BUILDING AN INFRASTRUCTURE FOR RESEARCH

LOMA LINDA UNIVERSITY
HEALTH
RESEARCH AFFAIRS

Human Subject Research Considerations

Amy L. Casey, MBA – Director, Human Research & Compliance

Human Subjects Research Considerations

Identify regulations for your specific country

- International Compilation of Human Research Standards
  - Features listing of over 1,000 laws, regulations and guidelines on human subject protections in 140 countries

https://www.hhs.gov/ohrp/sites/default/files/2018-International-Compilation-of-Human-Research-Standards.pdf

Country	Key Organizations	Legislation	Regulations	Guidelines
India For an overview of the clinical research regulations in India, see the ClinRegs report: http://clinregs.niaid.nih.gov/single_country.php?c_id=100				
General	Indian Council of Medical Research (ICMR): http://www.icmr.nic.in/human_ethics.htm			1. National Ethical Guidelines For Biomedical and Health Research Involving Human Participants (2017): http://icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf 2. National Ethical Guidelines for Biomedical Research Involving Children (2017): http://icmr.nic.in/guidelines/National_Ethical_Guidelines_for_BioMedical_Research_Involving_Children.pdf
Drugs, Biologics, and Devices	*Drugs*			
	1. Central Drugs Standard Control Organization, Office of Drugs Controller General of India (DCGI): http://cdsco.nic.in 2. Indian Council of Medical Research (ICMR): http://www.icmr.nic.in/human_ethics.htm	Schedule Y of the Drugs and Cosmetics Act (2005): http://www.cdsco.nic.in/writereaddata/Drugs&CosmeticAct.pdf	DCGI: 1. Good Clinical Practices for Clinical Research in India (2001): http://rgcb.res.in/wp-content/uploads/2014/07/Good-Clinical-Practice-Guideline.pdf 2. Permission for Clinical Trials: General Statutory Rules 63(E) 3. Ethics Committee Registration: General Statutory Rules 72(E) 4. A/V Consent – General Statutory Rules 611 (E) (2015) 5. Phytopharmaceutical Drug: General Statutory Rules 918(E) 6. Exemption for Academic Research and Animal Toxicity: General Statutory Rules 313(E) (2016)	ICMR: National Ethical Guidelines For Biomedical and Health Research Involving Human Participants, Section 7 (2017): http://icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf
	Devices			
	1. Central Drugs Standard Control Organization, Office of Drugs Controller General of India (DCGI): http://cdsco.nic.in 2. Indian Council of Medical Research (ICMR): http://www.icmr.nic.in/human_ethics.htm	Drugs & Cosmetics Act, 1940 (2005): http://www.cdsco.nic.in/writereaddata/Drugs&CosmeticAct.pdf	1. Rules: Schedule D & K (2014): http://www.cdsco.nic.in/writereaddata/GSR%20690(E),%2025th%20Sep.%202014.pdf 2. Rules: Schedule MIII (2016): http://www.cdsco.nic.in/writereaddata/GSR%20640%20(E)%20dated%2029_06_2016%20-%20Copy.pdf	ICMR: National Ethical Guidelines For Biomedical and Health Research Involving Human Participants, Section 7.7 (2017): http://icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf
Clinical Trials Registry	Clinical Trials Registry – India: http://ctri.nic.in/			Clinical Trials Registry – India: FAQs: http://ctri.nic.in/Clinicaltrials/faq.php Office of Drugs Controller General:

Country	Key Organizations	Legislation	Regulations	Guidelines
United Arab Emirates				
General	Health Authority - Abu Dhabi: http://www.haad.ae/haad/			Standard Operating Procedures for Research Ethics Committees (2012): http://www.haad.ae/HAAD/LinkClick.aspx?fileticket=UL7o8f5mukc%3D&tabid=820

Human Subjects Research Considerations

Local Oversight

- Institutional Review Board
- Research Ethics Committee
- Ministry of Health

Human Subjects Research Considerations

Assess resources

- Infrastructure
  - Social/Behavioral Studies
  - Clinical Research
    - Ancillary support (pharmacy, clinical lab, nursing)
- Faculty and/or Physicians as potential investigators
  - Research background
  - Interest
  - Support staff

Human Subjects Research Considerations

Know your population

- Language
  - Multiple languages represented in the community?
- Literacy
- Numbers
  - Number of patients with a specific disease
  - Estimate only 2-8% of patients will ultimately be eligible and consent to participate

Human Subjects Research Considerations

Policies and Procedures

- Policies are traditionally driven by regulations
  - Document retention
  - Data Management
  - Privacy

Human Subjects Research Considerations

Sample of Policy and Procedure Categories

General Administration	Protocol Management	Human Subject Management	Data Management	Quality Management
Policy Management	Study Initiation	Screening and Recruitment	Data Collection	Internal Audits
Job Descriptions	Ethics Submissions & Communications	Entering Subjects to Study	Data Submission	External Audits
Orientation and Education	Sponsor Communications	Monitoring Study Subjects	Data Maintenance	Study Misconduct
Budgets	Regulatory Documents	Follow up of Study Subjects		Notification of Subjects
Contracts	Subject Records Management	Communication with Subjects		Conflict of Interest
	Drug/Device Accountability	Special Procedures		
	Site Closure			**-SOCRA website**

Human Subjects Research Considerations

Questions?

Animal Use In Biomedical Research

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Obed B. Rutebuka, PhD, MSPH, CPIA
Director, Research Safety & Animal Welfare

Animal Welfare Act (AWA)

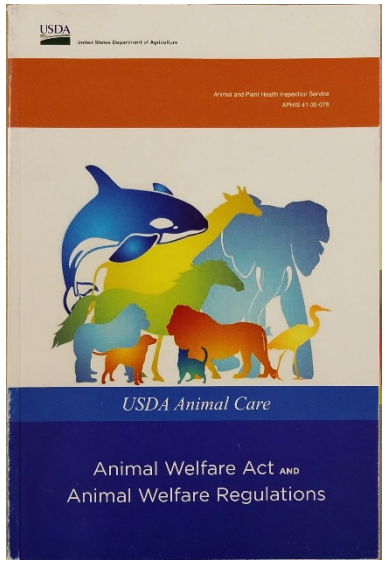
In United States of America, the use of animals in research is governed by laws and regulations on federal level:

- Animal Welfare Act enacted in 1966.
  - Regulates warm-blooded animals except mice and rats bred for research
  - Administered by United Department of Agriculture (Ministry of Agriculture)

Animal Welfare Act (AWA)

- Health Research Extension Act of 1985
  - Vertebrate animals funded by Public Health Service (PHS) under Department of Health and Human Services (National Institutes of Health, etc.)

Animal Welfare Act (AWA)

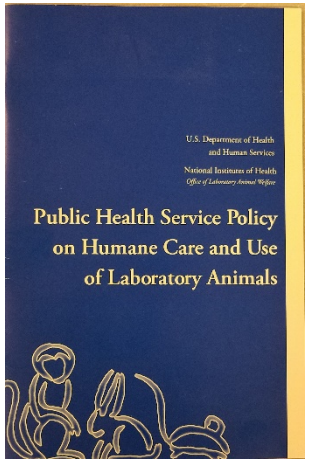


Humane treatment of animals used in research

- Bred for commercial sale
- Exhibited to the public
- Commercially transported
- Licensed or registered

Public Health Service Policies

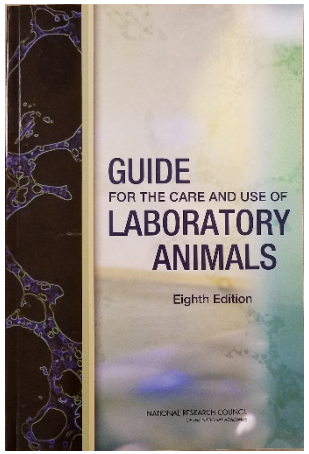
Public Health Service Policy on Humane Care and Use of Laboratory Animals
http://grants1.nih.gov/grants/olaw/references/phspol.htm



Endorses US Government Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research, and Training PHS-conducted or supported activities involving animals. It does not affect applicable state or local laws, refers to AWA and requires institutions to use the "Guide"

Public Health Service Policies

Guide for the Care and Use of Laboratory Animals
http://www.nap.edu/catalog.php?record_id=12910



Minimum standards

- Basis for developing and implementing program for animal activities
- Adopted by AAALAC International

Animal Use In Biomedical Research

- In addition to those federal agencies there is an accrediting agency for institutional animal care and use programs called AAALAC international. Initially incorporated as an American organization in 1965, it is now accrediting institutional programs worldwide (more than 45 countries).

- Both Office of Laboratory Animal Welfare (NIH- PHS Policy on Humane Care and Use of Laboratory Animals) and AAALAC International have adopted the Guide for the Care and Use Laboratory animals as a basis for minimum standards for humane care and use of Laboratory Animals.

Animal Use In Biomedical Research

- Both federal agencies (USDA, NIH) require that each institutional puts in place an oversight committee known in USA as Institutional Animal Care and Use Committee (IACUC) elsewhere as Oversight Board (OB).
- The most prominent function of IACUC is to approve and authorize the animal use when the request meets the laws and regulations mentioned above.
- Researchers are ethically bound to follow approved procedures in order to comply with laws, regulations and institutional policies.

Animal Use In Biomedical Research

- Considering the use of animals in an (your) institutional few questions must be answered first and foremost – Regulations, if any, regarding animal use in your country. Those regulations may include:
  - Facility –conditions regarding a location where animals can be cared for and used.
  - Researchers (investigators) – who is capable and willing to use animals in research.
  - Oversight Bodies (a committee to review and approve procedures to be conducted so that animals do not suffer unnecessarily)

Animal Use In Biomedical Research

Questions?

Creating a Compliance Program

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Jerri McIlhagga, MS, CHRC – Research Compliance Analyst, Human Research & Compliance

The Seven Elements of an Effective Compliance Program

- Standards and Procedures
  - Implement written policies, procedures and standards of conduct
- Oversight
  - Designate a compliance officer and committee
- Training and Education
  - Provide regular and relevant training and education
- Reporting
  - Develop open line of communication for reporting of complaints/incidents; protect anonymity; prevent retaliation
- Enforcement and Discipline
  - Enforce standards through well-publicized and utilized guidelines
- Auditing and Monitoring
  - Conduct internal audits and monitoring on a regular basis
- Investigation and Remediation
  - Respond promptly to reported and discovered non-compliance and require appropriate corrective action plans as needed

~Office of the Inspector General; see Federal Register, v63, n35 (1998)

The Cost of Non-Compliance

- Potentially massive fines and penalties
- Possible repayment of funds
- Bad publicity / Damaged reputation
- Lawsuits
- Operational restrictions
- Increased regulatory scrutiny
- Probation
- Criminal prosecution

The Three Purposes of a Compliance Program

- ❑Prevention
- ❑Detection
- ❑Correction

- **Prevention**
  - Written policies / code of conduct
  - Oversight /Compliance Official
  - Training / Education
- **Detection**
  - Confidential Reporting Hotline
  - Monitoring/Auditing/Internal Reporting
  - Protection through Non-Retaliation Policy
- **Correction**
  - Investigations / Remediation
  - Disciplinary Policies

Risk Assessment

An effective compliance program seeks to assess institutional compliance with the complex regulations that govern it. Some of these regulating entities are:

- Department of Health and Human Service (DHHS)
- Office of the Inspector General (OIG)
- Office of Human Research Protections (OHRP)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
- Centers for Medicare and Medicaid Services (CMS)
- Office for Civil Rights (OCR)
- Office of Research Integrity (ORI)
- Select Agents – Centers for Disease Control (CDC)
- Export Controls
  - Department of Commerce
  - Department of State
  - Department of Treasury, Office of Foreign Asset Controls (OFAS)
- International Students and Scholars – Department of Homeland Security (CIS, CBP, ICE)
- Accrediting Agencies (AAHRPP, AALAAC)

Risk Assessment Continued

Risk Assessment Steps

- Become Informed
  - What have other institutions received penalties for?
  - What types of settlements have been made?
- Determine Government Focus
  - OIG and other regulatory entities release their work plan/focus annually
- Identify and Prioritize Significant Institutional Risks
  - Choose among competing priorities
    - Human Subject Research Protection
    - Financial Conflicts of Interest
    - Animal Care and Welfare
    - Radiation Safety
    - International Student/Scholar Visa Compliance
    - Environmental Regulatory Compliance
- Develop a Work Plan
  - Prevent, manage, reduce, or eliminate risk
- Reassess Risk Annually and as Regulations Change

National Regulatory Authorities

- Argentina: National Administration of Drugs, Food and Medical Technology (ANMAT) https://www.argentina.gob.ar/anmat
- Mexico: Federal Commission for Protection against Sanitary Risks of the United Mexican States (COFEPRIS) https://www.gob.mx/cofepris
- Nigeria: National Agency for Food and Drug Administration and Control (NAFDAC) http:www.nafdac.gov.ng
- Peru: General Board of Medicines, Supplies, and Drugs (DIGEMID) http://www.digemid.minsa.gob.pe/
- United States: Food and Drug Administration (FDA) https://www.fda.gov/default.htm

Create a Culture of Compliance

"A culture of compliance is an environment that recognizes and acknowledges throughout its ranks that addressing compliance is a natural and integral part of research, such as setting up a study, collecting and analyzing data, or the disseminating of results through publications or presentations."

~Mark J. Rudin, PhD.

Compliance should be *informative*, rather than *punitive*.

- Set clear expectations and communicate these frequently
  - Involve stakeholders (administrators, faculty, students, etc.) in strategic planning
    - Promotes good will; encourages buy-in; develops vision
- Provide the highest quality customer service
  - Offer timely, comprehensive support and tools
    - Without this, research staff may bypass policies/procedures
- Empower staff
  - Resources for professional development
- Engage faculty
  - Recruit to serve on IRB, IBC, IACUC, etc.
- Provide education and mentoring at all levels
  - Formal and informal
- Address compliance problems appropriately
  - Consistency; timeliness; due process; follow established policies and procedures
- Promote compliance in the context of economic development
  - Necessary for developing research partnerships, entrepreneurship, infrastructure, instrumentation, expertise
  - Intellectual property, technology transfer, federal funding, sponsor requirements, institution interests must be protected
- Implement a continuous improvement process
  - Collect data by qualitative and quantitative methods
  - Determine if corrective actions plans (CAPs) needed
  - Evaluate success of CAPs and adapt as appropriate

Pre and Post Award

LOMA LINDA UNIVERSITY
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Aleta Savage, MBA, CRA - Executive Director

Pre & Post Award

- Staff of 9 with 80+ years combined experience in research administration
- Responsible for proposal submission and award administration
- Submit 200 proposals annually
- Manage 450+ awards
- Ensure we're following government regulations, sponsor and institutional policies…

✓ **We can continue the institution's mission through research and sponsored funding**

✓ **No one goes to jail**

Grant Life Cycle

Pre Award Functions…

- Institutional registrations
- Opportunity Scouting
- Proposal Development and Submission
- Post-submission Sponsor Inquiries

Opportunity Scouting

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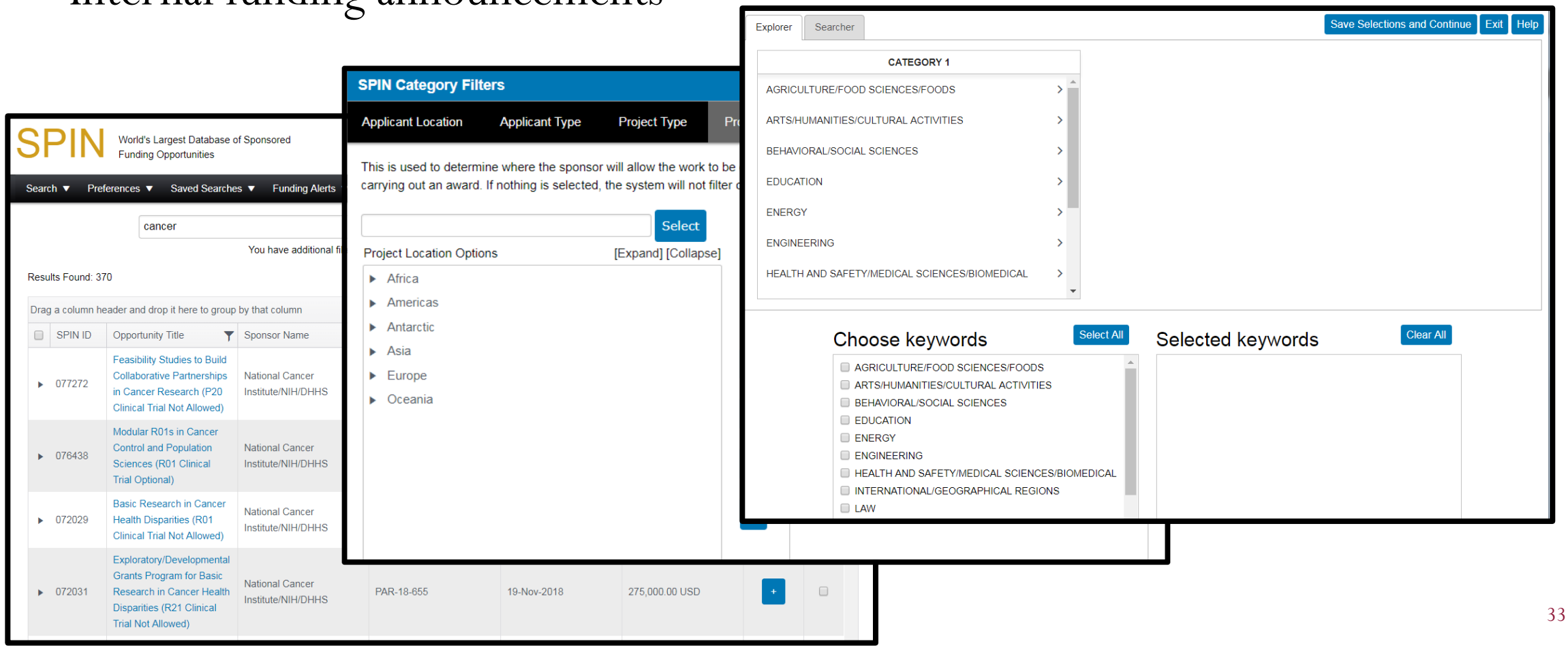
- Sponsored Programs Information Network (SPIN)
- Agency announcements
- Internal funding announcements



Proposal Development

- Provide technical assistance on policies, procedures, laws and guidelines
- Build application InfoEd for S2S submissions and provide assistance with entering information and uploading documents
- Provide budget templates and current rates for salaries,

fringe rates, F&A (overhead), etc.

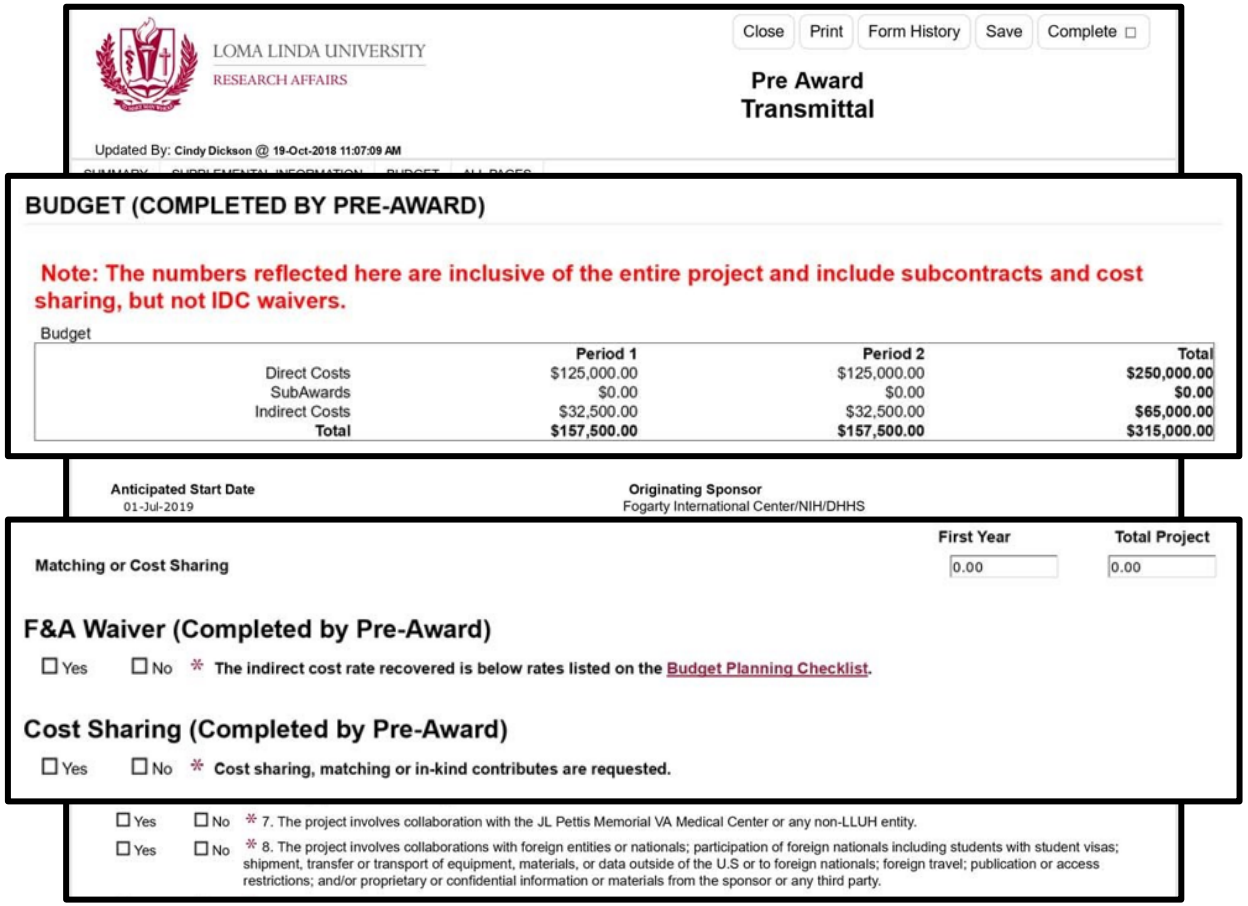
- Approve draft budget and justification
- Assist with responding to sponsor requests for

additional information: JIT Information, revised budgets, etc.

- Coming soon…grant writing, scientific editing

Proposal Submission

- Review for compliance with organizational policies and sponsor guidelines
- Finalize proposal and route for institutional approvals
- Ensure proposal is approved by stakeholders and cleared for submission
- Final review completed by Authorized Official (AO) for the organization
- AO submits the proposal on behalf of the organization



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Pre Award Transmittal

Updated By: Cindy Dickson @ 19-Oct-2018 11:07:09 AM

BUDGET (COMPLETED BY PRE-AWARD)

Note: The numbers reflected here are inclusive of the entire project and include subcontracts and cost sharing, but not IDC waivers.

Budget

	Period 1	Period 2	Total
Direct Costs	$125,000.00	$125,000.00	**$250,000.00**
SubAwards	$0.00	$0.00	**$0.00**
Indirect Costs	$32,500.00	$32,500.00	**$65,000.00**
Total	**$157,500.00**	**$157,500.00**	**$315,000.00**

Anticipated Start Date
01-Jul-2019

Originating Sponsor
Fogarty International Center/NIH/DHHS

	First Year	Total Project
Matching or Cost Sharing	0.00	0.00

F&A Waiver (Completed by Pre-Award)

☐ Yes ☐ No * **The indirect cost rate recovered is below rates listed on the Budget Planning Checklist.**

Cost Sharing (Completed by Pre-Award)

☐ Yes ☐ No * **Cost sharing, matching or in-kind contributes are requested.**

☐ Yes ☐ No * 7. The project involves collaboration with the JL Pettis Memorial VA Medical Center or any non-LLUH entity.

☐ Yes ☐ No * 8. The project involves collaborations with foreign entities or nationals; participation of foreign nationals including students with student visas; shipment, transfer or transport of equipment, materials, or data outside of the U.S or to foreign nationals; foreign travel; publication or access restrictions; and/or proprietary or confidential information or materials from the sponsor or any third party.

…all before the submission deadline

Proposals filed…

Fiscal Year	Amount requested	Applications submitted	Average amount per request
FY 2014	$94,043,114	175	$537,389
FY 2015	$137,701,431	171	$805,272
FY 2016	$146,008,957	182	$802,247
FY 2017	$171,885,868	202	$850,920
FY 2018	**$175,603,901**	**199**	**$882,432**
FY 2019 (through September)	$25,451,302	30	$848,377

Agencies applied to…

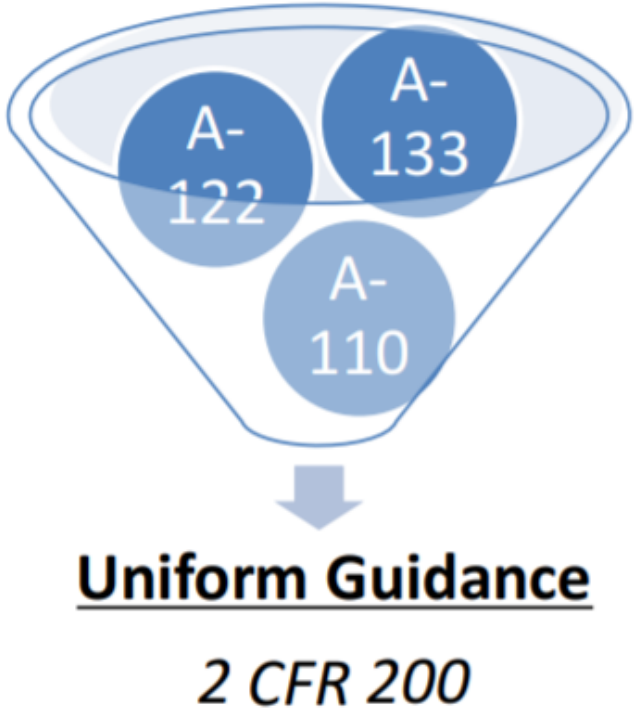
Sponsor	Amount requested FY2018
National Institutes of Health/DHHS	$97,124,255
National Aeronautics & Space Administration	$11,051,775
Office of Statewide Health Planning and Development/State of CA	$7,301,215
Chan Zuckerberg Initiative	$4,854,913
Health Resources and Services Administration/DHHS	$3,018,221
Tobacco-Related Disease Research Program	$1,779,835
Inland Empire Health Plan	$1,614,600
Department of the Army	$1,270,068

Post Award Functions…

- Administration and Oversight
- Financial Management
- Reporting
- Audits

Administration and Oversight

- Post Award compliance with Sponsor regulations/terms & conditions:
  - Effort reporting
  - Cost Sharing
  - Prior approval requirements
  - Program income
  - Fingerprinting/background checks
  - Suspension and debarment
  - Suprecipient monitoring
  - Procurement regulations/COI
  - Equipment management
  - Key personnel
  - Period of performance
  - No-cost extension
  - Record retention



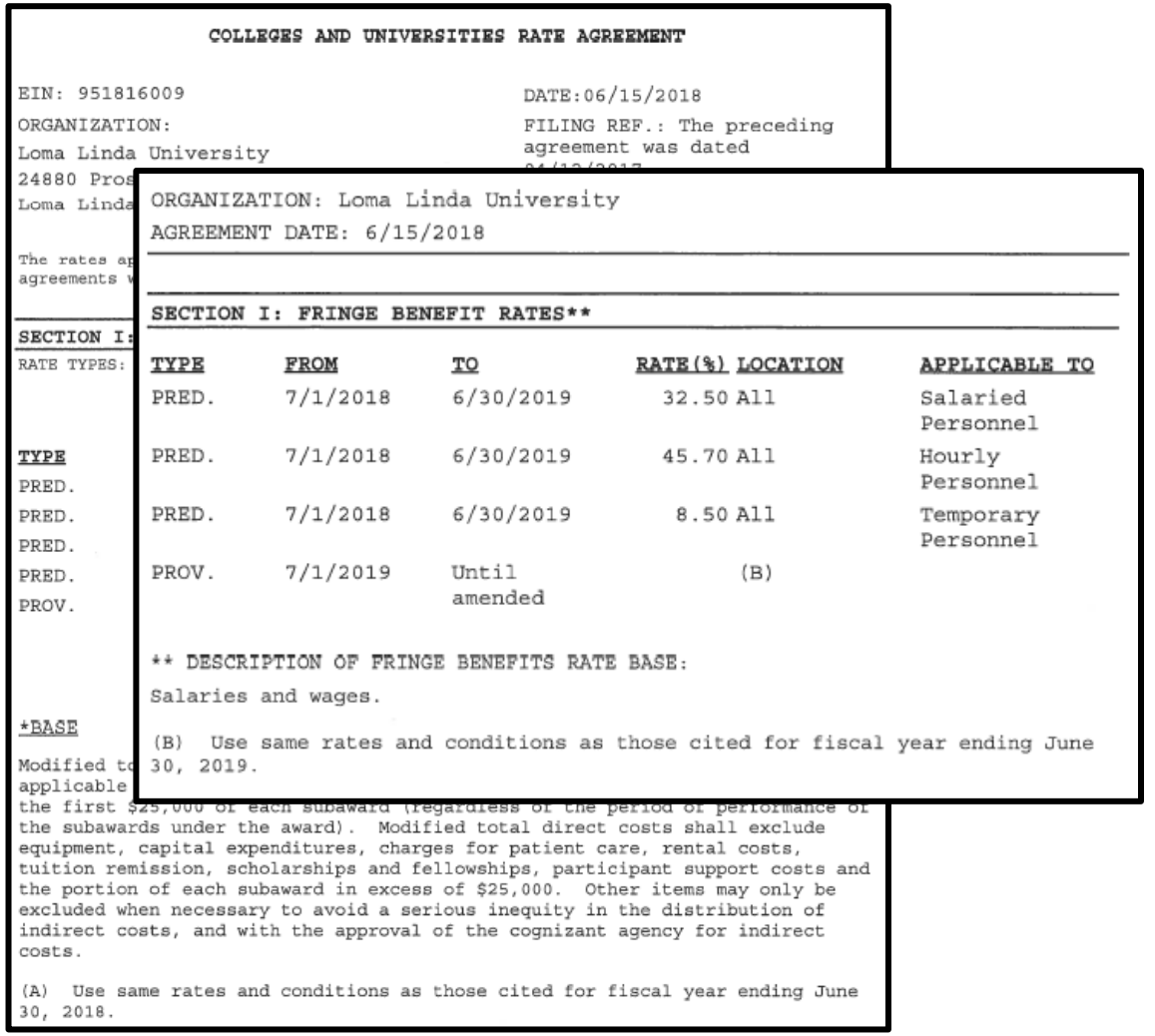
Every sponsor has unique terms and conditions

Financial Management

- FY2018 – 504 awards

$21M of expenditures

- Financial Management:
  - Cost allowability
  - F&A/fringe rates
  - Authorized transactions
  - Invoicing and accounts receivable
  - Cash management
  - 90-day transfers
  - Burn rates
  - Period of performance
  - Budget changes



COLLEGES AND UNIVERSITIES RATE AGREEMENT

EIN: 951816009
DATE:06/15/2018
ORGANIZATION:
Loma Linda University
FILING REF.: The preceding agreement was dated

ORGANIZATION: Loma Linda University
AGREEMENT DATE: 6/15/2018

SECTION I: FRINGE BENEFIT RATES**

TYPE	FROM	TO	RATE(%)	LOCATION	APPLICABLE TO
PRED.	7/1/2018	6/30/2019	32.50	All	Salaried Personnel
PRED.	7/1/2018	6/30/2019	45.70	All	Hourly Personnel
PRED.	7/1/2018	6/30/2019	8.50	All	Temporary Personnel
PROV.	7/1/2019	Until amended		(B)	

** DESCRIPTION OF FRINGE BENEFITS RATE BASE:

Salaries and wages.

(B) Use same rates and conditions as those cited for fiscal year ending June 30, 2019.

SECTION I:
RATE TYPES:

TYPE
PRED.
PRED.
PRED.
PRED.
PROV.

*BASE

Modified to
applicable
the first $25,000 of each subaward (regardless of the period of performance of the subawards under the award). Modified total direct costs shall exclude equipment, capital expenditures, charges for patient care, rental costs, tuition remission, scholarships and fellowships, participant support costs and the portion of each subaward in excess of $25,000. Other items may only be excluded when necessary to avoid a serious inequity in the distribution of indirect costs, and with the approval of the cognizant agency for indirect costs.

(A) Use same rates and conditions as those cited for fiscal year ending June 30, 2018.

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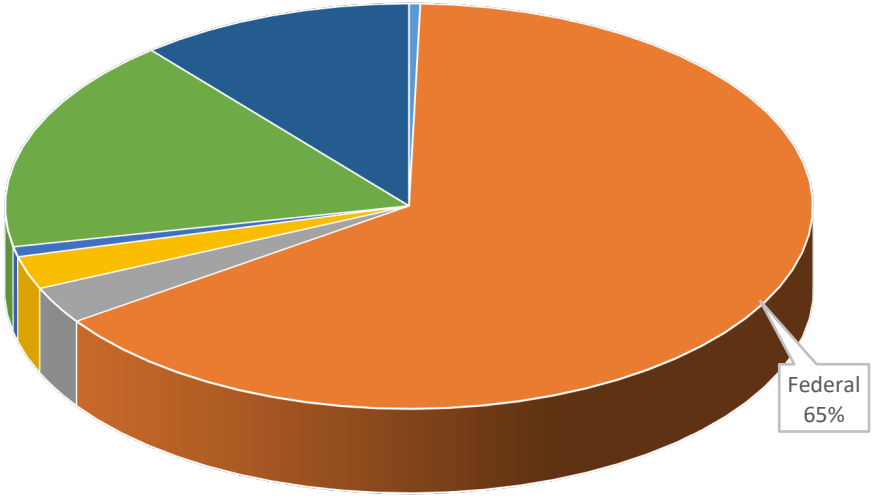
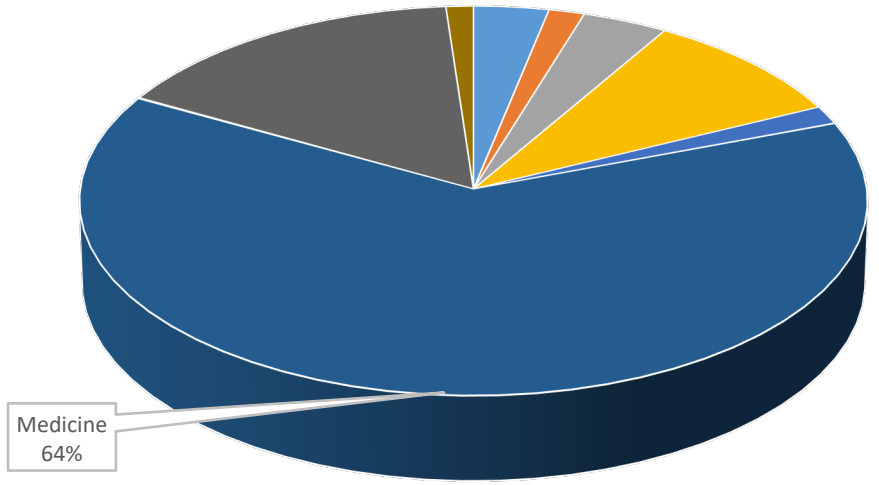
Funding sources

FY2018 - Total amount awarded - source type



- County
- Federal
- Federal Flow-through
- Foundation
- Industry
- Non-Profit
- State

FY2018 - Total amount awarded - entity receiving



- Behavioral Health
- Cancer Center
- Dentistry
- Institute for Community Partnerships
- LLUCH
- LLUMC
- Medicine
- Nursing
- Public Health
- San Manuel Gateway College

Reporting

- Submit progress and financial reports to sponsors
- Prepare quarterly cash reports to Federal agencies
- Other metrics and reports per sponsor requirements

Audits

- $750K+ expenditures – must have annual Federal audit
- Subject to IG audits, sponsor audits, site visits

Strategy & Measurements

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Michael R. Samardzija, PhD, JD
Vice President for Research Affairs

Strategy

Inventory

- Expertise
- Interest
- Resources
- Potential collaborators
- Funding opportunities

Align with mission

Forming Research Teams

Health Disparities/Global Health

Cancer

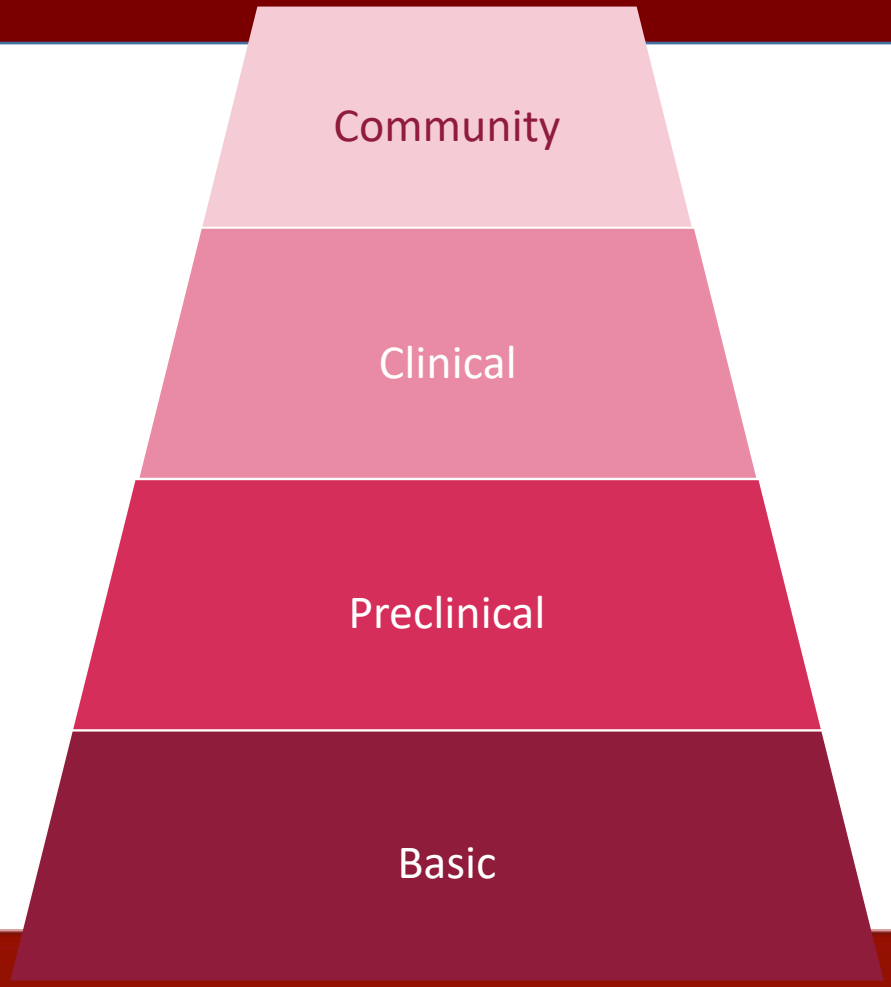
Neuroscience

Mental Health

Obesity/Diet

Prenatal/Perinatal/Neonatal

Aging Population



Measurements

Capacity – FTEs involved in research
Activity – income, publications, graduate students, post-docs
Intensity – activity/capacity
Efficiency – activities/expenditures
Quality – field-weighted citation index

BUILDING AN INFRASTRUCTURE FOR RESEARCH

Contact:
researchalliances@llu.edu