BASICS OF RESEARCH COMPLIANCE: RESEARCH INTELLECTUAL PROPERTY, FEDERAL GRANTS ADMINISTRATION, AND RESEARCH MISCONDUCT

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RESEARCH INTELLECTUAL PROPERTY

I. Legal Framework
  A. Bayh-Dole Act (P.L. 96-517, Patent and Trademark Act Amendments of 1980, as amended by P.L. 106-404, Technology Transfer Commercialization Act of 2000; codified at 35 USC 200-212)
    1. Principal objectives
      a. Stimulate the commercialization of federally-funded inventions by ensuring the transfer of federally-funded technology to the private sector
      b. Promote free competition and enterprise without unduly encumbering future research and discovery
    2. Grants first rights in an invention fully or partially funded by the federal government to the funding recipient
    3. When the funding recipient retains rights to an invention ("elects title"), the federal government retains a nonexclusive, nontransferable, irrevocable, paid-up license to practice (or have practiced) the invention world-wide
    4. Mandates reporting requirements to protect the rights of the federal government
  B. Rights to Inventions Made by Nonprofit Organizations and Small Business Firms Under Government Grants, Contracts, and Cooperative Agreements (37 CFR Part 401)
    1. Bayh-Dole Act implementing regulations
    2. Applies to all funding agreements between the federal government and nonprofit higher education institutions for experimental, developmental or research work
    3. Also applies to subcontracts under the funding agreement
  C. National Institutes of Health requirements (NIH Grants Policy Statement, "NIH Sharing Policies and Related Guidance on NIH-Funded Research Resources," (http://grants.nih.gov/grants/sharing.htm)
    1. General policy: Results and accomplishments of NIH funded activities should be made available to the public; researchers and grantee organizations are expected to make the results and accomplishments of their activities available to the research community and to the public at large

2. Inventions: If the outcomes of the research result in patentable inventions, the provisions of the Bayh-Dole Act apply
3. Research tools: Unpatented research products or resources may be made available through licensing to vendors or other reesarchers
4. Research data
    a. Defined as recorded factual material commonly accepted in the scientific community as necessary to validate research findings
    b. NIH endorses the sharing of final research data and expects and supports the timely release and sharing of final research data from NIH-supported studies for use by other researchers
    c. Researchers are expected to include a plan for data sharing or state why data sharing is not possible for certain awards over $500,000
5. Copyrighted works
    a. In general, grantees own the rights in data resulting from a grant-supported project and data may be copyrighted without NIH approval
    b. NIH must be given a royalty-free, nonexclusive and irrevocable license for the federal government to reproduce, publish or otherwise use the material (and to authorize others to do so) for federal purposes
    c. Sharing of copyrightable outcomes of research may be in the form of journal articles or other publications
6. Public Access Policy (http://publicaccess.nih.gov/policy.htm)
    a. Requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central (http://www.pubmedcentral.nih.gov) upon acceptance for publication
    b. Papers must be accessible to the public on PubMed Central no later than twelve months after publication

D. National Science Foundation requirements (NSF Grant Policy Manual (GPM) sec. 730, "Intellectual Property") (http://www.nsf.gov/pubs/2002/nsf02151/gpm02_151.pdf)
1. Inventions
    a. Disposition of rights governed by Bayh-Dole
    b. See also 45 CFR 650: Governs allocation of rights to inventions made in performance of NSF-assisted research (http://www.access.gpo.gov/nara/cfr/waisidx_08/45cfr650_08.html)
2. Copyrights
    a. NSF generally will only acquire rights to copyrightable materials as needed to achieve its purpose or comply with government-wide policy or international agreements
    b. To encourage dissemination, NSF generally will not restrict or take income from copyrightable materials
    c. NSF will a retain royalty-free, nonexclusive, nontransferable and irrevocable license for the federal government to exercise (or have exercised) on behalf of the U.S. worldwide all exclusive rights provided by the copyright
3. Research results

a. Researchers are expected to promptly prepare and submit for publication all significant findings of NSF-sponsored research
b. Researchers are expected to share all primary data gathered or created in the course of NSF-sponsored research
c. NSF generally allows researchers to retain principal intellectual property rights to provide incentives for development and dissemination

II. Invention Reporting Compliance

A. iEdison (https://s-edison.info.nih.gov/iEdison/)

1. To facilitate Bayh-Dole compliance, NIH developed Interagency Edison, "iEdison," an online invention reporting system
2. iEdison is a single interface for reporting institutions to interact with multiple federal funding agencies

B. Institutional responsibilities under 37 CFR Part 401

1. Require employees to make written disclosure of inventions to the institution (sec. 401.14(f)(2))
2. Make written disclosure of the invention to the funding agency within two months of inventor's disclosure (sec. 401.149(c)(1)); the disclosure must include:
   a. Inventor(s) name(s)
   b. Federal funding source
   c. Date of any public disclosure
   d. Technical details
3. Election of title (sec. 401.1(c)(2))
   a. Within two years of reporting the invention to the federal agency sponsor, the institution must notify the sponsor whether or not it will retain ownership
   b. Public disclosure of the invention may shorten the two year election period
4. Confirmatory license (sec. 401.14(f)(1)): Institution must confirm the rights of the government in the invention
5. Institution must share royalties with the inventor (sec. 401.14(k))
6. Assignment (sec. 401.14(k))
   a. Institution may not assign rights in the invention without approval of the federal sponsoring agency
   b. If rights are assigned to the inventor, the inventor as assignee must agree to comply with all terms imposed on institution
7. Patent prosecution
   a. Within one year after electing title, the institution must file its initial (nonprovisional) patent application (sec. 401.14(c)(3))
   b. Patent filings must include a statement of government support (sec. 401.14(f)(4))
   c. Sponsors may require institutions to provide the following (sec. 401.5(f)):
      i. Listing of all inventions under the funding, or statement that there were none;

ii. Filing date, patent application number and title, copy of patent application, and patent number and issue date
iii. Periodic listings of all inventions disclosed to the agency

d. Institution shall notify the agency of any decisions not to continue patent prosecution (sec. 401.14(f)(3))

8. Licensing
   a. Any licensee must agree that products embodying the invention will be substantially manufactured in the U.S. unless a waiver is granted by the agency (secs. 401.14(i))
   b. Institution must make reasonable efforts to license to small businesses (sec. 401.14(k))
9. "March-in rights" (secs. 401.6 & 401.14(j))
   a. The agency may require the institution, or if the institution refuses the agency may itself, license the technology to a "responsible applicant"
   b. Conditions for march-in
      i. Effective steps to achieve practical application of the invention
      ii. To alleviate health or safety needs
      iii. To meet requirements for public use
      iv. Non-compliance with U.S. manufacture requirements
10. Utilization reports must be submitted at least annually and include the following information (sec. 401.14(h)):
    a. Status of development
    b. Date of first commercial sale or use of a product incorporating the invention
    c. Gross royalties
11. At the close-out of the sponsored project, the institution may be required to report all inventions arising from the project, or state that there were none (sec. 401.5(f)(1))

FEDERAL GRANTS ADMINISTRATION

I. Types of Funding Instruments
   A. Procurement Contracts (31 USC 6303)
      1. Used when the principal purpose of the instrument is to acquire property or services for the direct benefit or use by the federal government
      2. Administrative framework provided by Federal Acquisition Regulation (FAR), 48 CFR Parts 1-51(*not covered in this outline)*
   B. Grants (31 USC 6304)
      1. Used when the principal purpose of the relationship is to transfer a thing of value to the recipient to carry out a public purpose instead of acquiring property or services for the direct benefit or use of the federal government, and substantial involvement is not expected between the federal agency and the recipient when carrying out the activity contemplated
      2. Administrative framework provided by Office of Management and Budget (OMB) Circulars

C. Cooperative Agreements (31 USC 6305)
   1. Used when the principal purpose of the relationship is to transfer a thing of value to the recipient to carry out a public purpose instead of acquiring property or services for the direct benefit or use of the federal government, and substantial involvement is expected between the federal agency and the recipient in carrying out the activity contemplated
   2. Administrative framework provided by OMB Circulars

II. OMB oversees and coordinates procurement, financial management, information and regulatory policies in the Executive Branch agencies
   A. OMB Circulars set forth the framework for federal research administration and oversight (http://www.whitehouse.gov/omb/circulars_index-education/)
      1. OMB Circular A-21: "Cost Principles for Educational Institutions" (2 CFR Part 220): Establishes the cost principles for universities and governs the direct and indirect charging of costs to sponsored awards
         a. Direct v. indirect costs:
            i. Direct costs: costs that can be identified specifically with a particular sponsored activity and with a high degree of accuracy
            ii. Indirect costs: costs incurred for common or joint objectives that cannot be identified readily and specifically with a particular sponsored project, *i.e.*, "Facilities and Administration" (F&A) costs
            iii. Sponsored project costs are comprised of allowable direct costs plus the allocable portion of allowable indirect costs
         b. Direct and indirect costs charged to a sponsored agreement must be reasonable, allocable, allowable and consistent
            i. Reasonableness
               1. Use Prudent Person Test: "A cost may be considered reasonable if the nature of the goods or services acquired or applied, and the amount involved therefore, reflect the action that a prudent person would have taken under the circumstances prevailing at the time the decision to incur the cost was made." (Sec. C.3)
            ii. Allocability
               1. "A cost is allocable to a particular cost objective . . . if the goods or services involved are chargeable or assignable to such cost objective in accordance with relative benefits received or other equitable relationship. (Sec. C.4.a)
               2. [A] cost is allocable to a sponsored agreement if it is incurred solely to advance the work under the sponsored agreement; it benefits both the sponsored agreement and other work of the institution, in proportions that can be approximated through use of

reasonable methods, or it is necessary to the overall operation of the institution and . . . is deemed to be assignable in part to sponsored projects." (Sec. C.4.a)

iii. Allowability; determined by:
1. OMB A-21 Sec. J, "General Provisions for Selected Items of Cost"
2. Agency specific policy
3. Award terms and conditions
4. University policy

iv. Consistency
1. Like costs cannot be direct charged in one case and indirectly charged in another
2. "All costs for the same purpose, in like circumstances, are either direct costs only or F&A costs only" (Sec. C.11.a)

c. Cost Accounting Standards (CAS) contained within OMB Circular A-21, Appendix A provide guidance and parameters for higher educational institutions when accounting for costs associated with federally sponsored projects

i. Fundamental principle of CAS 9905.502: Prohibit double counting of costs
1. "Double counting occurs most commonly when cost items are allocated directly to a cost objective without eliminating like cost items from indirect cost pools which are allocated to that cost objective." (CAS 9905.502, Sec. 1)
2. CAS 9905.502, Sec. 1 requires that "each type of cost is allocated only once and on only one basis to any sponsored agreement or other cost objective"

ii. Other applicable CAS provisions
1. CAS 9905.501: Consistency in estimating, accumulating and reporting costs
2. CAS 9905.505: Accounting for unallowable costs
3. CAS 9905.506: Cost accounting period

d. F&A Rate

i. The federal government uses an F&A rate established for each university to reimburse the university for indirect costs supporting organized research, *i.e.*, both federally-sponsored and non-federally sponsored research and development activities of an institution

ii. F&A is periodically negotiated between the university and its "cognizant agency"
1. OMB established the cognizant agency concept, under which a single agency represents all other others in dealing with grantees in common areas

2. Cognizant agency for non-profit organizations determined by calculating which federal agency provides the most grant funding;
3. Cognizant agency reviews and approves grantee's indirect cost rates

iii. F&A rate calculation formula =

$$\frac{\text{Indirect Costs Supporting Organized Research}}{\text{Direct Costs of Organized Research}}$$

iv. Indirect cost pool (numerator) comprised of facilities and administrative costs such as building and equipment depreciation/use allowance, interest, operations and maintenance, library, central administration, department administration, sponsored project administration, student services

v. Direct cost base (denominator) based on actual costs charged to research accounts

B. OMB Circular A-110: "Uniform Administrative Requirements for Grants and Other Agreements With Institutions of Higher Education, Hospitals and Other Non-Profit Organizations" (2 CFR Part 215)

1. Establishes uniform administrative requirements for federal grants and agreements to universities, hospitals and other non-profits
2. Provides guidance on:
   a. Pre-award requirements (Subpart B), including
      i. Appropriate award instrument
      ii. Applying for federal assistance
      iii. Debarment and suspension
      iv. Special award conditions
      v. Certifications and representations
   b. Post-award requirements (Subpart C)
      i. Financial and program management
      ii. Property standards
      iii. Procurement standards
      iv. Reports and records
      v. Termination and enforcement
   c. After-the-award requirements (Subpart D)

C. OMB Circular A-133: "Audits of States, Local Governments and Non-Profit Organizations"

1. Establishes the standards for obtaining consistency and uniformity among federal agencies for the audit of non-profit organizations expending federal awards
2. Non-federal recipient of federal funding is subject to annual audit
3. Auditee required (Subpart C § 300) to:

a. Identify all federal awards received and expended
b. Maintain internal control over federal programs "that provides reasonable assurance that auditee is managing Federal awards in compliance with laws, regulations, and the provisions of contracts or grant agreements"
c. Comply with laws, regulations and provisions of contracts or grant agreements
d. Prepare appropriate financial statements
e. Ensure that required audits are properly performed and submitted when due
f. Follow up and take corrective action on audit findings

III. National Institutes of Health (NIH) and National Science Foundation (NSF) Requirements
A. NIH Grants Policy Statement (NIH GPS) (http://grants1.nih.gov/grants/policy/policy.htm#gps))
1. Sets forth the policy requirements that serve as the terms and conditions of NIH grant awards
2. Changes in statutes, regulations, or policies that take effect before the next revision of the NIH GPS are published separately in the *NIH Guide for Grants and Contracts* http://grants.nih.gov/grants/guide/index.html
B. NSF Grant Policy Manual (NSF GPM) (http://www.nsf.gov/pubs/manuals/gpm05_131/index.jsp)
1. Sets forth NSF policies regarding the award and administration of grants
2. Applicable to NSF grants and cooperative agreements; does not apply to NSF contracts

IV. Debarment and Suspension
A. OMB Guidelines to Agencies on Government-Wide Debarment and Suspension (Nonprocurement) (2 CFR Part 180)
1. Provides guidance for federal agencies on the government-wide debarment and suspension system for nonprocurement programs and activities
2. Each federal agency required to issue regulations consistent with OMB guidance
B. Debarment and Suspension System
1. Purpose: To protect the public interest, the federal government ensures the integrity of federal programs by conducting business only with responsible persons and entities
2. Prohibits entering into transactions with excluded or disqualified individuals
3. Requires institutions to verify that they are not transacting business with excluded or disqualified persons or entities
C. Excluded Parties List System (www.epls.gov)
1. Maintained by General Services Administration (GSA) for the purpose of efficiently and conveniently disseminating information on parties that are excluded from receiving federal contracts and other assistance

RESEARCH MISCONDUCT

I. Regulatory Background
   A. December 6, 2000, Office of Science and Technology Policy (OSTP), Executive Office of the President, published the Federal Research Misconduct Policy (http://www.ostp.gov/cs/federal_policy_on_research_misconduct)
   B. OSTP required federal agencies and departments supporting research to implement research misconduct policies or regulations

II. Federal Office of Research Integrity (ORI) (http://ori.hhs.gov/)
   A. Oversees and directs Public Health Service (PHS) research integrity activities on behalf of the Secretary of U.S. Department of Health and Human Services (HHS)
   B. PHS composed of:
      1. Office of Public Health and Science
      2. National Institutes of Health
      3. Centers for Disease Control and Prevention
      4. Food and Drug Administration
         a. Allegations of misconduct in FDA regulated research are generally investigated by the FDA's Office of Regulatory Affairs, Bioresearch Monitoring Program Coordination; http://www.fda.gov/ora/compliance_ref/aip_page.html or http://www.fda.gov/ora/compliance_ref/bimo/default.ht
         b. ORI may also take actions related to FDA regulated research if the research is also supported by PHS funding
      5. Substance Abuse and Mental Health Services Administration
      6. Health Resources and Services Administration
      7. Agency for Healthcare Research and Quality
      8. Agency for Toxic Substances and Disease Registry
      9. Indian Health Service
      10. Office of Regional Health Administrators

III. HHS/ORI Regulatory Scheme
   http://ori.hhs.gov/documents/42_cfr_parts_50_and_93_2005.pdf
   A. Definition of research misconduct (42 CFR 93.103)
      1. Fabrication: "making up data or results and recording or reporting them"
      2. Falsification: "manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record"
      3. Plagiarism: "appropriation of another person's ideas, processes, results, or words without giving appropriate credit"
      4. Scientific misconduct does not include honest error or differences of opinion
   B. Requirements for finding of research misconduct (42 CFR 93.104)
      1. Significant departure from accepted practices

2. Intentional, knowing or reckless misconduct
3. Proof by a preponderance of the evidence

C. Institutional obligations (42 CFR 93.300-93.302)
1. Written policies and procedures for addressing allegations of research misconduct consistent with regulations
2. Respond to allegations in thorough, competent, objective and fair manner
3. Foster a research environment that promotes the responsible conduct of research, discourages research misconduct and deals promptly with allegations
4. Take reasonable and practical steps to protect good faith complainants, witnesses and committee members
5. Provide confidentiality
6. Take reasonable and practical steps to ensure the cooperation of respondents
7. Cooperate with HHS
8. Assist in administering and enforcing HHS administrative actions
9. Have an active assurance of compliance, *i.e.*, responsible institutional official must assure that the institution has written policies and procedures in compliance with regulations, and that the institution complies with its own policies and procedures
10. File an annual report with the federal Office of Research Integrity

D. Institutional Inquiry (42 CFR 93.307)
1. Purpose of inquiry: To decide if an allegation warrants an investigation
2. When to conduct an inquiry
   a. If the allegation falls within the definition of research misconduct
   b. PHS support is involved
   c. The allegation is sufficiently credible and specific
3. At the time of, or before, initiating an inquiry
   a. Notify the presumed respondent
   b. Take all reasonable and practical steps to obtain custody of all research records and evidence and sequester them in a secure manner
4. Following the inquiry
   a. Prepare a written inquiry report
   b. Provide the respondent with an opportunity to review and comment on the inquiry report
5. Timing: Inquiry must be completed within 60 days of initiation or document reasons for exceeding the 60 day period

E. Institutional Investigation (42 CFR 93.307-93.314)
1. When to conduct an investigation
   a. There is a reasonable basis for concluding that the allegation falls within the definition of scientific misconduct and involves PHS support
   b. Inquiry stage indicates the allegation may have substance
   c. If no investigation is warranted, the institution must keep detailed documentation of the decision not to investigate

2. Notice requirements
    a. Notify respondent, providing copy of inquiry report, regulations and institutional policies and procedures
    b. Notify complainant
    c. Report to ORI within 30 days, providing copy of inquiry report
3. Investigation steps
    a. Use diligent efforts to ensure the investigation is thorough and sufficiently documented and includes examination of all research records and evidence
    b. Take reasonable steps to ensure an impartial and unbiased investigation to the maximum extent practicable
    c. Interview each respondent, complainant and any other person having relevant information; record or transcribe each interview
    d. Diligently pursue all significant issues and leads
    e. Provide the respondent with a copy of the draft investigation report and copy of, or supervised access to, the evidence; the respondent has 30 days to submit comments
    f. A copy of the investigation report may be provided to the complainant, who has 30 days to submit comments
4. Investigation report requirements
    a. Describe the nature of the allegation
    b. Identify PHS support
    c. Describe the specific allegation
    d. Identify and summarize the research records and evidence reviewed
    e. Make a statement of finding for each allegation, including the type of misconduct and whether it was intentional, knowing or reckless
    f. Summarize the facts and analysis supporting the conclusion
    g. Identify whether publications need correction or retraction
    h. Identify the person responsible for the misconduct
    i. List respondent's current or pending PHS support
    j. Include comments provided by respondent or complainant on draft report
    k. Maintain and, upon request, provide records of proceeding, including transcripts or recordings of interviews
5. Timing
    a. Investigation must begin within 30 days after determining an investigation is warranted
    b. Investigation must be completed within 120 days unless ORI provides an extension
    c. Any institutional appeal must be completed within 120 days
6. Record retention: Institution must maintain records of the research misconduct proceeding for 7 years after completion of the proceeding (42 CFR 93.317)
7. Special circumstances requiring immediate notification of ORI (42 CFR 93.318)

a. Health or safety of public is at risk, including immediate need to protect human or animal subjects
b. HHS resources are threatened
c. Research activity should be suspended
d. Reasonable indication of possible violations of civil or criminal law
e. Federal action required to protect interests of those involved in research misconduct proceeding
f. Research misconduct proceeding may become public prematurely
g. Research community or public should be informed

F. HHS administrative actions (42 CFR 93.407)
1. In response to a research misconduct proceeding, HHS may impose the following:
a. Requirement to clarify, correct or retract the research record
b. Letter of reprimand
c. Certification or assurance requirements to ensure compliance with regulations or funding terms
d. Suspension or termination of funding
e. Restriction on specific award activities or expenditures
f. Certification in requests for PHS funding and reports to PHS
g. Prohibition on participation in any advisory capacity to PHS
h. Suspension or debarment
2. PHS may also seek to recover funds spent in support of activities that involved scientific misconduct

IV. Additional Regulations
A. In addition to HHS, the following agencies and departments have implemented research misconduct policies or regulations (as of May 1, 2009):
1. Department of Defense (http://www.dtic.mil/whs/directives/corres/html/321007.htm)
2. Department of Labor (http://www.dol.gov/federalregister/Search/GetHtml.aspx?DocID=8329)
3. Department of Transportation (http://ori.hhs.gov/documents/rmguidancefinal_228002.pdf)
4. Department of Veteran Affairs (http://ori.hhs.gov/policies/documents/ViewPublication-VAMisconduct.pdf)
5. Environmental Protection Agency (http://ori.hhs.gov/documents/epapolicy.pdf)
6. National Aeronautics and Space Administration (http://edocket.access.gpo.gov/2004/04-15432.htm)
7. National Endowment for the Humanities (http://neh.gov/grants/guidelines/researchmisconduct.html)
8. National Science Foundation (http://www.nsf.gov/oig/misconscieng.jsp)
9. Smithsonian Institution (http://www.si.edu/about/documents/sd604.pdf)

B. The following agencies are reportedly developing policies or regulations (as of May 1, 2009):

1. Department of Energy (http://www.sc.doe.gov/Program_Offices/Policy%20on%20research%20misconduct%20June%2028.pdf)
2. Department of Agriculture (http://edocket.access.gpo.gov/2008/pdf/E8-27834.pdf)
3. Department of Commerce
4. Department of Education
5. Department of Interior
6. Department of Justice

BASICS OF RESEARCH COMPLIANCE: EXPORT CONTROLS AND SELECTED SOURCES PERTINENT TO SPECIAL CATEGORIES OF RESEARCH

June 23 – June 27, 2009

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EXPORT CONTROLS

I. Background

A. The two primary export control rules with which institutions should be familiar include the International Traffic in Arms Regulations ("ITAR"), which regulate defense articles and services and are enforced by the Directorate of Defense Trade Controls ("DDTC") of the U.S. Department of State, and the Export Administration Regulations ("EAR"), which regulate commercial and "dual use" items and are enforced by the Bureau of Industry and Security ("BIS") of the U.S. Commerce Department. Other regulatory regimes that may be triggered depending on the nature of the export include, for example, the export restrictions administered by the Department of Energy, the Nuclear Regulatory Commission and the Food and Drug Administration.

II. ITAR / Department of State

A. Arms Export Control Act, 22 U.S.C. § 2778, available at http://www.pmddtc.state.gov/regulations_laws/aeca.html

B. Executive Order 11958, Administration of Arms Export Controls, available at http://www.archives.gov/federal-register/codification/executive-order/11958.html

C. ITAR, 22 CFR Parts 120 *et seq.*, available at http://www.pmddtc.state.gov/regulations_laws/itar.html

III. EAR / Commerce Department

A. EAR, 15 C.F.R. Part 730 *et seq.*, available at http://www.access.gpo.gov/bis/index.html

B. Lists to Check, available at http://www.bis.doc.gov/complianceandenforcement/liststocheck.htm

C. BIS, Introduction to Commerce Department Export Controls, available at http://www.bis.doc.gov/licensing/exportingbasics.htm

D. BIS, Frequently Asked Questions, available at http://www.bis.doc.gov/licensing/index.htm#faqs

SELECTED SOURCES PERTINENT TO SPECIAL CATEGORIES OF RESEARCH

I. Stem Cells

A. Executive Order 13505, Removing Barriers to Responsible Scientific Research Involving Human Stem Cells, available at http://www.whitehouse.gov/the_press_office/Removing-Barriers-to-Responsible-Scientific-Research-Involving-Human-Stem-Cells/

B. National Institutes of Health, Notice No. NOT-OD-09-085, Implementation of Executive Order on Removing Barriers to Responsible Scientific Research Involving Human Stem Cells, available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-085.html

C. Draft National Institutes of Health Guidelines for Human Stem Cell Research, available at http://stemcells.nih.gov/policy/2009draft.htm

D. Office for Human Research Protections, Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells and Stem Cell-Derived Test Articles, available at http://www.hhs.gov/ohrp/humansubjects/guidance/stemcell.pdf

E. U.S. Food and Drug Administration Regulations, 21 C.F.R. Part 1271, available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=1271

F. National Academies, Guidelines for Human Embryonic Stem Cell Research, available at http://www.nap.edu/catalog.php?record_id=12260

II. Biosafety

A. NIH Guidelines for Research Involving Recombinant DNA Molecules, available at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html

B. NIH, Office of Biotechnology Activities, Institutional Biosafety Committees, Information and Resource Page, available at http://oba.od.nih.gov/rdna_ibc/ibc.html

III. Select Agents

A. The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Public Law 107-188, available at http://www.selectagents.gov/otherLegislation.htm

B. Centers for Disease Control and Prevention Regulations, 42 C.F.R. Part 73, available at http://www.selectagents.gov/selagentRegulation.htm

C. U.S. Department of Agriculture, Animal and Plant Health Inspection Service Regulations, 7 C.F.R. Part 331, 9 C.F.R. Part 121, available at http://www.selectagents.gov/selagentRegulation.htm

D. National Select Agent Registry, available at http://www.selectagents.gov/

IV. Nuclear Safety

A. Nuclear Regulatory Commission Regulations, 10 C.F.R. Chapter I, available at http://www.nrc.gov/reading-rm/doc-collections/cfr/

BASICS OF RESEARCH COMPLIANCE: CONFLICTS OF INTEREST, HUMAN SUBJECTS RESEARCH, AND ANIMAL CARE AND USE

June 23 – June 27, 2009

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CONFLICTS OF INTEREST

I. Conflicts of Interest -- Real and perceived conflicts of interest can compromise or appear to compromise scientific judgment and undermine the public's trust in research. Federal regulations are intended to ensure that the design, conduct, or reporting of research funded by the Public Health Service (PHS) or the National Science Foundation (NSF) will not be biased by any conflicting financial interest of the investigators responsible for the research. 42 CFR 50.601

II. Federal Regulations
- A. PHS: Objectivity in Research 42 CFR Part 50
  FAQ at: http://grants.nih.gov/grants/policy/coifaq.htm
- B. NSF: Grant Policy Manual 510
  http://www.nsf.gov/pubs/2002/nsf02151/gpm5.jsp#510

III. Responsible Federal Agencies
- A. Public Health Service
- B. National Science Foundation
- C. Other funding agencies

IV. Compliance Issues
- A. Investigator Responsibility:
  1. Disclosure
     a. Must disclose "significant financial interest"
     b. Disclosure tied to submission, but investigators must update disclosures during period of award 42 CFR 50.604 (c)(2)
  2. Definitions 42 CFR 50.603
     a. "Significant financial interest" includes:
        1) Anything of monetary value
        2) Examples: salary, consulting fees, honoraria, equity interests, intellectual property rights
     b. "Significant financial interest" excludes:
        1) Salary and other payments from the university
        2) Income from seminars, lectures, teaching sponsored by public or non-profit entities

3) Income from service on advisory committees or review panels for public or non-profit entities
4) Ownership interest in SBIR applicant institution

c. "Investigator" is not just the Principal Investigator, but also anyone involved in the "design, conduct or reporting" of the research
1) Also must disclose conflicts of the spouse and dependent children of investigators

B. Institutional Responsibilities 42 CFR 50.604:
1. Written, enforced conflict of interest policy and disclosure process
2. Designate an institutional official to solicit and review investigator disclosures
3. Require investigators to submit appropriate conflict disclosures
4. Institutions must maintain and "manage, reduce or eliminate" conflicts
5. Maintain records
6. Establish appropriate enforcement mechanisms, with appropriate sanctions

C. Managing conflicts of interests
1. Public disclosure of conflict/financial interest
2. Monitoring by independent reviewers
3. Modification of research plan
4. Disqualification from participation in all/some of research
5. Divestiture of significant financial interest
6. Severance of relationship causing conflict
7. Disallow payments for attending industry-sponsored meetings and events
8. Prohibit gifts of any value from industry
9. Prohibit ghostwriting of professional presentations

D. AAMC/AAU Joint Advisory Committee Report https://services.aamc.org/Publications/index.cfm?fuseaction=Product.displayForm&prd_id=220&prv_id=268

V. Responsible Campus Units May Include:
A. Sponsored Projects (Research Grants and Contracts) Administration
B. Research compliance officer
C. Faculty conflict review committee
D. Procurement

VI. Sample Policies and Procedures
Johns Hopkins University: http://jhuresearch.jhu.edu/compliance-conflict.htm
Stanford University: http://rph.stanford.edu/4-2.html
University of California: http://www.universityofcalifornia.edu/compliance/ethics/COI_Researchers.html
University of Chicago: http://researchadmin.uchicago.edu/regulations/coi.shtml

VII. State Law: State conflict of interest statutes governing provision of goods and services by employees may apply and may have different definitions (e.g., of family/relative, significant interest) or disclosure requirements.

HUMAN SUBJECTS RESEARCH

I. Purpose of the regulatory framework: Protect the rights of people who volunteer to participate in research

II. Department of Health and Human Services, Office for Human Research Protections (hhs.gov/ohrp/humansubjects/guidance/45CFR46.htm)
   - A. 45 CFR Part 46
   - B. OHRP www.hhs.gov/ohrp/policy/index.html
   - C. See also: College/university policies

III. What "research" is covered?
   - A. Federal definition: Systematic investigation designed to develop or contribute to generalizable knowledge (also check institutional definition)
   - B. Federal regulations cover research supported with federal funding
   - C. College/university policy may apply to all institutional research involving people (regardless of funding)

IV. Levels of Institutional Review Board (IRB) review
www.hhs.gov/ohrp/humansubjects/guidance.exprev.htm
   - A. Exempt
   - B. Expedited
   - C. Full board

V. Key concepts
   - A. Informed consent – understand the nature of voluntary participation in the research and the possible risks and benefits (construed broadly)
   - B. Voluntary – no coercion (real or perceived)
   - C. Risks – include physical, emotional, financial, reputational, legal
   - D. Benefits – to the individual and to the public

VI. Social/ Behavioral Research and Medical/bioscience Protocols
   - A. General issues: research should be well-designed, participants should be selected to support meaningful research conclusion
   - B. Special populations – minors, prisoners, pregnant women and fetuses, mentally disabled, vulnerable
   - C. Certificates of confidentiality: Provide additional protection for participants in studies collecting information that, if disclosed, could have adverse consequences for participants, such as damage to their financial standing, employability, insurability, or reputation
      1. Certificate states that researcher can't be compelled to turn over information about participants (e.g., for use in lawsuits)
      2. Certificates are issued by NIH
      3. Additional information is available at: www.hhs.gov/ohrp/humansubjects/guidance/certconf.htm

D. All changes to protocols, consent forms, other approved documents or practices must be approved by the IRB

VII. Possible consequences of failing to follow regulations or poorly performed research
- A. Harm to individuals
- B. Misuse of resources
- C. Lessen the credibility of research

ANIMAL CARE AND USE

I. Animal Care and Use regulations are designed to provide guidelines for the care of animals used in research.

II. Responsible Agencies
- A. Office of Laboratory Animal Welfare ("OLAW") oversees compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals ("PHS Policy")
- B. U.S. Department of Agriculture's Animal and Plant Health Inspection Service ("APHIS") enforces the Animal Welfare Act ("AWA")
- C. Association for Assessment and Accreditation of Laboratory Animal Care International ("AAALAC") accredits animal care and use programs

III. Summary of Protections
- A. Federal Laws (Animal Welfare Act and PHS Policy) require institutions to:
  1. Designate an Institutional Official with responsibility for the animal care program (9 CFR § 1.1, PHS Policy Section III.G.)
  2. Appoint an Institutional Animal Care and Use Committee (IACUC) to oversee animal care programs, research, facilities (9 CFR § 2.31, PHS Policy Section IV.A.3.)
  3. Provide veterinary care (9 CFR § 2.33, PHS Policy Section IV.A.)
- B. General protections for animals used in research
  1. Protocol design must be relevant to human or animal health, advancement of knowledge, or the good of society
  2. Appropriate species, minimum number
  3. Not unnecessarily duplicate previous experiments
  4. No available alternatives to procedures that cause more than momentary/slight pain
  5. Avoidance and minimization of pain and distress

IV. Overview of Laws
- A. Federal
  1. Animal Welfare Act (AWA)
     a. 7 U.S.C. § 2131-2155

b. Humane care and treatment of animals intended for use in research facilities or for exhibition purposes or for use as pets (7 U.S.C. § 2131(1))
c. Implementing regulations at: 9 CFR Parts 1, 2(c) and 3
d. Covers research facilities, i.e., any school, institutions, organization or person that uses or intends to use live animals in research (9 CFR § 1.1) if:
    1) Purchase or transport live animals in commerce, or
    2) Receive federal funds to carry out the research (7 USC § 2132(e))
e. Applies to use of animals for research, teaching, testing, experimentation or exhibition (9 CFR § 1.1)
    1) Covers dogs, cats, non-human primates, guinea pigs, hamsters, rabbits and any other warm-blooded animal (9 CFR § 1.1)
    2) Excludes horses not used in research, farm animals used or intended for use as food or fiber, and livestock and poultry used for improving animal nutrition, breeding, management, production efficiency, and improving the quality of food and fiber (9 CFR § 1.1)
    3) Excludes birds, rats and mice bred for use in research (2002 Omnibus Farm Bill (H.R. 2646/ S.F. 1731))
f. Enforced by Animal and Plant Health Inspection Service (APHIS)
    1) Facilities must register and provide annual reports (9 CFR § 2.30 and § 2.36)
    2) APHIS has authority to inspect facilities
g. AWA FAQs: http://www.nal.usda.gov/awic/legislat/regsqa.htm

2. Health Research Extension Act of 1985
    a. 42 U.S.C. § 289d
    b. Proper care and treatment of animals used in biomedical and behavioral research funded by Public Health Service
    c. PHS Policy on Humane Care and Use of Laboratory Animals (http://grants.nih.gov/grants/olaw/references/phspol.htm
        1) U.S. Government Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research and Training (http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples)
        2) Guide for the Care and Use of Laboratory Animals (http://www.nap.edu/openbook.php?record_id=5140)
        3) PHS Policy applies to PHS conducted or supported activities involving animals (Sec. II)
        4) "Animal" includes any live, vertebrate animal used in or intended for use in research, research training, experimentation, or biological testing or for related purposes (Sec. III.A.)

5) Office of Laboratory Animal Welfare (OLAW) enforces PHS Policy
   a) Institutions file an assurance with OLAW (Section IV.A.)
   b) Institutions file annual reports (Section IV. A.)
6) PHS Policy on Humane Care and Use of Laboratory Animals, Frequently Asked Questions (Revised January 16, 2009), available at http://grants.nih.gov/grants/olaw/faqs.htm

3. Good Laboratory Practices (GLP) Act
   a. 21 CFR, Animal Care, Non-Clinical Studies and 40 CFR, Animal and other test systems, Clinical Studies
   b. Food and Drug Administration and the Environmental Protection Agency
   c. Requires separation of species, isolation of individual projects, storage areas for feed, bedding, supplies and equipment. Also required are written standard operating procedures for housing, feeding, handling and animal care. There should be appropriate identification of animals. Environmental records for each room are required. GLPs require establishment of a Quality Assurance Unit to conduct internal audits.

B. State laws – many states have laws that will also apply. See:
   1. Licensing and registration requirements
   2. Animal cruelty laws
C. Recent cases/developments: See www.nabr.org for current developments
D. Concerns about threats to safety due to public records and open meetings disclose information about the identity of researchers who work with animals
   1. Consider what information is necessary to include in records that may become public and be sure researchers understand extent to which information may become public
   2. State public records acts and open meetings laws (In Arizona, for example, protocols are subject to our public records act but meetings are not required to be open to the public.)
   3. Federal Freedom of Information Act (FOIA) 5 U.S.C. § 552
      a. Exemptions permit the protection of personal or private information about an individual but must balance the "foreseeable harm of invading that person's privacy against the public benefit that would result from the release." 45 C.F.R. § 5.67(b)
      b. *In Defense of Animals v. National Institutes of Health,* 543 F. Supp.2d 70 (D.D.C. 2008) (Court rejected NIH's use of the exemption to justify withholding information about floor plans, wiring diagrams and locations of animals)
   4. Laws that address damage, destruction, interference with animal research
      a. Animal Enterprise Terrorism Act, 18 U.S.C. § 43, extended the Animal Enterprise Protection Act of 1992 makes it a crime to

physically disrupt the functioning of an animal enterprise or intentionally cause lass of property, including animals and records (but protects peaceful demonstration)

b. See also state laws (e.g. California Penal Code § 422.4 and § 602.12)

V. Additional Resources

A. Applied Research Ethics National Association & OLAW, Institutional Animal Care and Use Committee Guidebook (2d ed. 2002), available at http://grants.nih.gov/grants/olaw/GuideBook.pdf

B. AAALAC Position Statements http://www.aaalac.org/accreditation/positionstatements.cfm

C. AAALAC Connection Newsletter http://www.aaalac.org/publications/newsletter.cfm