International Research
Does it keep you up at night?

Disclaimer

Conflict of Interest
We have no relevant personal/professional/financial relationship(s) with respect to this educational activity.

Commitment
This is intended to be an educational discussion to enhance awareness of international activity as it relates to research

Perspective
There is no one way to implement an international research program. This presentation is from the perspective of one institution highlighting success stories as well as lessons learned.
This presentation is intended to give you an insight into the process of defining, creating, and monitoring international research activities. The information here is based on the journey that my institution took with some lessons learned. There are many ways to approach this process based on the type of international activity, resource allocation, and the risk tolerance of your institution.

Objectives

**Who**
- Who owns it? Where does the responsibility live for identifying, assessing, and managing research activity?

**Manage**
- Discuss ways to manage and monitor research activities?
- Are there natural checkpoints?

**Assessment**
- Discuss ways to assess where research international activities occur within your institution.

**Define**
- What is international research? What does it mean to your institution?

**Regulation**
- Who has regulatory oversight over international research activities?

**Identify**
- How do you identify areas where international activities may occur?
**Regulatory review**

**Animals**
- PHS Policy on Human Care of Use of Laboratory Animals
- Foreign Assurance (from OLAW)
- CIOMS Guidelines

**Export Controls**
- Export Administration Regulations (EAR) 15 CFR 700-799
- Export Administration Act (EAA)
- Tax Reform Act (TRA)
- International Traffic in Arms Regulations (ITAR) 22 CFR 120-130
- Office of Foreign Assets Control (OFAC) 31 CFR 500-599
- Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES)
- Endangered Species Act
- Controlled Substances 21 CFR Chapter II

**Human Subjects Research**
- Federalwide Assurance (FWA)
- Institutional Review Board (IRB)/Ethics Board and local version of IRB/Ethics Board

**Investigational New Drugs (IND)**
- Declaration of Helsinki
- 21 CFR 312.120 Foreign Clinical Studies Not Conducted Under an IND
- Guidance for Industry and FDA Staff
- Investigational New Drug (IND) Application

**Foreign Corrupts Practice Act (FCPA)**

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**How do you define international research**

**Human Subjects**
**01**
Is it just clinical trials occurring outside of the US borders?

**Foreign Nationals**
**02**
Is your definition based on whether your PI is a foreign national or will be conducting research in a foreign country?

**Data**
**03**
Does your definition include sending or receiving data from a foreign location?

**Export Controls**
**04**
Is your definition based on whether you need an export control license?

**FCPA/OFAC**
**05**
Does your definition include checking the naughty lists?

Our definition is based on international activity occurring for research purposes.
Searching for international research activities

Regulation
Are there areas that are specifically called out in the regulation.

Usual Suspects
Areas that are always involved regardless of the type of research such as contracting.

Department Interviews
Checking in with departments within the institution to find out if they do business internationally.

What did we find

- Animals
- Bench research
- Contracting
- Data management
- Employment/Taxes
- Finance
- Foreign Nationals
- Grants
- Human Subjects Research
- IS/IT
- Labs
- Licensure
- Privacy/HIPAA
- Purchasing/Vendors
- Shipping
- Signing Authority
- Visas
What did we do with this information

- Collected info
- We talked
- We debated
- And then...
- Evaluated risk

What does it all mean?
We talked a lot about what this meant to the institution in terms of risk tolerance and things we felt were priorities to the organization.

How did we choose?
Once we did our assessment as to what we wanted to include and where it lived within the institution, we then assigned risk.

We wrote a policy

Easy right?

Where to start?
Who is going to own it? Who will draft it? Does it need to be a research policy? Who needs to be involved?

What to include?
Do we put every topic we can think of? Do we do bare bones? Do we just put a general framework? Do we only put the big stuff?

How much detail
Do we put everything in the policy? Do we have appendices? Do we do a SOP? Do we have guidelines?
Where we landed

Animal Subjects Research
Institutions that conduct animal research on live, vertebrate animals with Public Health Service (PHS) funds are required by the PHS Policy on Humane Care and Use of Laboratory Animals (PHS Policy) to have in place an Animal Welfare Assurance with the Office of Laboratory Animal Welfare (OLAW). If the research is being conducted outside the U.S. with PHS-funds, the PHS Policy requirements are applicable to the research (or the foreign entity must provide evidence to PHS that acceptable standards for animal care and use will be met). A Foreign Assurance from OLAW must be completed by the foreign institution and the foreign institution must comply with CIOMS Guidelines. Review the section below entitled Export Controls, Animals and Animal Products for additional information. See Appendix A for additional information on Animal Subjects Research.

Appendix A
Animal Subject Research

The BIDMC Investigator is responsible for the following:
The BIDMC Investigator must submit the research proposal to the BIDMC IACUC for approval. When submitting an application to the BIDMC IACUC that includes foreign animal research, the BIDMC investigator should include:
• veterinary qualifications at the foreign site,
• IACUC/oversight body requirements at the foreign site,
• animal pain/distress considerations in the host country, and
• whether the foreign site has a Foreign Assurance from OLAW.

The BIDMC Investigator should comply with the following policies and procedures:
• Investigator’s Training Manual
• Animal Welfare Act

For assistance on animal research issues at foreign sites, the BIDMC Investigator should contact the BIDMC Veterinarian at ________________.

What was our approach
Categorized
Provided regulatory or policy basis
Provided institutional information
Created appendices with additional information

What we included in our policy
• Responsibilities of the investigator
• Animal Subject Research
• Employment and Taxes
• Export Controls
  • EAR
  • Anti-boycott
  • ITAR
  • OFAC
  • Animals and Animal Products
  • Controlled Substances
• FCPA
• Funds
• Human Subjects Research
• FWA
• IRB/Ethics Board
• Investigational New Drugs (IND)
• Foreign Laws and Regulations
• Licensure
• Visa
• Privacy/HIPAA
• Securing Data
• Paper files
• Electronic data
• Local researchers/ translators
• Location of data collection
• Signing Authority
• Shipping
Next step...gap analysis

1. **Review of existing policy**
   Once we identified our categories, we looked at hospital policy to see if there was any overlap.

2. **Meetings**
   Met with individuals actually doing the work.

3. **Interviews**
   Interviewed key stakeholders in policy areas to evaluate their process. We then compared that to existing policy and to regulation to identify gaps.

4. **Survey**
   For topics where there was broad overlap among research groups, we conducted a survey.

5. **Overlap**
   Many categories were not stand-alone categories.

6. **Benchmarking**
   When gaps were identified, we reached out to colleagues to see what they were doing.

Next steps...developing and improving infrastructure

**Who is responsible?**
- International Office
- OGC
- Research Compliance
- Research Operations (IRB)
- PI/study staff

**When/where does it start?**
- Front-end vetting
- Pre/Post Grant application
- Pre/Post Award
- Contracting
- IRB Application/
- Approval

**Supporting Infrastructure—What do you need to be successful?**
What do you need to know

Questions to ask

• Ask about money—who is getting it and where is it coming from?
• Ask what is going to be done and where?
• Ask about personnel—where are they from and where will they be working—do they have the right visa, credentials, licensure, etc. Think about tax and employment law in all locations.
• What agreements are needed?
• What kind of data will be collected? Where is data stored? How will it be transferred? Who will have access?
• What equipment will be needed? Where will it be purchased?
• How will money be exchanged—carrying cash? Bank account? How will things be paid for abroad?
• Shipping of samples, equipment, etc.
• Are you prime or sub on the award, who is responsible for what?
• What space will you use—institution, collaborator, lease/rent, etc.

How do you monitor

Internal
Depending on your institutional risk tolerance and resources may determine what types of internal resources you have to monitor your international research program.

External
Some external may be requested like outside counsel or a consultant and others may invite themselves such as governmental agencies. Again, depending on resources, you may be able to enlist outside services to help with monitoring. The key with the external monitors is to be able to demonstrate due diligence.
What can go wrong

Harvard research in China
https://www.washingtonpost.com/archive/politics/2002/03/30/harvard-research-in-china-is-faulted/5a9a2538-93ea-43b4-b660-6c1498fc468c/?utm_term=.413c4c710ecd

Pfizer Trovan study in Nigeria
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4089044/

AZT trials in Africa
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4089044/

Clinical trial regulations in India
https://clinregs.niaid.nih.gov/country/india#_top

Other ideas, questions

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