

Policy 700 International Research – Policy Overview

<p>This document summarizes changes in <i>Policy 700 International Research</i> (referred to as Policy 700 in this document) that NIH investigators should be aware of, from the SOPs mentioned below.</p> <p>The policy describes the requirements and responsibilities of NIH investigators when conducting non-exempt human subjects research in foreign countries.</p> <p>Investigators are responsible for reviewing Policy 700 and complying with the requirements of the policy.</p> <p>Note: Text from the policy and other policy titles are italicized.</p>	
Policy 700 International Research	SOP Superseded by Policy:
Policy 700 partially supersedes	<p>SOP 20B NIH IRB Responsibilities When Reviewing Local Context Considerations for Offsite Research When inactivated, this SOP will be archived in the Policy Archive.</p>
<p>Applicability of Policy 700 - This policy applies to:</p> <ul style="list-style-type: none"> • NIH investigators conducting non-exempt human subjects research in foreign countries, and • the NIH IRB when reviewing non-exempt human subjects research that will be conducted in foreign countries. <p><i>This policy <u>does not</u> cover all federal and NIH policy requirements for non-exempt human subjects research conducted in a foreign country.</i></p>	
Policy Requirement	SOP Requirement
<p>Section E.1.f. – <i>NIH PIs must not initiate research until both the U.S.-based Reviewing IRB approval and the in-country IRB/EC (ethics committee) approval (if applicable) has been obtained.</i></p> <p>There is no change in regulatory obligations. Policy 700 adds specificity for clarity, making it explicitly clear the local IRB/EC approval is a requirement when such a committee exists. In addition, NIH IRB review can either precede or follow local IRB/EC approval.</p>	<p>SOP 20B, section 20.B.6.C. – <i>The NIH usually requires that the NIH IRB review and approve the protocol before it is submitted to the in-country IRB/EC.</i></p>
<p>Section C.1. – <i>Human subjects research conducted by NIH investigators is subject to federal law, regulation and policy, including</i></p>	<p>SOP 20B Appendix A, Standard F. – <i>Are there any issues related to differences in regulations between countries?</i> AND</p>

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<p><i>NIH policy, regardless of whether the research is conducted domestically or internationally.</i> AND Section C.2. – <i>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.</i></p> <p>There is no change in the obligation to comply with relevant international and domestic laws, regulations, and policies.</p>	<p>SOP 20B.6.A.¹. – <i>There should be no U.S. Government restrictions about conducting research in that country.</i></p> <p>Policy 700 is reorganized for clarity.</p>
<p>Section C.3. – <i>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.</i></p>	<p>Not applicable (NA) – This language has been added to Policy 700 for clarity.</p>
<p>Section C.4. – <i>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, 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.)</i></p> <p>There is no change in the obligation to comply with relevant international and domestic laws, regulations, and policies.</p>	<p>SOP 20B.6.B. – <i>In addition to the NIH IRB review, the research may also be subject to approval of a local IRB or Ethics Committee (EC)... Some countries require approval from the Ministry of Health or other government entities or officials.</i></p> <p>Policy 700 is reorganized for clarity.</p>
<p>Section C.6 – <i>Non-exempt human subjects research conducted or supported by the NIH IRP in a foreign country must be consistent with NIH’s Department of Health and Human Services (HHS) Federalwide Assurance (FWA).</i> AND Section C.6.a. – <i>Non-exempt human subjects research conducted in a foreign country with a</i></p>	<p>SOP 20B, section 20B.6.B. – <i>IRB/EC approval may be obtained from an institution/entity associated with that country that has a current approved FWA and an IRB/EC registered with OHRP.</i> AND SOP 20, section 20.4 B–2. – <i>Many research institutions in other countries do not have FWAs and instead follow the legal requirements of the</i></p>

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<p><i>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).</i></p> <p>Policy 700 makes it explicit that the local IRB/EC must be a registered IRB and that any collaborating institution must hold an active FWA with HHS. It also adds an exception to this policy statement which is contingent upon prospective NIH IO approval.</p>	<p><i>particular country. If, however, the NIH is supporting human subjects research at a foreign institution, the foreign institution must follow 45 CFR 46. This requires an FWA and IRB approval pursuant to those regulations.</i></p>
<p>Section C.7. – <i>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 it is the Reviewing IRB.</i> AND Section C.7.a. – <i>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.</i></p> <p>There is no change in the requirement to obtain in-country IRB/EC approval and/or local context review from the U.S.-based IRB.</p>	<p>SOP 20B, section 20B.6.C. described the requirement to obtain in-country IRB/EC oversight.</p>
<p>Section C.8. – <i>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</i></p>	<p>NA</p> <p>This language has been added to Policy 700 for clarity.</p>

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<p><i>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).</i></p>	
<p>Section C.9. – <i>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.</i></p> <p>Policy 700 does not change this obligation for local context review, but does now specify that if there is no local IRB/EC, the IRB will require a formal evaluation be provided to the IRB that assesses the appropriateness of the proposed research.</p>	<p>SOP 20B, section 20B.6.C. – <i>The PI should provide information about the culture, economic and political conditions, and specify any risks to subjects specific to that site that may impact research. The IRB may use consultants familiar with the population to aid in their deliberations.</i></p>
<p>Section C.10. – <i>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, <u>but in-country IRB/EC review is still required</u> (emphasis added).</i></p> <p>AND</p> <p>Section C.10.a. – <i>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.).</i></p> <p>Policy 700 clarifies that the NIH IRB is not required to review research in which NIH investigators are not formally engaged in the</p>	<p>SOP 20, section 20.4.B.2. – <i>If, however, the NIH is supporting human subjects research at a foreign institution, the foreign institution must follow 45 CFR 46.</i></p> <p>Policy 700 does not change the obligation to obtain in-country IRB/EC review before initiating the research.</p>

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<p>research. In such cases, the only IRB review required is review by the in-country IRB/EC review, which must be obtained before initiating the research.</p> <p>All other relevant NIH requirements still apply.</p>	
<p>Section C.11. – <i>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.</i> AND Section C.11.a. – <i>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.</i> AND Section C.11.b. – <i>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.</i> Policy 700 adds specificity for clarity.</p>	<p>NA Policy 700 incorporates the regulatory obligation to obtain in-country IRB/EC and/or U.S.-based IRB review before initiating the research.</p>
<p>Section C.12. – <i>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.</i></p> <p><i>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.</i></p> <p>U.S.-based IRB approval and in-country IRB/EC approval, (when applicable) are required prior to initiating the research. Policy 700 now specifies that NIH IRB approval will be rescinded if an in-country IRB disapproves the research.</p>	<p>NA This regulatory obligation has not changed</p>

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<p>Section E.1.a. – <i>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 21 CFR parts 50, 56, 312, and 812). In addition, all NIH investigators conducting non-exempt human subjects research in foreign countries, must comply with:</i></p> <p><i>I. All applicable foreign country laws and regulations (e.g., 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.);</i></p> <p><i>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 this policy. (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) such as, reporting research events, as compared to NIH policy; and</i></p> <p><i>III. The requirements of the U.S.-based Reviewing IRB.</i></p> <p>Regulatory, legal, and policy obligations have not changed. Policy 700 adds detail and specificity for clarity.</p>	<p>SOP 20B, section 20.B.6.B. – <i>In addition to the NIH IRB review, the research may also be subject to approval of a local IRB or Ethics Committee (EC). IRB/EC approval may be obtained from an institution/entity associated with that country that has a current approved FWA and an IRB/EC registered with OHRP. Some countries require approval from the Ministry of Health or other government entities or officials.</i></p>
<p>Section E.1.b. – <i>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></p> <p><i>I. Comply with FDA regulations for shipping test articles internationally;</i></p>	<p>NA</p> <p>These regulatory responsibilities have not changed.</p>

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<p><i>II. Comply with applicable NIH requirements (e.g., pharmacy, CC Office of Research Support and Compliance (ORSC));</i></p> <p><i>III. Comply with in-country regulatory requirements, approvals for test articles, and any necessary import requirements; and</i></p> <p><i>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.</i></p> <p>Policy 700 adds detail and specificity for clarity.</p>	
<p>Section E.1.c. – <i>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></p> <ul style="list-style-type: none"> I. PI/Lead Site Investigator(s) name; II. Rationale for conducting research in the foreign country; III. Information about the study population and what is required to enroll them in research. <p>See Policy 700 for additional detail, including protocol information necessary for NIH IRB review. The policy is also reorganized for clarity.</p>	<p>NA</p>
<p>Section E.1.d. – <i>Research that has been disapproved by an in-country IRB/EC, cannot be submitted to the U.S.-based IRB for approval.</i></p> <ul style="list-style-type: none"> I. <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.</i> <p>Policy 700 allows for more flexibility regarding timing of IRB submissions, and adds the</p>	<p>NA</p>

<p>requirement that the U.S.-based IRB be promptly notified of any in-country disapproval that occurs after U.S.-based approval.</p>	
<p>Section E.1.e. – <i>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></p> <p><i>I. Local context information that is not described in the protocol, including, but not limited to:</i></p> <p><i>i. A description of any laws, regulations, or local customs that impact the proposed research;</i></p> <p><i>ii. Whether the protocol also requires local approval by other in-country entities (e.g., institutions, drug and/or device oversight agencies).</i></p> <p><i>II. Documentation of in-country IRB/EC approvals, or a written assessment consistent with C.7., when there is no in-country IRB/EC;</i></p> <p><i>III. Any other materials needed by the NIH IRB.</i></p> <p>The policy specifies what information the PI must submit to the NIH IRB for review. The policy is also reorganized for clarity.</p>	<p>SOP 20, Appendix A outlined IRB review considerations for research conducted at foreign sites, including domestic and local regulatory standards; research setting; infrastructure and facilities; structural issues (e.g. monitoring and maintenance of records); subject safety; compensation; recruitment; and local norms such as age of consent, language barriers, and handling of specimens.</p>
<p>Section E.2.b. – <i>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></p> <p><i>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</i></p>	<p>SOP 20B, section 20B.6.B. – <i>IRB/EC approval may be obtained from an institution/entity associated with that country that has a current approved FWA and an IRB/EC registered with OHRP.</i></p> <p>AND</p> <p>SOP 20B, section 20B.6.A. – <i>The IRB may use consultants familiar with the population to aid in their deliberations. Consultants should include individuals with knowledge of the local research context.</i></p>

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<p><i>NIH IRB to consider prior to review and approval of the research.</i></p> <p><i>AND</i></p> <p>Section E.2.c. – <i>The NIH IRB must not approve collaborative research occurring in a foreign country that 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.</i></p> <p>Policy 700 now clarifies the IRB’s authority and responsibility when the in-country IRB disapproves the research.</p>	<p>SOP 20B did not specify IRB actions after in-country IRB/EC disapproval.</p>
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