Mass General Brigham

HUMAN RESEARCH AFFAIRS

CONSIDERATIONS FOR INTERNATIONAL RESEARCH

All human research that involves Mass General Brigham Investigators or members of the research team traveling internationally to recruit, consent, conduct research activities and / or collect data must be submitted to the Mass General Brigham IRB for review. Additionally, research funded by the Mass General Brigham investigator or the investigator's grant, designed by Mass General Brigham investigators, or research occurring in another country under the direction of the Investigator must be submitted for IRB review.

Conducting human research outside of the United States (U.S.) poses complex regulatory and ethical challenges. To protect participant's rights and welfare, the research must follow the ethical standards, legal requirements, and cultural norms of the country where the research will be conducted. If research will be conducted in an embargoed country or involve an export control issue, investigators should contact Research Compliance.

Preparing for submission to the IRB should start at the initial planning stages of the research to allow time to obtain the necessary approvals from the country in which the research will take place. These approvals can take several months depending on the requirements of the country. Depending on the type of study and the country's legal requirements and cultural norms, the IRB may require additional information to complete their review.

Local Context

When developing materials related to recruitment, consent, data collection and the overall research, investigators should consider the local customs, cultural and religious norms. If culturally appropriate, the IRB will consider alternative consent formats. In some instances, it may be appropriate for the IRB to waive some or all requirements for written consent in favor of a verbal consent for cultural, religious or literacy reasons (e.g., cultures where signing consent is not the norm). Investigators must describe the cultural norms or conditions requiring such a waiver and explain how consent will be documented.

If the study provides compensation, investigators must take care to avoid unduly influencing participants. Investigators should consider local context when determining the amount, type, and/or method of payment. The remuneration should be described in the IRB application and protocol.

Ethics Committee (EC)/Institutional Review Board (IRB)

The U.S Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) International Program works to ensure that research participants outside of the U.S. who participate in research projects conducted or funded by HHS receive an equal level of protection as research participants in the U.S.

If a country has a local EC/IRB qualified to review and oversee the research, approval from this committee is required. The approval documentation must be provided to the Mass General Brigham IRB.

The approval documentation must be in English. Both the translated and original version should be submitted to the IRB along with the translator's certification

If there are no known local or national regulations or requirements, investigators are expected to consult with local experts, Regulatory Officials, or community leaders about the project and to secure their support for the conduct of the research. Investigators should get documentation of this support. Documentation may include reference to a country's laws or policies online or an email/letter or statement from the appropriate authority in the country. Investigators should review OHRP's International Compilation standards to understand local and/or national regulatory requirements.

There are differences across and within Countries. Each place where the research is conducted should be treated as a separate entity and may be subject to different regulatory requirements. Local collaborators should be able to advise on the necessary regulatory requirements to conduct a study in that country. There are often country or national-level approvals that are needed in addition to the institutional IRB approval (i.e., in Uganda, you also need approval from the Uganda National Council for Science and Technology). There may also be other approvals needed to conduct the study. For instance, in Kenya, if you are submitting a proposal that involves study drugs or participant samples, you will need approval from the Pharmacy and Poisons Board (PPB).

The Mass General Brigham IRB does not serve as the Single IRB for international sites. It is often helpful to submit to the local IRB prior to submitting to the Mass General Brigham IRB to account for any changes the local IRB may request.

Federally funded Research

All institutions (U.S. and international) engaged in the conduct of research funded by a U.S. federal agency must obtain a federal-wide assurance (FWA) with HHS. FWA is an assurance of compliance with the U.S. Federal Policy for the Protection of Human Subjects ("Common Rule"). Common Rule and the applicable subparts apply to international sites engaged in non-exempt research supported by HHS. See the *Resources* section below for additional information about obtaining FWAs.

A study funded by the FDA or subject to FDA regulations must comply with FDA regulations pertaining to human research or clinical investigations.

Mass General Brigham IRB Review

The IRB will review the research, taking into consideration the local context review, if required, and other legal requirements. The application should include a description of Mass General Brigham's role in the research, as well as information about the procedures that will be conducted at the international site and the name of the EC/IRB that will provide oversight. All modifications and reportable events (even if they occur at an international site) must be submitted to the Mass General Brigham IRB according to the IRB policy. The EC/IRB's approval or acknowledgment for amendments and reportable events should also be submitted. Submissions should be submitted to the EC/IRB at the international site before being submitted to the Mass General Brigham IRB. If the EC requires documentation of Mass General Brigham IRB approval, Mass General Brigham IRB may provide an approval contingent upon receipt of the EC approval letter.

Reportable events that occur at international sites (e.g., unanticipated problems, major deviations) must be submitted to the Mass General Brigham IRB in accordance with IRB policies. Even if limited or preliminary information is available and the study team is still collecting information, the IRB must be informed within the specified reporting window (i.e., within 5 business days) by submitting an Other Event in Insight.

Consent Form:

- The consent form approved by the local EC/IRB should be translated into English and submitted for review. The consent documents should be uploaded as 'Other' attachments and a blank document may need to be uploaded in the 'Consent' attachment section. The consent form will not be stamped by the Mass General Brigham IRB.
- When the study is federally funded, the consent form must include the key information section, and language about certificate of confidentiality.
- If a study is subject to FDA regulations, the consent form must include all elements of consent as required by the FDA.

Other Considerations

Data privacy laws and regulations are quickly evolving and may impact research conducted in international settings. Requirements for data privacy and security may vary between countries. One example includes the General Data Protection Regulation (GDPR), a European data privacy law that protects the person data of people located in the European Economic Area. GDPR is a European law that went into effect on May 25, 2018 and establishes protections for privacy and security of "personal data" about individuals in European Economic Area ("EEA")-based operations and certain non-EEA organizations that process personal data of individuals in the EEA. GDPR has strict requirements for transfer of data collected from citizens of the EEA (most countries in Europe including the United Kingdom) and transferred outside of Europe. The IRB has developed language to include in the informed consent form that complies with the GDPR. For more information on GDPR, see United States Health and Human Services OHRP's website: https://www.hhs.gov/ohrp/international/gdpr/index.html or https://gdpr.eu/
GDPR does not apply if the data is anonymous.

Investigators must ensure that data is collected, managed, and shared in compliance with the law where the data was collected. For guidance on foreign laws impacting data security and privacy, refer to OHRP's International Compilation of Human Research Standards. If this guidance does not address the foreign site, then consult with an informed local partner.

Contact Research Management to determine whether an agreement would be required to share or transfer data between countries.

Additional Resources for Investigators

- International Compilation of Human Research Standards: OHRP provides a listing of over 1,000 laws, regulations, and guidelines on human subject protections in over 100 countries and from

several international organizations. This document should be consulted to determine country level guidelines on human subject research.

- Federalwide Assurance (FWA) Requirement: Review applicability for international sites.
- Obtaining FWAs