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Procedural Challenges In International Collaborative Research

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Abstract

There is tremendous promise for a rewarding experience in an international research project due to the collaboration, mutual learning and cultural bridging that intrinsically occur. However, knowledge of the procedural requirements for international research is not widely disseminated to investigators who may not have been involved in the administration of a federal grant with a foreign component. The purpose of this article is to highlight the major challenges in administrative, procedural and equipment management aspects of grant implementation when federal funding is involved in international collaborative research. It is hoped that awareness of these difficulties and demystification of the process for future investigators can minimize the potential encumbrances in a rewarding journey towards realizing the scientific goals in an international collaborative research project.

Keywords

International collaborative research; maternal and infant mental health; grant administration; foreign clearance; IRB; Graduate Medical Education; physician education

Introduction

It has long been recognized that many of the challenges that confront public health services of any given country are not unique to that nation, as diseases permeate territorial demarcations, highlighting common grounds to address universal health concerns. Furthermore, with urbanization and lifestyle changes, the threats from non-communicable diseases (e.g. stress-related illnesses and cancer) resonate across the world. It is thus acknowledged that the systematic understanding of the risk factors, etiologies, and the quest for solutions to these problems, may entail a broadening of scope for investigators to collaborate globally, and to put hypotheses to the test at the sites offering the experimental conditions (be it a foreign country or a highly endemic area) (1–5). In maternal and child health research, for example, the specific investigations may include the effects of social discrimination from HIV, the impact of environmental toxic exposure on child development, and post traumatic stress after a natural disaster. In these themes of investigation, one can identify or allude to similar concerns applicable to the context of the U.S.

Rhode Island Congressman John Fogarty had the prescient understanding of the importance of U.S. investment in international health research more than 40 years ago. The visions to foster global health research and reduce health disparities gave rise to the NIH Fogarty International Center (FIC) (6–9). Today, funding for international collaborative studies is supported by the majority of the 27 centers and institutes of NIH. In general, investigators have to be U.S. citizens

or permanent residents to receive funding from NIH, but some award applications and special programs are open to foreign nationals as well. A search on the NIH Computer Retrieval of Information on Scientific Projects (CRISP) database for fiscal year 2008 reveals 1357 activities, including 408 research projects (mainly R01, U01 and R03 grants), 121 career awards (K series), 132 center grants (P series), and 138 Trainee and Fellowship awards (T and F series) involving international collaboration.

In this framework of a supportive and organized system to fund international collaborative studies, there are a number of administrative, budgetary, and performance requirements from both U.S. and foreign institutions and agencies that need to be considered by investigators. Unfortunately, knowledge of the procedural requirements for international research is not widely disseminated to investigators who may not have been involved in the administration of a federal grant with a foreign component. Without gaining a coherent outlook of longer-term plans, a piecemeal approach may be the only visible avenue, but adoption of such a strategy may lead to loss of time, if it does not place the grant in jeopardy. Knowing what to expect in the process can help the investigator with the tools for problem-solving that will be counted upon. This article discusses the difficulties of grant implementation, and the potentially time-consuming steps in seeking approvals from various domestic and foreign agencies, when federal funding is involved in global research.

In the Beginning

The receipt of a priority score in the fundable range can be the beginning of a rewarding journey towards the eventual obtaining of results generated from the research proposal (10–13). Readers seeking clarification on priority scores and paylines can refer to general information on NIH websites, the article by Berg et al (2007)(14), and but more specific guidance can be obtained from the program official. While awaiting the Notice of Grant Award (NOGA), the investigator should be aware of the foreign clearance aspects of the grant. The investigator may check with the program official if foreign clearance can be initiated, and approximately how long it may take. The Institutional Research Board (IRB) and Federal Wide Assurance (FWA) procedures as specified in the sections below can be initiated as well.

The investigator should also be aware that if research equipment and/or collection of samples and specimens involved in the research, there are special requirements and permits needed for shipment and handling that have to be addressed prior to the implementation of the research plans. Failure or delay in obtaining of these permits or clearance of these procedures can jeopardize the project, especially if the use of the equipment or the collection/analysis of specimens needs to be timed according to the recruitment and follow-up schedule. Requirements for contractual agreements with the foreign collaborating site also have to be taken into consideration. The procedural steps to consider are summarized in Figure 1 and explained in the sections below.

Foreign Clearance

For studies that involve a foreign grant or contract, foreign clearance of the grant has to be obtained through the Fogarty International Center (FIC). Depending on the country where the foreign site is slated, this process may vary, and there are uncontrollable factors of the geopolitical climate that can prolong the process, even if the research is independent of politics by its design. The program official will usually be the person initiating the process for foreign clearance, and will be able to inform the principal investigator of the status of the approval. The Notice of Grant Award cannot be issued without issuance of foreign clearance through FIC's Division of International Relations (<http://www.fic.nih.gov/about/dir.htm>).

Depending on the nature of the project, there are other approvals that may need to be considered, such as safety monitoring, certificate of confidentiality, and clinical trials registration. The National Heart, Blood, and Lung Institute's (NHBLI's) website contains information for these requirements. There may be similar or additional requirements from the overseas institution and their system of monitoring and oversight. These may include the local Ministry of Health and entities performing similar functions to the Centers for Disease Control or Food and Drug Administration. It is prudent to check with the NIH program official, the foreign collaborator/s and the IRB and clinical trials specialists at the principal investigator's institution, for which approvals are needed.

IRB and FWA Requirements

The investigator must address the cultural and ethical barriers to conducting research in non-Western countries, the protection of human rights in research, and the compliance to informed consent procedures, as they may apply to the foreign site (15–24). There are also special IRB requirements for government-funded grants with foreign components. For human subjects research conducted or supported by U.S. Department of Health and Human Services (HHS), a Federalwide Assurance (FWA) (25,26) is required from the Office for Human Research Protections (OHRP). An assurance of compliance is a written document submitted by an institution, not by its Institutional Review Board. Obtaining an approved assurance from OHRP is a two-step process. First, the investigator must ensure that the IRB(s) designated under the Assurance are registered with OHRP. The lists of registered domestic and international IRB's are available on the website. If the foreign IRB is already registered, the next step is to complete the assurance application.

Registration of the IRB is initiated by the foreign collaborator's IRB chairperson. The IRB has to meet the minimum requirements for membership, which include having at least five members. It has to include at least one member whose primary concerns are in scientific areas, at least one member whose primary concerns are in nonscientific areas (a 'layperson'), and at least one member who is not otherwise affiliated with the institution. There are other requirements listed on the website (27).

The international FWA application can be submitted by paper or online. The FWA is signed by a high-level individual within the institution (e.g. the Chief Executive Officer, or Chancellor), committing the institution to abide by the Terms of Assurance whenever it is engaged in human subjects research conducted or supported by HHS. The instructions, submission and the status for a FWA application can be found online, on the HHS FWA website.

The research protocol will not be approved by the IRB at the principal investigator's institution (U.S.) unless the international FWA has been issued. In addition, the protocol needs to be reviewed and approved by both the U.S. and foreign IRB's. At some institutions, the U.S. IRB may require the foreign IRB approval first, before it issues its own approval.

Shipping of Equipment and Customs

Research equipment is not easily imported into certain countries. Major academic centers in the U.S. will usually have an office (e.g. Purchasing Department or Office of Research Administration) that can assist in the shipping of research equipment overseas. Unfortunately, the role of that office in assisting investigators with the shipping, including their needed expertise with export control regulations, may not be well advertised or generally known to staff and personnel at the academic center.

Further to the export regulations of the U.S., the investigator should also be aware of the import regulations of the foreign site. Even if the research equipment is just one unit and not intended for resale, it may still be subject to import-export regulations. The university office that assists investigators with the shipping of equipment overseas, may have contracts with vendors which handle the procedures, administration and paperwork needed for export and import for specific countries or regions.

Electrical Compatibility and Power Configuration

For equipment manufactured in the U.S. to be used in the foreign country, a number of adaptations and knowledge of the local resources need to be considered. Depending on the sensitivity of the equipment and the reliability of the power source, adapting the equipment to a higher voltage AC system may have to involve the use of a heavy duty transformer. Other issues include the availability of electrical outlets and supply, the grounding of the equipment, and the possible electromagnetic interference from the power lines in the new environment. It is advisable to have a local technical specialist be available for assistance with troubleshooting and repair, and to have access to consultation with experts familiar with the equipment.

Samples and Specimens

Samples and specimens fall under regulated materials and commodities. These cannot leave or enter the country without the documentation, approvals and checks. Investigators who receive human etiological agents and genetic elements must comply with import and transfer requirements of the U.S. Centers for Disease Control and Prevention (CDC). The U.S. Animal and Plant Health Inspection Service (APHIS) regulates shipments when importing and exporting plants, animals, animal products and biologics. A Toxic Substances Control Act (TSCA) Export Notification Form is required for chemicals listed on the U.S. Environmental Protection Agency's (EPA) "Chemicals on the Reporting Rule" Database (30). When institutions and firms collaborate, they often sign a Material Transfer Agreement (MTA) that further limit shipments of proprietary and other research materials (31). These are the U.S. requirements, but the investigator will also have to conform to the standards and regulations of the foreign collaborator's institution and country. These protocols and approvals will have to be reviewed and obtained in advance to ensure the safe passage of the shipments. If the shipments lack the proper approvals to leave the country, or become mired in customs, the efforts in collection are essentially forfeited.

Contractual agreements

The contracts and terms of payment for an international collaboration funded by NIH or other federal agencies need to be reviewed and approved by both the investigator's and collaborator's institutions. Within the contract, the intellectual property rights for the results generated from the project should be specified. Prior to this stage, the delineation of the contract terms and intellectual property rights issues (32,33), including the publication authorship, should be discussed with the collaborator. Although the investigator and collaborator may have worked and published together prior to grant funding, and understand each other's perspectives, there may be additional requirements and demands from both domestic and foreign institutions that need to be addressed in the formal contractual agreement process. Details of the contractual discussions should also include the fluctuations in exchange rate (34). Usually, the contract terms are stated in fixed dollar amounts that will not float according to the exchange rate at a later time.

Conclusion

This report highlights the major challenges in administrative, procedural and equipment management aspects of grant implementation when federal funding is involved in international collaborative research. It is hoped that future investigators will be able to avoid delays and implementation pitfalls by timely resolution of these difficulties.

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Figure 1.
Summary of Procedural Requirements and Steps to Consider