Mapping African Research Capacity (MARC)[4] initiative is also seeking to approach the question of how to make ethics review work better. It initially identified and mapped capacity for ethics review in Africa, then moved into an on-going interventional phase in 2012.

Trust

In many contexts a lack of trust pervades the research process: this is inter-institutional, inter-governmental, international, and in many instances the public harbour a deep lack of trust in research as well. Institutions and governments frequently have different goals and interests from researchers and/or participants, hampering trust in research; collaborations between high and low- and middle-income countries may also lead to distrust where power differentials arise. There is a need to clarify the value of research as it is not always clear it is a social good, build the trustworthiness of systems and regulations, and to disseminate good standards of research ethics to develop trust over time.

- Understanding of research and research purposes

[3] http://bioethics.iu.edu/programs/arep/
[4] http://onlinelibrary.wiley.com/doi/10.1111/j.1471-8847.2012.00325.x/pdf

In Africa and Latin America in particular, a history of exploitation leads countries, institutions and individuals to be wary of influence and research from outside. For example, in Latin America there have been calls to reject the Declaration of Helsinki as it is thought not to be sensitive to the context of this region. Public wariness of research broadly is in part explained by there often being few tangible benefits of research, owing to poor translation into practice: there is a continued lack of access to treatments, substantial and continuing public health issues and little evident implementation of research findings into policy and healthcare. There is also a perception that research is industry driven and concerned with profit, as medicines remain costly. Those who do participate in research often give consent on the basis of trust, not knowledge or understanding of the science, and it is crucial to maintain the trustworthiness of research and researchers in these circumstances.

The H3Africa[5] initiative is attempting to overcome some of these issues of trust through ensuring that there is African leadership and ownership of the research collaborations. It is imperative that credible and trustworthy governance structures are created: as part of the effort to build trust and capacity in Africa there is a period of exclusivity for African researchers to samples and data.

Some types of community engagement can held to develop trust, but these also require confidence to be earned in the systems governing research. For instance, Community Advisory Boards can be a model for enhancing collaboration, but can also create demands, holding up research particularly if distrust of the researchers and the processes in place to protect participants remains. Community engagement needs to be fair, effective, inclusive and accountable whilst being sensitive to different contexts and situations in which the research is being undertaken.

- Issues between institutions and across borders

Substantial challenges exist to developing trusted and trustworthy relationships between different institutions, regions and countries undertaking collaborative research. There are many layers to these collaborations, all of which can generate issues with trust and political problems for researchers. There are particular concerns in Africa about the storage and shipment of samples to other countries, and how this could and should be regulated.

Power differentials create significant barriers to developing trust, and it is imperative to understand both how dynamics of power influence collaborations but also the extent to which the collaborative relationship, with human interactions, is important in developing or undermining trust between different parties. It is important to question what kinds of relationships are fair and equitable, especially with respect to contracting, resources and access to information, if relationships of trust are to be established.

- Collaboration with industry

Collaborations with industry mean that there are increasing demands for speed and efficiency in ethics review, and these demands are being encapsulated in the EU regulation on clinical trials. The issue of funding of trials and other research from the pharmaceutical industry remains a larger issue for the global research community: it is not clear whether it is possible to reach consensus about the influence that industry could or should have over research. Where it is felt that research is driven by industry, gaining public trust in research is particularly challenging.

[5] www.h3africa.org

The international research environment

- Dynamics of collaboration between LMICs and HICs

It is difficult to define collaboration, particularly where there are differences in power between different stakeholders. Collaboration may be different from co-operation or partnership: the latter imply working together equally and caring about the relationship, which is not always true of collaboration. Most ethical discussions about collaboration are dominated by US researchers and bioethicists, which may mean that the perspectives of those in LMICs on the ethics and processes of collaboration have not been widely heard.

There are specific ethical issues arising from international collaborations, specifically around high income countries sponsoring clinical trials in LMICs, many of which may not have high functioning systems of ethical review. In contexts in which potential participants have low levels of familiarity with medical concepts, and there are cultural and linguistic barriers, exploitation is a real possibility – whether intentional or not. Furthermore, the political realities of the conduct of research across borders need to be acknowledged and understood: politics is just as important as procedures and policies.

Although different approaches will be appropriate in different contexts, there are some key lessons to be drawn from experiences of international research. For example, researchers need to discuss the research with local collaborators at an early stage while developing the research protocol in order to be alert to the local context and any ethical issues that may arise from doing research in that area or with specific populations. A vivid example of this arose following Typhoon Haiyan in 2013, which brought a lot of well-meaning international disaster research to the Philippines, and it was not always beneficial as the researchers had not had previous contact with local communities. On a more promising note, the H3Africa model, supported by UK and UK funders, works by creating on-going discussions between expert working groups across African countries, consolidating the available expertise and additionally building their capacity to apply for internationally competitive research grants.

- Substantive ethical issues of international collaboration

There are frequent concerns expressed about the procedural aspects of ethics review, but what counts as appropriate process inevitably varies between contexts; this makes it difficult to establish common ground. However, whilst details of process legitimately differ there may be substantive ethical issues that affect and challenge collaborative research across the world and these could provide fertile ground upon which to seek consensus and unity. Substantive ethical issues such as fairness and justice are universalisable: if we can reach agreement on what these are and what they mean, the processes for handling them can be different in different places while maintaining standards across review systems.

There may be new or unique substantive issues arising from international collaborative research, particularly as collaborations high income and LMI countries become more commonplace. It is anticipated that questions of global justice and health inequalities will come to the fore in these contexts, for example in questions around sample sharing and access to data and samples across borders.

It is nonetheless important to acknowledge and respect different interpretations of ethical principles in diverse regions and countries. For example, views about what is ethically important will vary between locations in a single study, as will the acceptability of different choices and solutions. Furthermore, some research is not conducted in a liberal democratic

environment. This may undermine some of the assumptions that are made about 'ethical research' as a whole, as there will be very different political contexts to consider.

However, there is a tension between sensitivity to local contexts and the need to ensure coherence across study sites in international collaboration: some issues cannot be devolved to a local level, because of the need for accountability of the project as a whole and the need for shared moral responsibility. There are practical questions to address here about relativism for practical ethics and project management.

Communication and information sharing

With technological innovations, new groups not bounded by geography will be able to form, that can share capabilities, competencies, best practice and challenges. The research community could make more of technological solutions to create communities of practice and expert support systems across the world, although language may remain a barrier. New technologies can also be used to help address some of the challenges of multiple ethics review, for example, software and training programmes have been developed to assist with automating some parts of the process and develop ethics review capacity.

There are already good examples of the use of technological innovations to assist and support researchers:

- the Clinical Trials without Borders (ECRIN)[6] initiative is an attempt to support clinical trial collaborations within academia to develop protocols and assist with monitoring and reporting.
- Research Ethics Web[7] is an online resource for African RECs that is also widely used in Latin America and the Caribbean.
- COHRED[8] has worked to generate useful tools for ethical review: the RHInnO[9] initiative includes EthiCALL, a system to connect REC members with the research ethics world via closed discussion groups, enabling consultation with the global ethical community; and EthiXPERT, providing information to research ethics reviewers worldwide on updates to guidelines and regulations in real-time.

Conclusions

Ethics review processes continue to be a source of significant ethical and practical concern in many different contexts, and these challenges are often magnified in international collaborative research in which issues of power dynamics, trust and fairness come to the fore.

There may be different forms of ethics review sensitive to their particular contexts that can nonetheless achieve 'equivalence' or 'reliance agreements' and thereby adhere to the same standards. GFBR participants have begun to build tools for collaborative research and ethical review, and the GFBR could help to create networks of members to pilot different models or tool. Empirical pilot work needs to be done to explore how the right systems can be developed in different settings. This would ensure the GFBR is utilised as a way to take ideas forward for piloting and reporting back.

[6] http://www.ecrin.org/
[7] http://www.researchethicsweb.org/
[8] http://www.cohred.org/
[9] http://rhinno.net/

The GFBR could also potentially take a lead in developing key competencies for international research ethics.

Other key issues

The focus on medical research ethics can risk leaving out issues of public health, which makes it difficult to incorporate discourses around social sciences and biotechnologies (such as genetic modification).

The line between what counts as research – and is therefore subject to ethical review – and what is clinical care or public health, particularly surveillance, is also blurred. Healthcare and research are becoming more integrated and so the issue of whether there is a divide between them will become more pressing in time.

GFBR Inaugural Award

Finally, at the end of the meeting Dr Ruth Macklin was awarded the inaugural Global Forum on Bioethics in Research Award for "Contributions to Progress in International Research Ethics" and received a commemorative trophy. The GFBR intends to make this an annual award for outstanding researchers in the field of international bioethics.

Dr Ruth Macklin (centre) receives the inaugural award for Contributions to Progress in International Research Ethics from Doug Wassennar (l) and Florencia Luna (r) in Mexico City, 24 June 2014.