

# Conducting International Research: Ethical and Policy Concerns

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# Session Overview

- Who are we and why is this relevant?
- What is “International Research”?
- Ethical and Policy Issues; Laws, international conventions, policies
- Animal Research
- Human subject research: consent issues
- Collecting/developing genetic resources/traditional knowledge
- Intellectual Property
  
- Q&A
- Quick survey

# RPAC's Role

- Who we are: Research Policy Analysis & Coordination
- What we do:
  - Policy development
  - Guidance on implementation of UC and external policies/rules
  - Systemwide leadership and representation beyond UC
  - Systemwide coordination and resources
    - International research:
      - International research listserv
      - UCGO.org
- Subject matter expertise is broad and deep

# RPAC covers a *BROAD* range of issues

- Animal Research
- Biodiversity/Genetic Resources
- California Institute for Regenerative Medicine (CIRM)
- Citizenship Restrictions
- Clinical Trials
- Conflict of Interest
- Copyright
- Data Rights
- Equity in Licensing
- Export Control Clauses/ITAR
- Federally Sponsored Research
- Gifts and Grants Classification
- HIPAA in Research Agreements
- Human Subjects/Institutional Review Boards
- Indirect Cost Policy
- Industry Sponsored Research
- Intellectual Property (IP)
- IP Issues in Global Health Access
- International Research Issues
- Legislation Affecting Research
- Material Transfer Agreements
- Multi-campus Research
- NAGPRA
- National Laboratory/Campus Awards
- Non-profit Sponsored Research
- Publication Restrictions
- State-sponsored Research
- Tax Exempt Bonds: Intellectual Property
- UCOP Contracts & Grants Administration

# RPAC's Role

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      - International research listserv
      - UCGO.org
- Subject matter expertise is broad and deep
- Emerging issues

# What is “International Research”?

Historically:

Activities and informal collaborations of our faculty abroad

- Consultations
- Site visits
- Conferences
- Exchange of research materials
- Co-authorship
- Conducting small-footprint research in another country, usually without local partnership

Recent expansion includes:

International Research Collaborations / cross-national teams

Jointly initiating and conducting larger and more complex research projects

Two people from different countries collaborating on a project



Major ventures of international teams involving substantial investment from participating countries

(e.g. Large Hadron Collider)

# What is “International Research”?

## Research Conducted Outside U.S.:

Driven by:

- Desire to work with specific experts
- Object of scientific study
- Specialized infrastructure
- Research funding



+

Perception of weaker regulatory requirements, and/or lower costs of collecting research data outside the U.S.



## Foreign Researchers at U.S./UC:

Driven by:

+

Potential to increase the impact and recognition of their scientific work  
E.g. Horizon 2020 (The Marie Skłodowska-Curie actions (MSCA) Fellowships)

# Ethical and Policy Issues

## 1. Human subject research issues

- Consent: concept of vulnerability (age of consent, group assent vs. individual consent)
- Using placebo
- Topic of research/stigmatized populations
- Providing study drug or device after the study, etc.

## 2. Research involving vertebrate animals

## 3. Intellectual Property

## 4. Research Data and Privacy Protection

## 5. Research Misconduct

## 6. COI and COC

## 7. Publication Restrictions



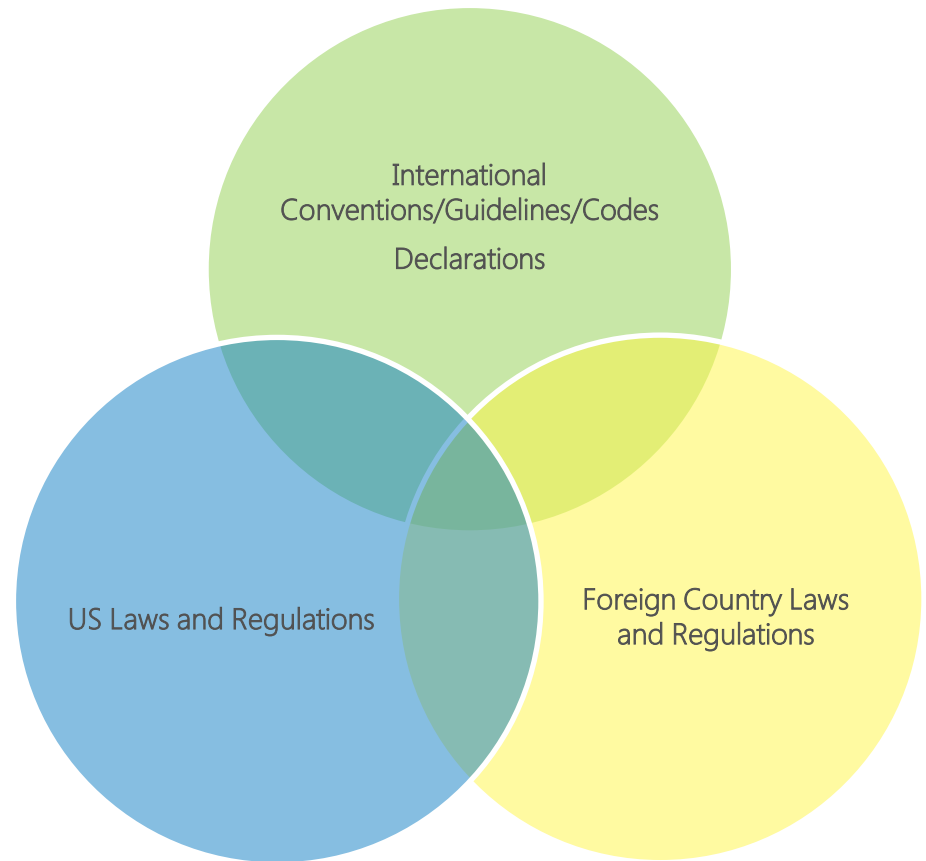
# Ethical and Policy Issues: Laws, International Conventions, Codes, Guidelines, and Policies

(Bio)ethical standards ⇒  
basis for regulations

US signatory of some  
international conventions

US Federal Grants: US  
laws and foreign country  
regulations

Challenge:  
When laws mismatched:  
whose laws apply?



# International Animal Research

# Animal Research

Why conduct animal research outside of the US?

Ethical considerations related to research with animals



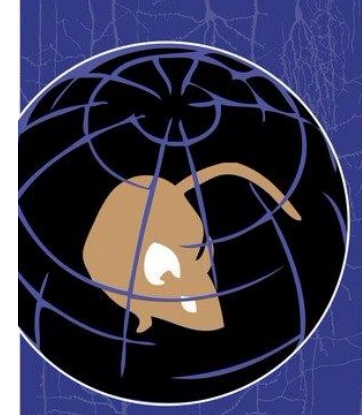
Regulatory framework:

- US regulations
- Local country regulations
- International standards

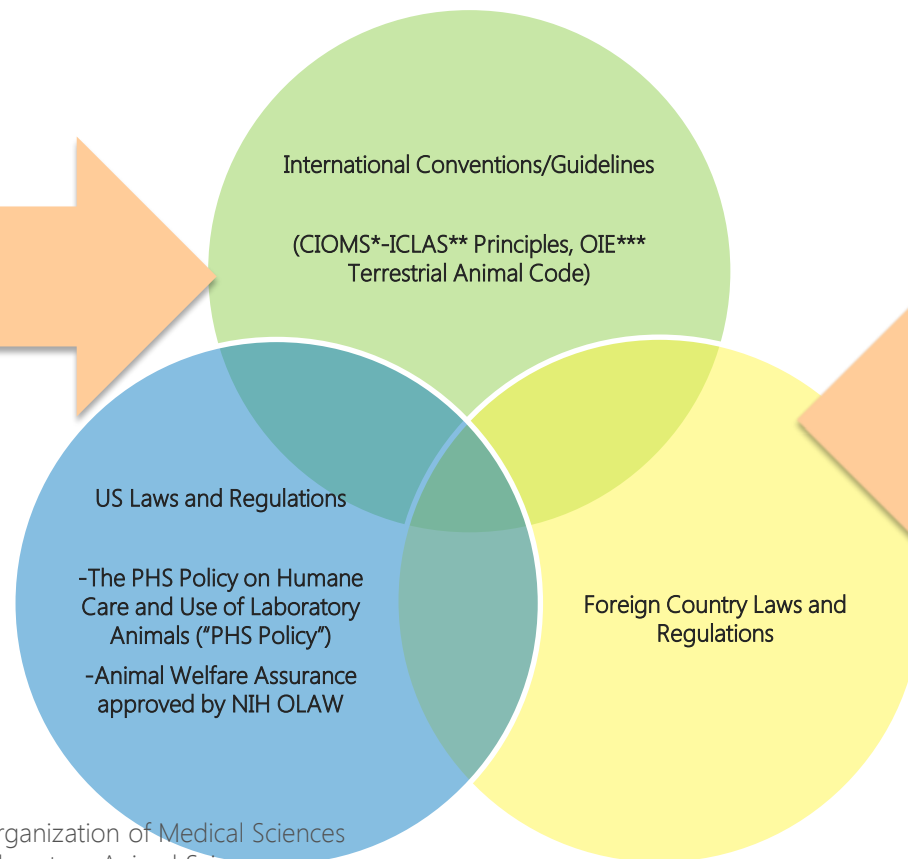
Contractual considerations:

- Material Transfer Agreements
- Subaward Management

# Animal Research: Regulatory Framework



- Harmonization vs. standardization
- Assurance that standards of animal care & use are comparable
- Science as the common language



Variances  
between  
countries in:

- Veterinary qualifications
- IACUC/ oversight body requirements
- Animal pain /distress considerations

\*CIOMS=Council for International Organization of Medical Sciences

\*\*ICLAS=International Council for Laboratory Animal Science

\*\*\*OIE=World Organization for Animal Health

# Contractual Considerations

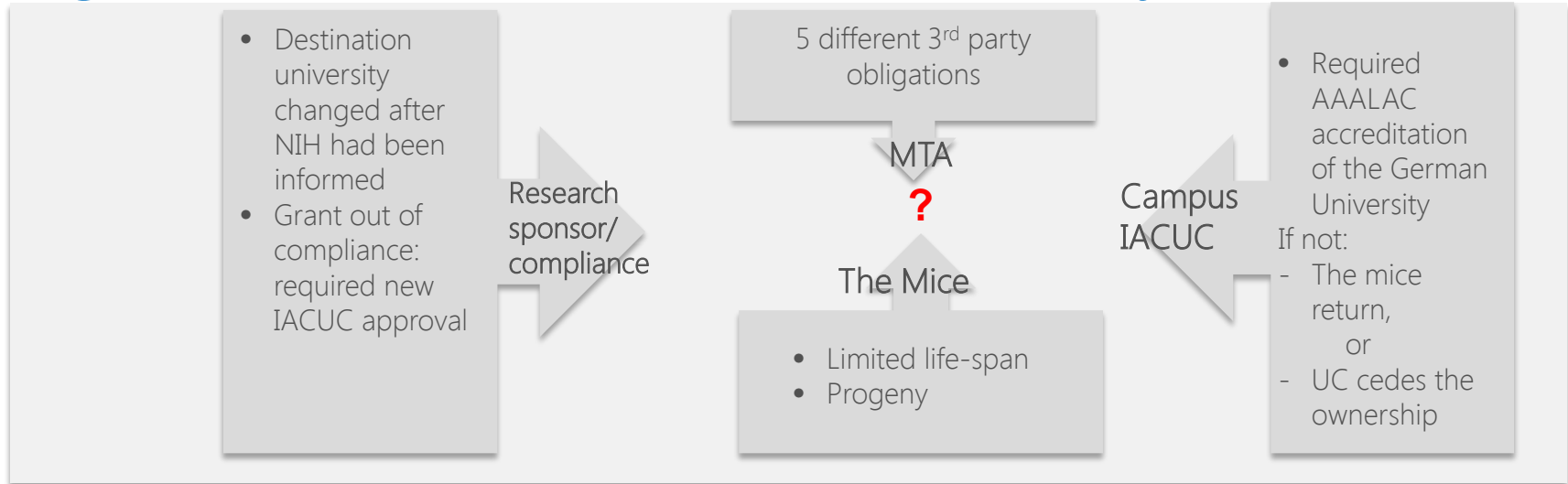
## 1. Material Transfer Agreements



+ shipping/export/import considerations

# UC Case:

## Eight mice travelled to Germany in 2011...



The German University **not AAALAC accredited**:

- o Returning the mice would be detrimental to the research project, so PI was against it
- o Ceding ownership problematic because of the 3<sup>rd</sup> party obligations

**Epilogue (19 months later):**

- The original mice reported dead by the German PI
- The progeny are no longer breeding and would be euthanized

# UC Case:

## Eight mice travelled to Germany in 2011...

- Destination university changed at NIH had been informed
- Grant out of compliance required new IACUC approval

5 different 3<sup>rd</sup> party

### Many Lessons Learned:

#### For Faculty:

If preparing for international research, even if it means just sending mice to a foreign institution- do your due diligence well in advance, contact the right offices to learn about the approvals you will need and seek assistance.

#### For Administrators:

Importance of cross-silo work for capturing all the details critical for making a decision regarding international research.

- Required AAALAC accreditation
- If not:
  - The mice return, or
  - UC cedes the ownership

- The German University
- Returning to
  - Ceding ownership

PI was against it

Epilogue (19 months later).

- The progeny are no longer breeding and would be euthanized

# Contractual Considerations

## 2. Subaward Monitoring



Federal Grant		Responsibility
Prime Awardee	UC	<ul style="list-style-type: none"> <li>• PHS Animal Welfare Requirement applicable</li> <li>• UC responsible for animal activity at foreign site=                             <ul style="list-style-type: none"> <li>• UC IACUC approval that certifies that foreign performance site is acceptable to UC</li> <li>• Responsible to report non-compliance at the foreign site</li> </ul> </li> <li>• Allowed to audit the subawardee; physical monitoring of the facility</li> </ul>
	Foreign Institution	<ul style="list-style-type: none"> <li>• UC IACUC approval is not required</li> <li>• Must complete Foreign Assurance from OLAW</li> <li>• Must comply with CIOMS Guidelines</li> </ul>



# Human Subject Research

# Some Consent Basics

UC IRBs/Committees for the Protection of Human Subjects will apply the same ethical and regulatory standards to research conducted abroad as to domestic research

## Elements of the consent process

- The informed consent process involves:
- giving a subject adequate information concerning the study,
- providing adequate opportunity for the subject to consider all options,
- responding to the subject's questions, ensuring that the subject has comprehended this information, obtaining the subject's voluntary agreement to participate and,
- continuing to provide information as the subject or situation requires.

To be effective, the process should provide ample opportunity for the Investigator and the subject to exchange information and ask questions

The regulatory requirements for Informed Consent:

General Requirements 45 CFR 46.116; 45 CFR 46.117, 21 CFR 50 Subpart B

# Is the consent process culturally appropriate? what is the local research context?

- Consider local culture, tradition, and language, current political and social climate.
- Research must be conducted in compliance with the host country's laws protecting human subjects and any requirements for local IRB approval must be met.
- Consent process and participant protections must be appropriate for the level of risk and the nature of the proposed research setting in which the research will be conducted
  - Determine culturally appropriate ways to disclose information necessary to meet the ethical standard of informed consent
  - Pay particular attention to disclosures relating to diagnosis and risk, research design, and possible post-trial benefit
  - Include in the informed consent process and consent documents information about what benefits, if any, will be available to research participants when their participation in the study in question has ended.

# What could go wrong?

Tribal members consented to allow blood samples to be taken for use for a study on the genetics of diabetes. However, the samples were also used for studies on schizophrenia, inbreeding, and possible migration patterns of the tribe's ancestors from Asia to America. Tribe sued the researchers' institution, charging that researchers misused blood samples taken from tribal members.

This case caused many AI/AN communities to enact tribal laws and regulations to require "community consent" in some instances and other provisions intended to control how their communities are portrayed in publications or presentations by researchers.

# What could go right?

In Senegal, researchers seeking to consent participants for a vaccine study overcame a barrier to participants' adequate understanding of the scientific/technical aspects of research protocols, given their culture and belief systems. They explained the concept of the role of immune cells in an immune response by talking about people who guard houses, a particular kind of watchman. The immune cells were described as a particular kind of watchman in the participant's blood. Even in countries with very low literacy rates, widespread illiteracy is not a barrier to comprehension. Informed consent is more an interactive process than one that depends on reading.

To illustrate the principle of randomization and the possibility that one of the vaccines might fail, the researchers used a familiar agricultural example: the evaluation of fertilizers or of seed varieties on randomized plots, a procedure familiar to farmers in the area.

# A Few Tips for Investigators

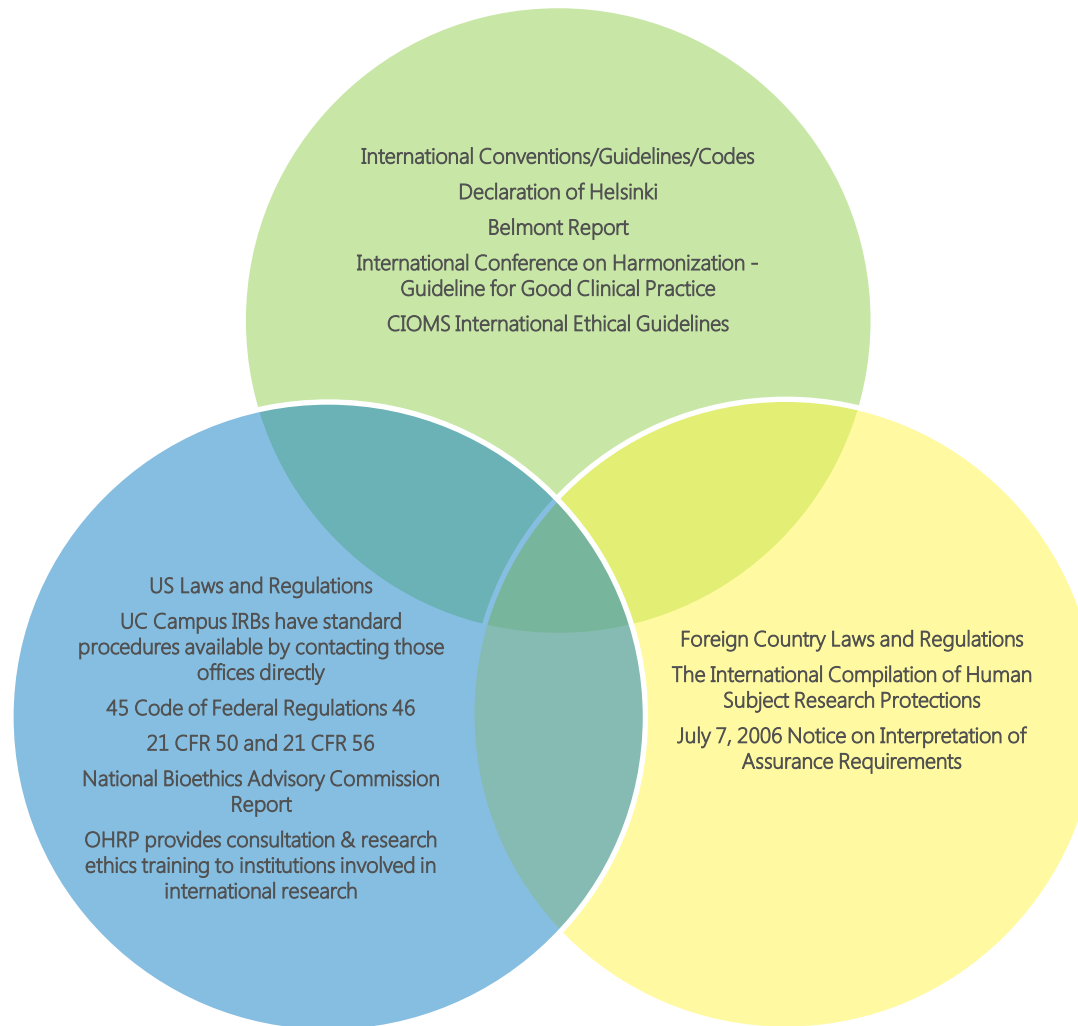
- Anticipate that informed consent development will take longer, and require more complex evaluation, than for domestic studies
- Consider partnering with local researchers in order to ensure understanding of, and compliance with, relevant laws protections for human subjects in the host country
- Anticipate translation needs
- Consider making more use of visual material to supplement written material for informed consent processes, particularly for populations with low literacy levels.
- Use IRB resources to access human subjects training options in commonly used international languages for international co-investigators
- Provide local PI and any international study staff and students conducting research at the international site with training in human subject protections.
- Collaborate with the local IRB to develop a workable plan for post-approval monitoring

# A Few Tips for IRBs

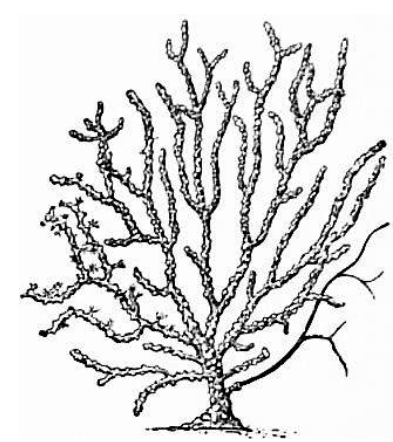
- Consider providing investigators examples of creative use of visual materials to supplement the informed consent processes.
- As appropriate, consider linguistic status as a vulnerable subject population category.
- Promote use of the CITI site by international collaborators, which has human subjects training in several languages
- Examine oversight and training for international studies with students on the research team.

Human Research studies conducted abroad must be carefully justified, reviewed, and approved -- often with additional protections added.

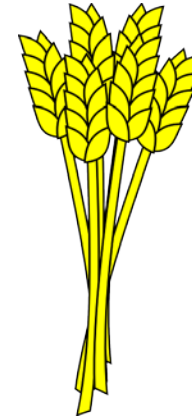
# For information about some informed consent requirements for research conducted abroad:







# Genetic Resources/Traditional Knowledge



“Utilization of genetic resources” = to conduct research and development on the genetic and/or biochemical composition of genetic resources, as well as subsequent applications and commercialization

# Changing Landscape Affects Researchers

International agreements and individual countries' implementation = different laws/rules in different countries

Nagoya Protocol on Access to Genetic Resources and Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity effective 12 October 2014  
<https://www.cbd.int/abs>

- Access and Benefit-sharing (ABS) Clearing-House provides some information on national procedures for ABS
- National focal point in countries can assist with process
- Laws/rules still in flux

US is not party to Nagoya Protocol, but country laws still affect international research and ability to turn discoveries into future useful products (e.g. patent disclosure requirements)

Education of researchers prior to bioprospecting and international collaboration is critical to ensuring compliance

# 1. Documentation of Source/Origin

Laboratory notebook documentation

- Origin of material (e.g. country, location, indigenous community)
- Source (trace back to origin as much as possible)
- Permissions documents

Researchers should ask international collaborators for documentation of source/origin of (and permissions for) genetic resources used in research

May be required under patent disclosure requirements under patent laws of certain countries

National focal point or ABS Clearing-House may provide information or procedures to assist with compliance

## 2. Prior Informed Consent

Obtain informed consent *prior* to collection or utilization

Identify who has the authority to provide informed consent; ideally from authority who provides access to the genetic resource

- National focal point
- Indigenous cultural practices may need separate consent

Obtain informed consent in writing for research and educational purposes, as well as potential future commercialization; can be coupled with Access and Benefit Sharing Agreement

Recommendation: more is better than less

# 3. Access and Benefit Sharing (ABS) Agreements

Main focus of Nagoya Protocol

Work with the proper local authorities in the country to negotiate ABS agreement

- National focal point
- Indigenous cultural practices
- ABS Clearing-House

Benefits arising from utilization of genetic resources, including subsequent applications/commercialization, shall be shared in fair/equitable way with provider of resource that is country of origin or party that acquired genetic resource in accordance with CBD.

- Benefits may include monetary and non-monetary benefits
- Mutually agreed terms

# Some Tips for Researchers:

- If you plan to conduct research overseas, contact campus administrators *as early as possible*. Laws may need to be researched, agreements negotiated, permissions obtained, protection secured, and/or projects examined. Notify administrators if you expect to collect or conduct research on genetic resources or the scope of projects start to overlap.
- Consider collaborating with a local researcher who likely will know the local rules. Country laws usually apply to what occurs in that country regardless of the venue or governing law written in the agreement.
- Carefully consider requirements associated with bioprospecting or collecting genetic resources from another country. Keep clear and comprehensive documentation in laboratory notebooks of country of origin, source, permissions, and other relevant information.
- Obtain any necessary permissions in advance and in writing.
- When conducting research overseas, avoid signing any documents regarding IP, genetic resources, or ABS without advance review and approval from campus authorities.

# Some Tips for Administrators:

- If genetic resources are obtained in field studies or through a material transfer agreement, collect and maintain proper documentation as it may be needed in filing of patent applications years later.
- Start investigation as early as possible as laws may need to be researched, agreements negotiated, permissions obtained, protection secured, and/or projects examined. Consult with authorized licensing office (ALO) if patent or royalty-sharing requirements are involved.
- Be aware that the country laws (and/or Nagoya Protocol provisions) apply in the country where research occurs, even if you or your researchers do not know the relevant laws. Also country laws may differ, e.g. if filing for patent protection in the European Patent Office, individual member states may have different rules.
- Carefully review ABS agreements for other restrictions re: publication, use, or sharing with others. If a prospective licensee or company collaborator is involved in the research, bring it into the conversation about ABS.
- Educate, educate, educate researchers long before they consider international research.

# Some Resources

## Nagoya Protocol

- <https://www.cbd.int/abs/about/default.shtml>

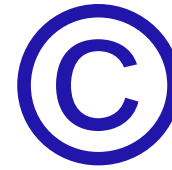
## ABS Clearing-House

- <https://www.cbd.int/abs/theabsch.shtml>

## Biotechnology Industry Organization (BIO) information, Bioprospecting Guidelines, and industry model MTA

- <http://www.bio.org/category/biodiversity-bioprospecting>
- [http://www.bio.org/sites/default/files/BIO\\_Model\\_MTA\\_0.pdf](http://www.bio.org/sites/default/files/BIO_Model_MTA_0.pdf) (can extract any appropriate or relevant provisions for use in UC MTA)





# Intellectual Property (IP) Issues

**Research  
Data**



# Types of Intellectual Property

## Patents

- Useful processes, machines, manufactured items or compositions of matter (utility patents)
- Generally plant breeders' rights (US plant patents/plant variety protection)
- Ornamental designs for articles of manufacture (design patents)

## Copyrights

- Original works fixed in a tangible medium of expression including scholarly works, images, sound recordings, and software

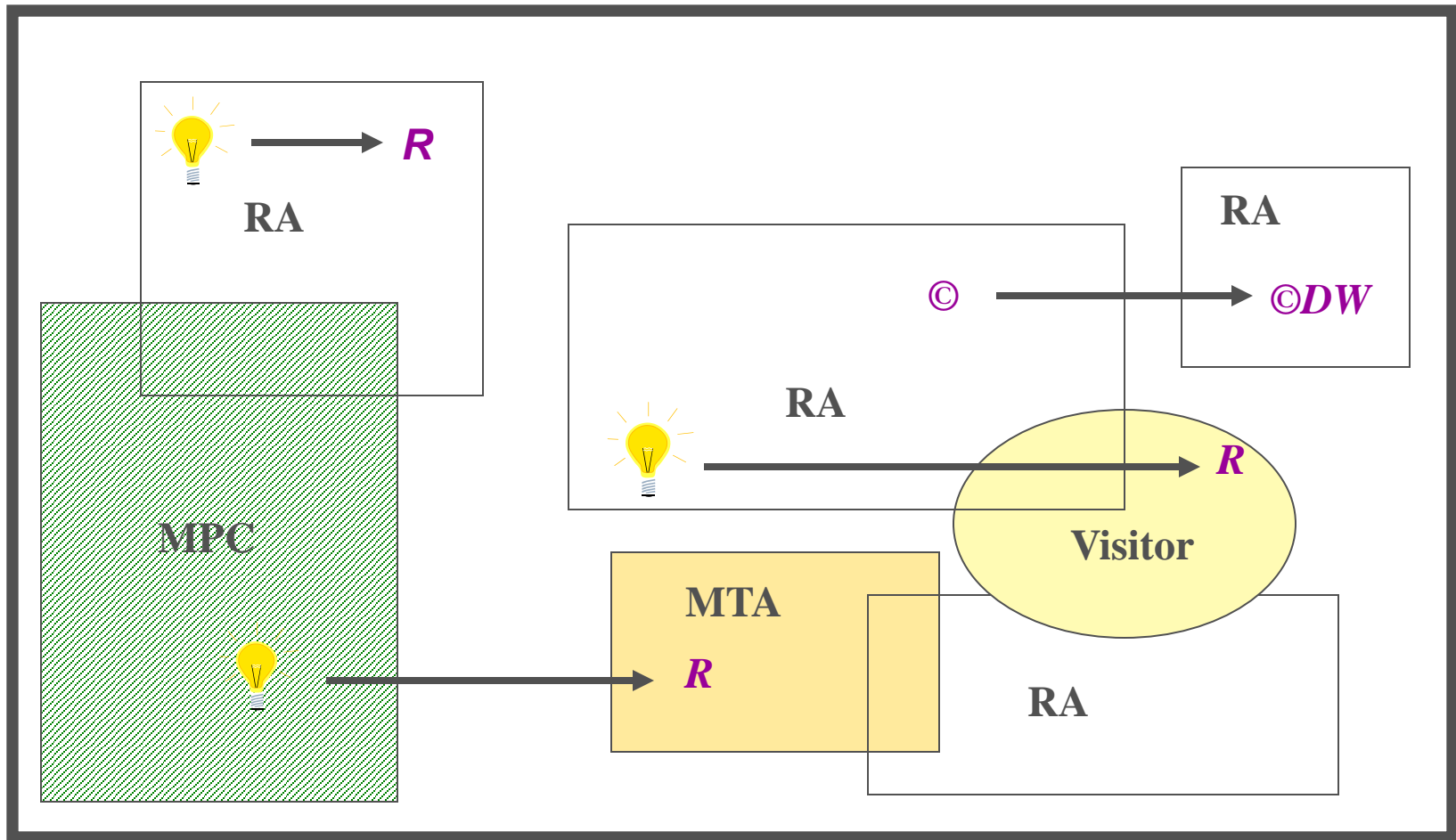
## Trademarks


- Words, names, symbols, sounds that identify the source of, and distinguish, goods or services

## Trade Secrets

- Advantageous "secret" formulas, processes, products, business information

# Research Program-IP Portfolio



-  CONCEPTION
- R** REDUCTION TO PRACTICE
- © COPYRIGHTABLE WORK
- ©DW DERIVATIVE WORK
- RA RESEARCH AGREEMENT
- MTA MATERIAL TRANSFER AGREEMENT
- MPC MULTI-PARTY COLLABORATION



# Some Main Issues to Consider

## Evaluate scope of research/scope of rights

- Review existing research projects/agreements for overlap in scope, including material transfer agreements
- Avoid incorporating existing intellectual property
- Consider appropriate handling of future research results

## Identify potential conflicting legal obligations

- Where overlap in scope with other projects/agreements, check for obligations

## Raise awareness among researchers

- Discuss in advance rights, responsibilities and existing obligations under projects

## Carefully consider differences in IP rights among different countries

## Limit any impact to individual researcher and specific project

# Patents, Patent Applications and Inventions

## UC Patent Policy/Patent Acknowledgment:

- Disclosure of inventions to UC authorized licensing office (ALO)
- UC ownership of inventions made by UC employees within course and scope of employment, during use of UC research facilities, or through use of UC gift, grant or contract research funds, even if working overseas
- Researchers should have signed 2011 Patent Amendment (hired before 11/1/11) or 2011 Patent Acknowledgment (hired 11/1/11 or later)

## Host entities in other countries may want certain rights

- Rights to use or license background IP or future research results
- Sole or joint ownership of future research results

## Different laws in different countries

- Example: Laws in other countries may override your contract terms
- Joint ownership complications: need to clarify assignment, use by owner, licensing, accounting to co-owners

# Copyrights

## UC Ownership of Copyrights Policy

- Scholarly works by designated academic personnel generally owned by such personnel, though there are key exceptions
- Sponsored works generally owned by UC

## Different laws in different countries

- Example: Jointly authored scholarly works – may need permission from co-owners to give rights to others

# Research Results – Data

Data = building blocks for intellectual property (although not necessarily protected under IP laws)

- Use in filing patent applications
- Forms essence of scholarly works
- Backbone for future research endeavors and conclusions

Be aware of restrictions on use of personal health data (laws in other countries may be more stringent)

Different laws in different countries

- Example: May need permission to use jointly owned data if contract is silent on how data can be used
- Ensure UC still owns our own data that we contribute to a larger data set.

# Trademarks and Trade Secrets

Few isolated situations where trademarks would be involved, especially in research

UC generally does not engage in trade secrets, but may receive such under confidentiality agreement

- Review of any confidentiality agreements by campus authorities
- Use standard confidentiality clause with the usual “outs”
- Better to accept only what one actually *needs* for research
- Best to maintain option to decline accepting confidential information that is not needed for research



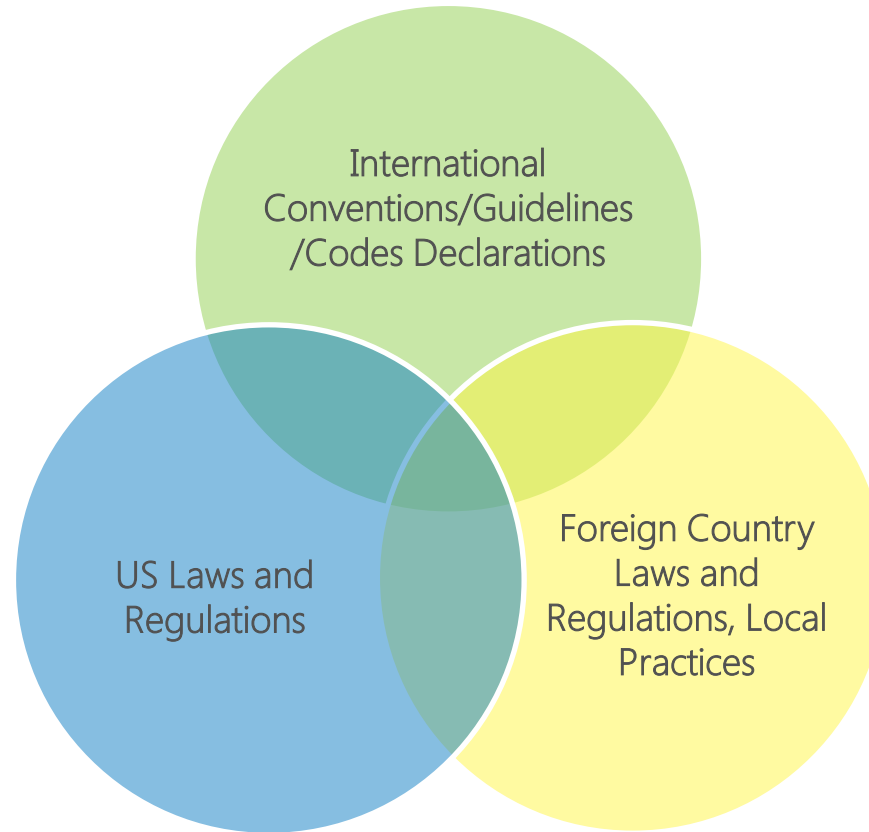
# Some Tips for Researchers:

- When conducting research overseas, avoid signing any documents regarding IP without advance review and approval from the ALO and/or contracts and grants office (C&G office).
- If you plan to conduct research overseas, contact campus administrators *as early as possible*. Agreements may need to be negotiated, permissions or protection may need to be secured, and projects may need to be examined. Notify administrators if projects start to overlap in scope.
- Carefully consider implications of bringing existing materials/data/IP into another country, particularly if acquired from a third party. Avoid using existing IP in international research w/o contacting ALO. May need permission if bringing other UC IP.
- Country laws usually apply to what occurs in that country regardless of the venue or governing law written in the agreement. Consider collaborating with local researchers who likely will be familiar with local requirements.

# Some Tips for Administrators:

- In a collaboration, clarify in an agreement the specific scope of project, who is contributing what, who owns what, and what rights and uses are permitted, e.g. if UC-owned data will be incorporated into a dataset in EU, clarify UC does not lose ownership.
- Check for potential conflicting obligations; as one looks at a research project, remember to consider the full research program.
- Be aware that if other laws take precedence, the laws of that country govern, even if you or your researchers (or UC attorneys!) do not know the country's laws.
- Know who campus experts are. For IP issues, consult with ALO.
- Ensure researcher has signed Patent Amendment or 11/2011 Patent Acknowledgment.
- In relevant contracts, try to specify application of US laws and/or California as the venue for disputes. But even if governing law or venue is foreign, maintain usual UC defenses under CA law.
- Carefully consider how to balance valuable research collaborations with protection of IP and typical academic rights and expectations.

# International Research Occurs at the Intersection of Various Laws, Rules, International Conventions, etc.



# Questions?

# Survey

# Thank You!

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