HRPP POLICY APPROVAL & IMPLEMENTATION

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

Policy Number: 700

SOP Title: International Research

Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB Chairs, IRB Administrators, Protocol Navigators

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POLICY

A. PURPOSE
1. Describes the requirements and responsibilities of NIH investigators when conducting non-exempt human subjects research in foreign countries.

B. SCOPE
1. This policy applies to NIH investigators conducting non-exempt human subjects research in foreign countries.
2. This policy applies to the NIH Institutional Review Board (IRB) when reviewing non-exempt human subjects research that will be conducted in foreign countries.
3. This policy does not cover all federal and NIH policy requirements for non-exempt human subjects research conducted in a foreign country. For more information about other NIH policy requirements for international research, consult the Fogarty International Center website.
4. This policy generally does not apply to NIH intramural support for foreign research where no NIH investigator is conducting non-exempt human subjects research (see C.10 below).

C. POLICY
1. Human subjects research conducted by NIH investigators is subject to federal law, regulation and policy, including NIH policy, regardless of whether the research is conducted domestically or internationally.
2. Research may not be conducted by NIH investigators in any foreign country that is contrary to any U.S. Government prohibitions or restrictions on conducting research in that country.  
3. When the NIH IRB is reviewing research conducted collaboratively with foreign investigators and/or institutions, its oversight responsibilities extend only to the activities of those investigators covered by the NIH FWA as specified in Policy 100.
4. When conducting non-exempt human subjects research in a foreign country, NIH investigators must comply with all applicable in-country laws and regulations. If U.S. law,  

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1 Contact Fogarty International Center for additional information about international research collaborations.
regulation, or policy (including NIH policy) differs from the foreign requirements, the most
restrictive approach should be used - so long as it is not contrary to U.S. law or policy. (For
more information, see the International Compilation of Human Research Standards.)

5. When international research will involve the study of test articles (e.g., drugs, biologics,
nutritional products or devices) in a foreign country and the test articles will be shipped from
the United States to the foreign site, the NIH Principal Investigator (PI) will comply with all
requirements detailed in E.1.b. below.

6. Non-exempt human subjects research conducted or supported by the NIH IRP in a foreign
country must be consistent with the applicable Department of Health and Human Services
(HHS) Federalwide Assurance (FWA).

a. Non-exempt human subjects research conducted in a foreign country with a foreign
institution, must be with an institution that holds an active FWA and reviewed by an
IRB/Ethics Committee (EC) registered with the HHS Office for Human Research
Protections (OHRP) or has equivalent procedures consistent with 45 CFR 46.101(h). (See
OHRP database for FWA and IRB/ECs.) Any exception to this policy statement requires
a compelling justification and must be approved in advance by the NIH Institutional
Official (IO).

7. Non-exempt human subjects research conducted by NIH investigators in a foreign country,
must be approved by an in-country IRB/EC prior to receiving final approval by the NIH IRB,
when the NIH IRB is the Reviewing IRB.

a. If reviewed by an external U.S.-based IRB and approved by that IRB prior to in country
IRB/EC approval, NIH research may not commence until the NIH Investigator receives
approval from the in-country IRB/EC, or if no in-country IRB/EC, until the reviewing
IRB requirements for local context review (if any) have been met.

8. When the NIH IRB is the reviewing IRB, its review will be limited to determining if the
proposed research meets the requirements of U.S. federal law, regulation and policy. The
NIH IRB will not make determinations whether the research is compliant with the laws or
regulations of any foreign nation, which will be determined by the in-country IRB/EC (see
C.11., below), unless there is no in-country IRB/EC (and so C.9. applies).

9. When the NIH IRB is the Reviewing IRB, and when there is no in-country IRB/EC, the NIH
IRB will require a written assessment of the research for its consistency with foreign country
laws and regulations, or local customs and culture, by an individual with appropriate
expertise in the foreign country’s culture, who is independent of the research team.
10. If the NIH Intramural Research Program (IRP) is supporting non-exempt human subjects research conducted in a foreign country, but the NIH is not otherwise engaged in the human subjects research, then the NIH IRB is not required, but in-country IRB/EC review is still required. As noted in B.4. above, other NIH requirements may still apply. (See OHRP Engagement of Institutions in Human Subjects Research.)

a. If reviewed only by an in-country IRB/EC, that IRB must be registered with OHRP and conduct its review compliant with 45 CFR 46 or has equivalent procedures consistent with 45 CFR 46.101(h). (See OHRP database for FWA and IRB/ECs.)

11. Research may not be initiated in a foreign country until both U.S.-based Reviewing IRB approval and in-country IRB/EC (if applicable) approval has been obtained.

a. In the absence of in-country IRB/EC review, NIH PIs cannot initiate research until approval of the U.S.-based Reviewing IRB has been received.

b. If US based IRB review is not required as no NIH or other US based investigators are engaged in human subjects research, then only in-country IRB/EC review is required and research may not commence until such approval has been received.

12. The NIH IRB will not approve research occurring in a foreign country that has been previously disapproved by, or otherwise conflicts with the determinations of, the in-country IRB/EC. If previously approved by the NIH IRB and a later determination by the in-country IRB/EC disapproves the research, the NIH IRB approval will be rescinded.

D. DEFINITIONS

1. **Federalwide Assurance (FWA)** – A written commitment that human subjects research conducted on behalf of an institution will comply with the protections for human subjects specified in the Common Rule regulation (e.g., 45 CFR 46). The FWA is filed with the US Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP).

2. **NIH Investigator** – An NIH federal employee (intramural or extramural), Special Volunteer, Intramural Research Training Awardee (IRTA) and Cancer Research Training Awardee (CRTA) who is conducting NIH human subjects research on behalf of the NIH. This may include a contractor in accordance with policy.
E. RESPONSIBILITIES AND REQUIREMENTS

1. NIH Principal Investigator (PI) and Investigator Responsibilities

   a. NIH Investigators must comply with federal law, regulation, and policy, including NIH policy, regardless of whether the research is conducted either domestically or internationally (e.g., 45 CFR 46, and FDA regulations at 21 CFR parts 50, 56, 312, and 812). In addition to these requirements, all NIH investigators conducting non-exempt human subjects research in foreign countries, must comply with:

   I. All applicable foreign country laws and regulations consistent with C.3. above (e.g., the foreign country regulations for human subjects protection, for drugs and devices, collection and transportation of biological specimens and, as applicable, ICH or CIOMS standards). (For more information, see the International Compilation of Human Research Standards);

   II. The requirements of the in-country IRB/EC (if applicable), so long as the requirements are no less restrictive than, and are not counter to the standards in E.1.a.I. above. For example, all NIH investigators must have a clear understanding regarding policy differences between the in-country IRB/EC and the U.S.-based Reviewing IRB, (e.g., as detailed in the protocol or other written agreement) such as, reporting research events, maintaining proper research records, and non-compliance, as compared to NIH policy; and

   III. The requirements of the U.S.-based Reviewing IRB.

b. When international research involves the study of test articles (e.g., drugs, biologics, nutritional products or devices) in a foreign country, and the test articles will be shipped from the United States to the foreign site, the NIH PI must:

   I. Comply with FDA regulations for shipping test articles internationally;

   II. Comply with applicable NIH requirements (e.g., pharmacy, CC Office of Research Support and Compliance (ORSC));

   III. Comply with in-country regulatory requirements, approvals for test articles, and any necessary import requirements; and

   IV. Provide written documentation from the foreign site indicating all necessary approvals for use of a test article under the local laws have been obtained to the NIH IRB.
c. For research conducted in a foreign country, the NIH PI must describe in the protocol, the rationale and the plan (e.g., scope of research, facilities) for conducting non-exempt human subjects research at the foreign site(s), and relevant local context information, including but not limited to:

   I. The name of the foreign PI/Lead Site Investigator(s) (if collaborating with a foreign institution);

   II. The rationale for conducting research in the foreign country;

   III. Information about the foreign study population and what is required to enroll them in research, (e.g., legal age at which subjects can provide consent to participate in research, capacity to consent standards, legally authorized representative standards, local processes for obtaining research informed consent, local languages or dialects, and vulnerable populations).

d. Research that has been disapproved by an in-country IRB/EC, cannot be submitted to the U.S.-based IRB for approval.

   I. If the U.S.-based IRB has already approved the research the NIH PI must promptly notify the U.S.-based IRB that the in-country IRB has disapproved the research.

e. When the NIH IRB is the reviewing IRB, in addition to the submissions requirements specified in Policy 205 Requirements for IRB Submissions, the NIH PI must submit the following items to the NIH IRB (including, as applicable, certified/back- translations of any foreign-language documents into English):

   I. Local context information that is not described in the protocol, including, but not limited to:

      i. A description of the foreign country laws and regulations or local customs that impact the conduct of the proposed research;

      ii. Whether the protocol will require, in addition to any necessary local IRB/EC approval, local review and approval by any other in-country entities (e.g., institutions, offices, departments, Scientific Committees, drug and/or device oversight agencies).
II. Documentation of in-country IRB/EC (if applicable) review determinations and approvals, or a written assessment consistent with C.7 above, when there is no in-country IRB/EC; and

III. Any other materials needed by the NIH IRB to complete its review.

f. NIH PI’s must not initiate research until both the U.S.-based Reviewing IRB approval and the in-country IRB/EC approval (if applicable) has been obtained.

2. Responsibilities of the NIH IRB

a. When reviewing international research, the NIH IRB must take local context information into consideration when making its determinations

b. The NIH IRB must not issue a final approval for research conducted in a foreign country until approved by an in-country IRB/EC, if one exists

I. If the foreign country does not have an IRB/EC, the IRBO will require the submission of an independent assessment of the protocol by an individual with knowledge of the foreign country laws and regulations, or local culture and customs, which must be submitted to the NIH IRB to consider prior to review and approval of the research.

c. The NIH IRB must not approve collaborative research occurring a foreign country that has been previously disapproved by, or otherwise conflicts, with the determinations of the in-country IRB/EC. If previously approved by the NIH IRB and a later determination by the in-country IRB/EC disapproves the research, the NIH IRB approval will be rescinded.

F. REFERENCES

1. Federal Regulation:
   HHS: 45 CFR 46
   FDA: 21 CFR parts 50, 56, 312, and 812

2. NIH Policy:
   Policy 100
   Policy 205 Requirements for IRB Submissions
   Policy 500 Research Involving Drugs, Biological, and Nutritional Products
   Policy 501 Research Involving FDA Regulated Devices
   Policy 502 Expanded, Including Emergency Use of Investigational Drugs, Biologics and Medical Devices (Test Articles)
3. **Guidance:**
   - Fogarty International Center, Division of International Relations
   - International Compilation of Human Research Standards
   - OHRP database for FWA and IRB/ECs
   - Institute/Center (IC) Technology Development Coordinators

G. **APPENDICES:** NA

H. **REVISION HISTORY:** NA

I. **SUPERSEDES DATE:** 11/09/2020
   - SOP 20B NIH IRB Responsibilities Reviewing Local Context Considerations for Offsite Research