PUBLIC CONTRACTING INSTITUTE

Life Sciences Contracting 101

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Topics

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"Common Rule" for Clinical Trials

- U.S. Department of Health and Human Services sets requirements for protection of human subjects at 45 C.F.R. Part 46
- Heightened requirements compared to U.S. Food and Drug Administration regulations
- Most federal agencies adopt Common Rule requirements for federally funded clinical trials
- Requirements changed in 2018, and existing third-party agreements may still be following old requirements
- Additional guidance is available at https://hhs.gov/ohrp

"Common Rule": Coverage

- In general, extends to human subjects research performed or "supported" by the U.S. Government
  - Research is broadly defined to sometimes even cover evaluation/demonstration activities
  - Extends to just obtaining individually identifiable private information from living individuals (i.e., allows the identity of the individual to be directly or readily ascertained)
  - Support can take the form of collaboration or funding
  - Governmental entities can be covered by the requirements
- Limited to those "engaged" in human research:
  - Obtain data about subjects through intervention or interaction
  - Obtain for research purposes individually identifiable private information (including identifiable biospecimens) about subjects
  - Obtain informed consent of subjects
  - *Prime agreement recipients are also automatically covered regardless of actual activities*

"Common Rule": Requirements

- Must have an assurance of compliance in place and approval of institutional review board (IRB) before engaging in research
- IRB approval (only 1 board permitted for U.S.-based activities):
  - At least 5 members
  - At least 1 member with scientific expertise
  - At least 1 member with nonscientific expertise
  - At least 1 member not affiliated with covered institution or family members
- Broader mandatory reporting to IRB, covered entity officials, agency, and HHS:
  - Unanticipated problems involving risks to subjects or others
  - Serious or continuing noncompliance with Common Rule or IRB determinations
  - Suspension or termination of the IRB
- Informed consent requires specific disclosures, which are supplemented by the Privacy Act
- Additional protections for pregnant women, fetuses, neonates, children, and prisoners can apply

"Common Rule": Individual Investigator Agreements

- Covered lower-tier entities that do not have an Assurance can be covered under an individual investigator agreement if:
  - A principal investigator from an entity with an Assurance directs and supervises the work; and
  - The lower-tier entity without an Assurance does not routinely conduct covered research
- Extends higher-tier Assurance to lower-tier work
- Can be used for non-employee and employee investigators at lower-tier entity that does not have an Assurance
- Each lower-tier investigator must enter into the agreement when not covered by an Assurance
- Form agreement is not required as long as key provisions are included, including written confirmation by entity without Assurance that the research is permitted at its facilities
- Assurance holder and applicable IRB need to approve the extension through individual investigator agreement

"Common Rule": Ex-U.S. Research

- Requirements apply to work and entities outside the United States
- Individual investigator agreements are typically used to address concerns raised by ex-U.S. sites
- Federal department or agency can provide approval to only comply with ex-U.S. requirements
- Federal department of agency can sometimes waive Common Rule requirements for specific activities or classes of activities
- Grants of either exception are rare and must be published

Common Rule Coverage Exceptions *(Applied at Institution Level)*

- Commercial services typically performed by entity for non-research purposes *(e.g., commercial laboratory services or hospital staff drawing blood for investigator)*
- Non-site medical services dictated by protocol and typically performed by institution as part of routine clinical monitoring or follow-up
- Non-site limited study intervention that occurs on a one-time or short-term basis, with investigator determination that limited intervention in subject's best interest *(e.g., subject travel or emergencies)*
- Providing preliminary study information about availability, contact information, or consent to contact *(e.g., referring a subject to a study)*
- Solely permit use of facilities by a covered institution *(e.g., nursing homes or businesses)*
- Only releasing personally identifiable private information (including identifiable biospecimens)
- Obtaining coded private information or biospecimens from a covered entity without being able to readily ascertain identity
- Limited access to information when visiting, auditing, reporting to FDA, or publishing

* For each exception, generally cannot engage in study intervention, activities meriting professional recognition for publication, obtaining informed consent, enrolling subjects, overseeing protocol, or reporting of data

Investigator Financial Conflicts of Interest

- Applies in addition to U.S. Food and Drug Administration disclosure requirements
- Covers research funded by grant, cooperative agreement, or procurement contract (except Small Business Innovation Research Phase I agreements)
- Directly applies to the Public Health Service (e.g., NIH, FDA, CDC, and potentially BARDA), with other agencies like DoD able to trigger requirements by contract
- Nearly identical regulations at 42 C.F.R. Part 50, Subpart F (grants and cooperative agreements) and 45 C.F.R. Part 94 (procurement contracts)
- Research is very broad and covers clinical and non-clinical work
  - Chemistry, manufacturing, and controls activities likely not covered
  - *In vitro* work and animal studies often covered
- Individual coverage is broad, including anyone with responsibility for designing, conducting, or reporting covered research (directly supervised individuals may not be covered if they do not have sufficient responsibility)

Investigator Financial Conflicts of Interest

Requirements	Covered Interests
1. Maintain policy on entity's publicly accessible web site 2. Require employees to report significant financial interests to internal designee 3. Report financial conflicts of interest to awarding agency 4. Manage financial conflicts of interest* 5. Train before engaging in research, every 4 years, and upon revisions to or noncompliance with policy 6. Require lower-tier entities to adhere to higher-tier policies or implement their own	Significant Financial Interests • Reasonably related to duties • Includes interests held by spouse and dependent children • Not renumeration from and for-profit equity in employer reporting entity • Not investments controlled by others Financial Conflicts of Interest • Related to covered agreement • Interest could directly and significantly affect the design, conduct, or reporting of research under covered agreement

* Management requires retrospective review when undisclosed interests are discovered

Other Support and Ex-U.S. Components of Work

- The National Institutes of Health and other agencies have significantly ramped up disclosure requirements for “other support” and ex-U.S. components of work
- Contractors that have employees performing work with other entities (e.g., universities) need to follow detailed disclosure requirements
- Other support disclosures are generally focused on support received by individual investigators (e.g., not subcontracts under an award)
- All contractors sending data, samples, or work outside the United States should review agency disclosure requirements before engaging in ex-U.S. work that is not clearly identified in a proposal or award
- Although not inherently problematic, joint publications or patents with other entities that include a statement of U.S. Government funding can raise red flags and should be reviewed for potential violations

Animal Research Requirements

- PHS Policy on Humane Care and Use of Laboratory Animals
  - Applied to federal agency work and by contract, typically in awards from components of the Public Health Service
  - Requires compliance with Guide for the Care and Use of Laboratory Animals, which extends to all vertebrate animals including birds, fish, rats, and mice not covered by the Animal Welfare Act
  - Similar to the Common Rule, requires submission of assurance of compliance to the Office of Laboratory Animal Welfare
  - Assurance can cover facility generally up to 5 years and can be based on review of the Association for Assessment and Accreditation of Laboratory Animal Care or an Institutional Animal Care and Use Committee (IACUC)
  - IACUC membership requirements are similar to IRB requirements for clinical research
- Components of the Department of Defense follow similar requirements, with component-specific approvals replacing broad assurance process

Recombinant or Synthetic Nucleic Acid Molecules

- NIH Guidelines apply to research involving recombinant or synthetic nucleic acid molecules when:
  1. In the United States, entity receives funding or support from NIH for covered research, triggering compliance requirement for all covered research conducted or sponsored by the same entity (i.e., including commercial work)
  2. Outside the United States, entity receives funding or support from NIH for covered research, with only supported or funded research covered unless No. 3 below applies
  3. In or outside the United States, research involves testing in humans of materials containing covered materials developed with NIH funds to the extent entity that developed the materials participates in research (i.e., requirements are carried by recipient for subsequent phases of research, but mere provision of materials through transfer agreement not enough)
- Imposes detailed facility requirements and mandates review by institutional biosafety committee, with representation of local health and environmental interests
- Ex-U.S. work must follow host country rules, generally while still complying with NIH requirements unless reasonably consistent with NIH requirements
- May be required in agreements with other agencies

The Privacy Act and Other Protections

- Privacy Act applies in addition to traditional privacy requirements (e.g., HIPAA and GDPR) when a procurement contract involves the operation of a "system of records"
  - Systems of records are controlled directly or indirectly by a federal agency with information that is retrieved by name or other personally identifying particular
  - Must obtain written consent to disclose an individual's records
    - Cannot use blanket consent; must identify specific recipients
    - A number of exceptions apply across systems or under specific system of record notices (e.g., disclosures to other federal agencies for performance of their duties)
  - Training is required for contractor employees, which can be subject to criminal penalties for willful and knowing noncompliance with the Act
- Certificate of confidentiality prohibits disclosure in proceedings (e.g., in response to subpoena)
  - Now automatically issued for research funded in whole or in part by the U.S. Government (individually identifiable information is defined by "very small risk" of identification)
  - Some uncertainty about new state and local law exception (e.g., for state open records laws)

Export Controls, DURC, and Public Access

- International Traffic in Arms Regulation
  - Category XIV(f)(2) – equipment and software for detecting, identifying, or monitoring chemical or biological agents identified in DoD agreement
  - Category XIV(n) – developmental countermeasures or sorbents supported by DoD agreement
  - DoD agreements can be exempt from (f)(2) and (n) by expressly referencing development for both civil and military applications
  - Category XIV(b), (g), (h) – separate coverage for certain genetically modified biological agents, detection materials, and vaccines involving viruses and bacteria like Ebola, Bacillus anthracis (anthrax), Marburg, Variola virus (smallpox), and Yersinia pestis (plague)
- Dual Use Research of Concern
  - Imposed by contract, requiring internal process for reviewing and reporting categories of research involving at least 1 of 15 covered agents in all operations (including commercial)
  - Requirements are triggered for entities in the United States when receiving <u>any</u> federal life sciences funding
- Peer-reviewed articles need to be available on Government database, often with underlying data sets freely accessible

DURC Coverage

Agents and Toxins	Activities
1. Highly pathogenic avian influenza virus	A. Enhances harmful consequences
2. Bacillus anthracis (anthrax)	B. Disrupts immunity or effectiveness of immunization without clinical/agricultural justification
3. Burkholderia mallei (glanders)	C. Confers resistance to interventions or ability to evade detection
4. Burkholderia pseudomallei (melioidosis)	D. Increases stability, transmissibility, or ability to disseminate
5. Ebola virus	E. Alters host range or tropism
6. Foot-and-moth disease virus	F. Enhances susceptibility of host population
7. Francisella tularensis (tularemia)	G. Generates or reconstitutes an eradicated or extinct agent or toxin
8. Marburg virus	
9. Reconstructed 1918 influenza virus	
10. Rinderpest virus	
11. Toxin-producing strains of Clostridium botulinum (botulism)	
12. Variola major virus (smallpox)	
13. Variola minor virus (smallpox)	
14. Yersinia pestis (plague)	

Service Contract Act

- Requires prevailing wages and fringe benefits for service employees
- Also triggers additional requirements like paid sick leave
- Historically only applied to procurement contracts, but the U.S. Department of Labor has been pushing an aggressive interpretation extending to cooperative agreement
- No blanket exemption for research and development
  - Look for FAR 52.222-41, Service Contract Labor Standards
  - Exemption can apply if 80-90% professional, administrative, or executive employees performing work on agreement and only 10-20% service employees
  - Exemption can apply if only minor or no work in the United States
  - Wage and fringe benefit minimums may easily be met for covered employees, but documentation is needed and many life sciences contractors do not track hours
  - Paying cash in lieu of fringe benefits may make sense if fringe benefits are self-funded
- Laboratory and data services at higher risk of being covered than manufacturing or clinical work

Government Property and Risk of Loss: Procurement

Type	Government Title	Risk of Loss
Contractor Acquired (Fixed-Price)	Upon acceptance of deliverables	Transfers to Government upon later of acceptance or delivery
Contractor Acquired (Cost-Reimbursement and Time-and-Materials)	Extends to any item eligible for reimbursement	Always with Government except to the extent: • covered by insurance or reimbursement; • resulting from willful misconduct; or • revoked based on failure to follow property management requirements
Government-Furnished	Always retained even if incorporated or combined	Always with Government as above, except when under competed or commercial item fixed-price contracts

*Alternative framework can apply by agreement.

Government Property and Risk of Loss: Grants and CAs

- Title and risk of loss generally remain with contractor subject to conditions:
  - Can only be used for project purposes during performance
  - Cannot be encumbered (e.g., with liens)
  - Must provide access for other federal purposes
  - Cannot use in services for less than fair-market fees
  - Must go through disposition procedures generally resulting in transfer to the U.S. Government or another awardee, sale, or retention by the original awardee, with the U.S. Government obtaining a portion of any fair market value received by the original awardee
- Exceptions exist for low-value items (e.g., ≤$5,000 per unit value)

Questions?

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