Research conducted outside of the United States by LSUHSC-NO investigators must offer research subjects the same or equivalent levels of participant protection as offered subjects of research conducted domestically at LSUHSC-NO. Investigators must ensure that the research complies with the policies set forth by the LSUHSC-NO Human Research Protection Program, with the relevant HHS and FDA regulations, and when appropriate with ICH Good Clinical Practice guidelines. Research conducted outside of the United States must also respect the customs and comply with the laws of the foreign setting where the research will take place. All aspects of the research must take into account the cultural context of the foreign setting. See the Office of Human Research Protections (OHRP) International Compilation of Research Standards for a listing of key organizations, laws, regulations, and guidelines governing human subjects research in various countries (http://www.hhs.gov/ohrp/international/intlcompilation/intlcomp2013.pdf.pdf).

A. LSUHSC-NO IRB Review

Research conducted outside of the United States by employees or agents of LSUHSC-NO must be approved by the LSUHSC-NO IRB before the research can be initiated. The LSUHSC-NO IRB is responsible for monitoring the conduct of the research, including continuing reviews, amendment reviews, and additional post-approval monitoring. In order to ensure pertinent information will be provided to the LSUHSC-NO IRB in a timely fashion, the LSUHSC-NO investigator must submit to the LSUHSC-NO IRB information regarding how communication will be maintained between the investigator, study team, and the LSUHSC-NO IRB.

B. Foreign Review and Engagement

The LSUHSC-NO investigator must provide the LSUHSC-NO IRB with information regarding whether or not foreign IRB, ethics committee (EC), or any other form of review and approval is available and required in the foreign setting. If additional approval is required, the investigator must provide the LSUHSC-NO IRB with documentation that the approval was granted. The investigator may not initiate the study until both LSUHSC-NO IRB approval and all required foreign approvals have been granted. Foreign approval does not guarantee approval by the LSUHSC-NO IRB. When applicable, the LSUHSC-NO IRB will enter into a written agreement with the foreign IRB detailing respective responsibilities as deemed appropriate for the specific study, and will maintain communication with the foreign IRB/EC to the extent appropriate for the given study.

LSUHSC-NO will consider an institution outside of the United States to be engaged in a non-exempt research project when its employees or agents for the purposes of the research project obtain: 1) data about the subjects of the research through intervention or interaction with them; 2) identifiable private information about the subjects of the research; or 3) the informed consent of human subjects for the research. See the OHRP Guidance on Engagement of Institutions in Human Subjects Research for more detailed scenarios of institutional engagement and non-engagement (http://www.hhs.gov/ohrp/policy/engage08.html).

According to HHS regulations [45 CFR 46.103(a); 45 CFR 46.103(b)], if an institution will be engaged in a non-exempt research project and the research project is conducted or supported by a U.S. federal department or agency, that institution must: 1) provide written assurance satisfactory to the

department or agency head that it will comply with the requirements set forth in the regulations; and 2) certify to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB.

If an institution outside of the United States will be engaged in the research study, the LSUHSC-NO investigator must provide the LSUHSC-NO IRB with the following: 1) documentation of the foreign institution's OHRP-approved FWA, 2) a copy of the policies and procedures of the IRB provided for in the assurance, and 3) any other information the LSUHSC-NO IRB deems necessary to understand the policies, procedures, and practices of the institution, its IRB, and its employees or agents that will be involved in the research.

The investigator must also provide to the LSUHSC-NO IRB evidence that all non-LSUHSC-NO investigators and study team members possess the qualifications to offer subjects the appropriate human subjects research protections and adhere to the applicable standards set forth for conducting human subjects research in the country (see the OHRP International Compilation of Human Research Standards for a listing of such standards, http://www.hhs.gov/ohrp/international/intlcompilation/intlcomp2013.pdf.pdf).

C. Exempt Research

The LSUHSC-NO IRB Chair or his/her designee will determine if a study can be given Exempt status or if the study requires continued oversight by the IRB. Emphasis will be placed on the foreign setting's local context when considering the study's risk-benefit ratio and all other aspects of the research project. Due to variations in local context, a study that would qualify for exempt status when conducted domestically at LSUHSC-NO might not necessarily qualify for exempt status when conducted outside of the United States. If the study is determined to qualify for Exempt status by the LSUHSC-NO IRB, the study team must uphold all ethical principles expected of Exempt research conducted domestically at LSUHSC-NO while taking into consideration the local context of the foreign setting. If any factors or relevant events alter the risk-benefit ratio of the research project, the LSUHSC-NO investigator must notify the LSUHSC-NO IRB immediately.

D. Local Context

In order to conduct thorough and appropriate reviews, the LSUHSC-NO IRB must possess the appropriate knowledge and expertise regarding the country, culture, and subject population that will be involved in the research project. In cases where the LSUHSC-NO IRB does not possess sufficient expertise regarding the local context of the foreign setting, an expert consultant may be invited to advise members of the LSUHSC-NO IRB about the culture and context, to review experimental protocols and materials, and to provide any other relevant information as deemed necessary. If an expert consultant is invited to a Full Board meeting, the consultant may serve in a non-voting, advisory-only capacity.

The research study must be conceptually and methodologically appropriate in the given local context of the foreign setting. Additionally, the research team must be qualified to perform the research in that setting. Therefore the LSUHSC-NO investigator must demonstrate to the LSUHSC-NO IRB that: (1) the research is appropriate given the local context of the foreign setting, and (2) the investigator and the other members of the research team possess sufficient experience and expertise regarding the country, culture, and subject population that will be involved in the research project.

The LSUHSC-NO investigator must also provide the LSUHSC-NO IRB with information regarding each of the following topics:

- The country and region/community where the research will take place (including current social, economic, and political conditions)
- Whether or not participating in the research poses any additional risks for subjects due to the local context of the foreign setting (and if so, how those risks will be minimized)
- The performance sites where the research will be conducted
- The country's organizations that provide oversight for human subjects research
- Legislation, regulations, and guidelines in place regarding the conduct of human subjects research in the foreign setting
- Country and other approvals that are needed to conduct human subjects research in the foreign setting
- Any form of compensation that will be provided to subjects for participation (including an explanation of the significance of the compensation in terms of relative local context)
- The contact person that will be available in the foreign setting to address subjects' questions or concerns (and how that person can be contacted by subjects)
- The age of majority in the country
- Languages spoken by potential subjects and which members of the research team are fluent in those languages
- Whether or not translators will be needed, qualifications of translators, and relationship of translators to research subjects

If translated consent forms or other translated experimental materials are needed, the LSUHSC-NO investigator will provide the LSUHSC-NO IRB with copies of both the translated and English documents. The investigator must also provide documentation of verification of the translations.

E. Informed Consent

Investigators conducting research outside of the United States must obtain informed consent from every subject or their legally authorized representative in a manner that offers equivalent protections as would be offered subjects consented domestically, while respecting the customs and laws of the foreign setting. Additionally, the informed consent information must be given to the subject or representative in a language understandable to the subject or representative (45 CFR 46.116; 21 CFR 50.20). The LSUHSC-NO investigator must provide the LSUHSC-NO IRB with a detailed description of the informed consent process, including all of the following information:

- Where the consenting process will take place
- What language will be used during the consenting process
- Who will be administering consent
- Whether or not any individuals other than the subject will be providing consent for the subject to participate
- Any other relevant factors (e.g. subject illiteracy, potential unwillingness of subjects to document consent due to local culture, etc.)

Documentation of consent will be expected unless the investigator shows that the study meets the criteria for a waiver of consent [45 CFR 46.116(c) and (d)] or the criteria for a waiver of documentation

of consent [45 CFR 46.117(c); 21 CFR 56.109(c)(1)]. These criteria must be fulfilled in light of the cultural context of the foreign setting. If the LSUHSC-NO IRB determines that a waiver of documentation of consent is appropriate for a particular study, the investigator must submit to the LSUHSC-NO IRB an explanation of how subjects will be provided information regarding the research. This includes submitting both English and translated copies of any language that will be used during the (undocumented) consenting process.

F. HIPAA Authorization

LSUHSC-NO will consider any individually identifiable health information collected in the context of international research and transmitted to LSUHSC-NO (a covered entity) to be protected health information (PHI) as defined by 45 CFR 160.103. Therefore, investigators conducting international research which utilizes such information must abide by the regulations of the HIPAA Privacy Rule (45 CFR Parts 160 and 164) when appropriate.

In cases where language and cultural barriers may impede the population of subjects in the foreign setting from fully understanding the concepts presented in the standard HIPAA Authorization form, the investigator may submit a request for alteration of Authorization to the LSUHSC-NO IRB. Such an alteration would consist of a simplified version of the elements of authorization. The investigator must provide a satisfactory rationale for requesting the alteration.

When appropriate, the investigator may choose to request a waiver of HIPAA Authorization from the LSUHSC-NO IRB. As part of this request, the investigator must provide a satisfactory rationale for requesting the waiver.

The use of an alteration or waiver of HIPAA Authorization must be appropriate in the context of the foreign setting. Additionally, the following criteria set forth by 45 CFR 164.512 (i)(2)(ii) must be fulfilled in order for a request of alteration or waiver of HIPAA Authorization to be approved: (1) the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals; (2) the research could not practicably be conducted without the waiver or alteration; and (3) the research could not practicably be conducted without access to and use of the protected health information.

The investigator must submit to the LSUHSC-NO IRB both English and translated copies of any HIPAA forms that will be presented to subjects, along with documentation of verification of translations.

G. Research Involving Children

If research conducted outside of the United States will involve children as subjects, investigators must demonstrate that the research meets standards of such research conducted domestically [see 45 CFR 46 Subpart D; 21 CFR 50 Subpart D], while respecting the customs and laws of the foreign setting. The LSUHSC-NO investigator must provide the LSUHSC-NO IRB with information regarding children in the context of the foreign setting. Specifically, the investigator must provide the LSUHSC-NO IRB with information regarding the following topics:

- The relationship between parents and their children in the country
- An acceptable and effective parental permission process in the foreign setting
- An acceptable and effective child assent process in the foreign setting

- Laws of the foreign setting pertaining to children as research subjects
- Laws of the foreign setting pertaining to orphans/wards as research subjects, if applicable

H. Application

LSUHSC-NO investigators who wish to conduct research outside of the United States must submit the Supplementary Application for International Research along with a standard research application. The Supplementary Application for International Research and the standard research applications are posted on the LSUHSC-NO IRB website at http://www.lsuhsc.edu/administration/academic/ors/irb.aspx.