Research Compliance: 2016/2017 Year In Review

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Presented To:

Agenda

- OIG Work Plan FY2017
- Research Related Guidance Documents/FAQs/Q&A Documents
- Integrated Addendum to ICH GCP
- Clinical Trials Registration & Results Final Rule
- Revised Common Rule
- National Academies of Sciences, Engineering and Medicine Report
- 21st Century Cures Act
- Legislative Actions Taken to Reduce Regulatory Burden
- Human Research Subjects Protections Enforcement Actions
- DOJ/HHS OIG Actions/Settlements
- Research Misconduct Enforcement Actions
- Removing Barriers to Clinical Research Act of 2016

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OIG Work Plan FY2017

OIG Work Plan FY2017 Overview

- The Work Plan highlights the priorities that the OIG's more than 1,700 employees will have as they:
  1. Conduct audits, evaluations, investigations;
  2. Provide guidance; and
  3. Impose civil monetary penalties, assessment and administrative sanctions.
- Familiarity with the focus of the OIG work plan is crucial. For FY 2016, the OIG reported
  1. 3,635 exclusions (individuals and entities);
  2. 844 criminal actions; and
  3. 708 civil actions.
- For FY 2016, the OIG
  - Reported expected recoveries of over $5.66B, consisting of nearly $1.2B in audit receivables and about $4.46B in investigative receivables; and

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OIG Work Plan FY2017

CMS Other Providers and Suppliers

- **Data Brief on Financial Interests Reported Under the Open Payments Program (New)**

  The Physician Payments Sunshine Act requires that manufacturers disclose to CMS payments made to physicians & teaching hospitals. Manufacturers & group purchasing organizations must also report ownership & investment interests held by physicians. OIG will analyze 2015 data extracted from the Open Payments website to determine:

  1. The number & nature of financial interests;
  2. How much Medicare paid for drugs and DMEPOS ordered by physicians who had financial relationships with manufacturers and group purchasing organizations; and
  3. The volume and total dollar amount associated with drugs & DMEPOS ordered by these physicians in Medicare Parts B and D for 2015.

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OIG Work Plan FY2017

CMS Other Providers and Suppliers

- **Review of Financial Interests Reported Under the Open Payments Program**

  OIG will determine:

  1. The extent to which data in Open Payments System is missing or inaccurate;
  2. The extent to which CMS oversees manufacturers' and group purchasing organizations' compliance with data reporting requirements; and
  3. Whether the required data for physician & teaching hospital payments are valid.

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OIG Work Plan FY2017

Public Health Reviews - CDC

- **CDC – Oversight of the Federal Select Agent Program**

  OIG will examine CDC's inspections of entities registered with the program & CDC's oversight of entities' annual internal inspections. In specific, OIG will:

  1. Examine number, frequency & results of CDC inspections and CDC's response to and follow-up on noncompliance with regulatory requirements identified during inspections (Part 1); and

  2. Examine extent to which CDC ensures that sampled entities comply with annual internal inspection requirements & that identified observations are corrected. OIG will also identify any differences and/or similarities b/t observations identified in CDC's and the entities' inspections for sampled entities (Part 2).

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OIG Work Plan FY2017

National Institutes of Health (NIH)

- **Review of NIH Data Controls to Ensure Privacy & Protection of Volunteers in Precision Medicine Initiative (New)**

  Precision Medicine Initiative plans to have more than 1 million volunteers provide their personal health information to NIH so researchers, providers and patients can develop individualized care. Maintaining data security and privacy is paramount to retaining the volunteer's trust and participation in the initiative. OIG will determine the controls that NIH has developed to ensure privacy and protection of the volunteer's personal health information.

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OIG Work Plan FY2017

NIH

- **Controls Over Subcontracting of NIH Grant and Contract Work**

  OIG will assess colleges' and universities' controls over the subcontracting of NIH grant and contract work. Specifically, OIG will determine whether colleges and universities effectively monitor the services subcontracted to other organizations and ensure that Federal funds are spent on allowable goods and services in compliance with selected cost principles and the terms and conditions of the grants and subcontracts. Cost principles for Educational Institutions at 45 CFR 75 are used in determining the allowable costs of work performed by colleges and universities under sponsored agreements.

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OIG Work Plan FY2017

NIH

- **Colleges' and Universities' Compliance with Cost Principles**

  OIG will assess colleges' and universities' compliance with selected cost principles. OIG will conduct reviews at selected colleges and universities on the basis of the dollar value of Federal grants received and input from HHS operating divisions and the offices of the Assistant Secretary for Financial Resources and the Assistant Secretary for Administration.

OIG Work Plan FY2017

NIH

- **Superfund Financial Activities for FY2015 – Mandatory Review**

  The NIH National Institute of Environmental Health Sciences (NIEHS) provides Superfund Research Program funds for university-based multidisciplinary research on human health and environmental issues related to hazardous substances. Federal law and regulations require OIG to conduct an annual audit of the Institute's Superfund activities. OIG will review payments, obligations, reimbursements, and other uses of Superfund money by NEIHS.

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OIG Work Plan FY2017

NIH

- **Review of NIEHS' Funding for Bisphenol A (BPA) Research**

  OIG will determine the extent to which NIH's NIEHS has conducted and funded research on the safety of BPA since 2000 as well as roles that other HHS programs and agencies play in planning, funding and conducting NIEHS's BPA research. OIG will also determine the extent to which NIEHS followed its grant application processes related to peer review when awarding funds for BPA research.

Slide 11

A1 May want to add the OHRP audit initiative. I believe the audience would be interested in this topic. See page

Author, 12/1/2015

OIG Work Plan FY2017

Public Health Legal Activities

- **Violations of Select Agent Requirements**

  In 2005, HHS issued final regulations on possession, use and transfer of select (biological) agents and toxins that applies to academic institutions; commercial manufacturing facilities; and Federal, State, and local laboratories. 42 CFR Part 73. The final regulations authorize OIG to conduct investigations and impose civil monetary penalties against individuals or entities for violations of 42 CFR Part 73. OIG is continuing to coordinate efforts with CDC, FBI, and USDA to investigate violations of Federal requirements for the registration, storage, and transfer of selecte agents and toxins.

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Financial Reviews

- **OIG Reviews of Non-Federal Audits**

  Pursuant to the Uniform Grant Guidance at 2 CFR Part 200, certain entities receiving Federal awards are required to have annual organization-wide audits of all Federal funds that they receive. OIG will continue to review the quality of audits conducted by non-Federal auditors, such as public accounting firms and State auditors, in accordance with the uniform grant guidance.

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Research Related Rules/Guidance Documents/FAQs/Q&A Documents

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2016 Research Related Documents

Date	Title	Type of Document	Issuing Agency
3/16	**NIH / FDA Draft Guidance Protocol Template for Phase 1 & 2 IND/IDE Applications**	Draft Guidance	NIH/FDA
5/16	Use of Electronic Health Record Data in Clinical Investigations – Guidance for Industry	Procedural	FDA
6/16	Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies – Draft Guidance for Industry and FDA Staff	Draft Guidance	FDA
6/16	**FDA Categorization of IDE Devices to Assist CMS with Coverage Decisions – Draft Guidance for Sponsors, Clinical Investigators, Industry, IRBs and FDA Staff**	Draft Guidance	FDA
6/16	**Expanded Access to Investigational Drugs for Treatment Use – Qs & As; Guidance for Industry**	Procedural	FDA
6/16	**NIH Single IRB (sIRB) Policy**	Final Policy	NIH
6/16	Charging for Investigational Drugs Under an IND – Qs & As	Procedural	FDA
7/16	Adaptive Designs for Medical Device Clinical Studies – Guidance for Industry and FDA Staff	Final Guidance	FDA
8/16	**IRB Written Procedures – Draft Guidance for Institutional and IRBs**	Draft Guidance	FDA/OHRP
9/16	**GCP Training for NIH Awardees Involved in NIH Funded Clinical Trials**	Policy	NIH
10/16	Collection of Race and Ethnicity Data in Clinical Trials – Guidance for Industry and FDA Staff	Final Guidance	FDA
12/16	**Use of Electronic Informed Consent –Qs & As – Guidance for IRBs, Investigators, and Sponsors**	Procedural	FDA/OHRP

NIH / FDA Draft Guidance Protocol Template for Phase 2 & 3 IND/IDE Applications

NIH / FDA Draft Guidance Protocol Template for Phase 2 & 3 IND/IDE Applications

- Scope: An instructional and sample text protocol template for NIH funded investigators to use in writing protocols for phase 2 or 3 clinical trials that require Investigational New Drug application (IND) or Investigational Device Exemption (IDE) applications.
- Goal: Encourage and make it easier for investigators to prepare protocols that are consistently organized and contain all the information necessary for the clinical trial to be properly reviewed.
- NIH and FDA sought public comment on draft template; comment period ended April 2016

FDA Categorization of IDE Devices to Assist CMS with Coverage Decisions

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FDA Categorization of IDE Devices – Draft Guidance

- Modifies FDA's policy on categorizing investigational device exemption (IDE) devices into either Category A (experimental/investigational) or Category B (non-experimental/investigational) which will assist CMS in determining whether an IDE device should be reimbursed by CMS.

- New guidance needed because:
  1. FDA's 1995 policy regarding categorization of IDE devices did not adequately articulate criteria relevant to categorizing certain studies involving IDE devices such as feasibility studies;
  2. FDA's 1995 policy did not provide sufficient guidance regarding how a category designation may change from A to B;
  3. FDA's previous criteria did not consider all applicable regulatory pathways. (e.g. de novo submission);
  4. CMS changed from local Medicare Administrative Contractor review/approval of IDE studies to centralized review.approval of IDE studies effective January 1, 2015; and
  5. Interactions between FDA and CMS since that time have highlighted a need for changes to categorization in order to improve consistency.

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FDA Categorization of IDE Devices – Draft Guidance

- New Category A: Experimental Guidelines - …device for which 'absolute risk' of device type has not been established, i.e., initial safety and effectiveness (S&E) questions have not been resolved, & FDA is unsure whether device type is safe and effective. (42 CFR 405.201(b))

- FDA will consider a device to be in Category A if one or more of following:
  1. No PMA approval, 510(k) clearance or de novo request has been granted for proposed or similar device, and non-clinical and/or clinical data on proposed device do not resolve initial S&E questions.
  2. Proposed device has different characteristics compared to legally marketed device & information related to marketed device does not resolve initial S&E questions of proposed device. Available non-clinical and/or clinical data on proposed device also do not resolve these questions.
  3. Proposed device is being studied for a new indication/intended use for which information from proposed or similar device related to the previous indication does not resolve initial S&E questions. Available non-clinical and/or clinical data on proposed device relative to the new indication/intended use also do not resolve these questions.

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FDA Categorization of IDE Devices – Draft Guidance

- New Category B: Nonexperimental/Investigational Guidelines - …device for which incremental risk is primary risk in question (i.e., initial S&E questions are resolved) or it is known that device type can be safe and effective because, e.g., other manufacturers obtained FDA premarket approval or clearance for device type. (42 CFR 405.201(b))

- FDA will consider a device to be in Category B if one or more of following:
  1. No PMA approval, 510(k) clearance or de novo request granted for proposed or similar device; but available clinical data (e.g., feasibility study data) and/or non-clinical data for proposed or similar device resolve initial S&E questions.
  2. Proposed device - similar characteristics to legally marketed device & information related to marketed device resolve initial S&E questions for proposed device.*
  3. Proposed device being studied for new indication/intended use; but information from proposed or similar device related to previous indication resolves initial S&E questions.*

*Additional non-clinical and/or clinical data on proposed device may be used in conjunction with the leveraged information to resolve these questions.

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FDA Categorization of IDE Devices – Draft Guidance

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

	1995 Interagency Agreement	Draft Guidance
Changes	Detailed criteria were used to designate an IDE device category.	Criteria have been simplified to ensure that devices fall into the correct category.
Changes	Limited or no visibility to how a category change may occur as knowledge is gained.	Draft guidance provides an explanation of how a category change may occur.
Changes	No examples provided.	Examples provided.
The same	FDA review team makes the category designation.	Unchanged
The same	Category designation is to be based on the degree to which initial questions of safety and effectiveness are resolved.	Unchanged
The same	The categorization will then be used by CMS as part of its determination of whether or not items and services will be covered.	Unchanged

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Expanded Access to Investigational Drugs for Treatment Use – Qs & As

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FDA Expanded Access to Investigational Drugs for Treatment Use - & As

- Expanded access - use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient (with a serious or immediately life-threatening disease or condition who lacks therapeutic alternatives) rather than obtain information about a drug generally derived from clinical trials
- In 2009, FDA revised its IND regulations by removing the existing regulations on treatment use and creating subpart I of part 312 to consolidate and expand the various provisions regarding expanded access to treatment use of investigational drugs
- Under FDA's regulations, there are three categories of expanded access:
  1. Expanded access for individual patients, including emergency use (21 CFR 312.310);
  2. Expanded access for intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol (21 CFR 312.315); and
  3. Expanded access for widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) (21 CFR 312.320)

FDA Expanded Access to Investigational Drugs for Treatment Use – Qs & As

- Document developed to provide information to interested parties about most FAQs pertaining to implementation of FDA's regulations on expanded access to investigational drugs for treatment use under an IND. Document provides answers to 31 FAQs, including:

1. What is expanded assess?
2. Which regulatory submissions can be used to obtain expanded access to a drug under the 3 expanded access categories?
3. When should an expanded access protocol vs. an new expanded access IND be used?
4. What information should be included in an expanded access submission? See 21 CFR 312.305(b) and 312.310(b) for individual patient submissions or 312.315(c) for intermediate-size patient population submissions or 312.320(b) for treatment submissions.
5. Whether prospective IRB review/approval is required for all expanded access categories?

FDA Expanded Access to Investigational Drugs for Treatment Use – Qs & As

6. Whether expanded access submissions are subject to informed consent requirements?
7. How FDA categories/subcategorizes expanded access submissions?
8. Who can make a submission for individual patient expanded access? Either the sponsor of an existing IND or a licensed physician.
9. What are the roles of the patient's physician and FDA in determining if expanded access of an individual patient is appropriate?
10. Whether there can ben more than one intermediate-size patient population expanded access IND or protocol for a particular drug for the same disease or condition?
11. When can access for emergency use begin?
12. When can treatment begin under expanded access protocols not for emergency use?

NIH Single IRB Policy

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NIH Single IRB Policy

- June 21, 2016 – NIH Single IRB (sIRB) Policy for multi-site research of non-exempt human subjects research protocols funded by NIH and are carried out at more than one site in the United States
- Applies "only to studies where the same research protocol is being conducted at more than one site; it does not apply to studies that involve more than one site but the sites have different roles in carrying out the research."
- Per NIH email correspondence (12/2/16): If one site involved in a study has a different role than other sites, that site may elect to use a different IRB for reviewing and approving research; however, exception does not exempt remaining sites from the expectation that they will use a single IRB.

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NIH Single IRB Policy (cont'd)

- Policy criticism - Little guidance provided to facilitate Policy implementation
- NIH will issue guidance and provide resources to assist awardees in adapting to the change before policy's effective date and post guidance at: http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/models-irb-review

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NIH Single IRB Policy (cont'd)

- Guidance will address:
  - How costs are charged as direct vs. indirect costs;
  - sIRB selection considerations;
  - Content of sIRB plan submitted with applications/proposals;
  - Exemption request process;
  - Roles and responsibilities of the sIRB and participating sites;
  - Model authorization agreement, e.g., SMART IRB Model;
  - Models for gathering and evaluating information from reliant sites re: community attitudes and acceptability of proposed research;
  - Model communication plan identifying documents to be completed and shared with those involved
- December 2016: NIH announced a revised effective date from May 25, 2017 to September 25, 2017

IRB Written Procedures

FDA/OHRP Draft Guidance – IRB Written Procedures

- Highlights that written IRB procedures should:
  - Be detailed so IRB members/staff understand how to carry out duties consistently and effectively in ways that ensure that the rights and welfare of subjects are protected, and that the IRB operates in compliance with the regulations;
  - Identify who carries out specific duties by reference to position title (e.g., IRB Administrator) rather than by employee name;
  - Be available to investigators so investigators are aware of IRB's requirements and facilitate investigator compliance with IRB requirements; and
  - Help regulators understand how IRB operates/fulfills its regulatory responsibilities.
- Includes an IRB Written Procedures Checklist that incorporates both HHS and FDA regulatory requirements for IRB written procedures and additional topics that FDA and OHRP recommend including in IRB written procedures, including IRB Scope and Authority; IRB Membership; IRB Functions and Operations; and IRB Records.

NIH GCP Training Policy

NIH GCP Training Policy

- Scope: Applies to NIH-funded **investigators** and **clinical trial staff** who are responsible for the conduct, management and oversight of NIH-funded **clinical trials ("CTs")**

  - Investigator: Individual responsible for the conduct of CT at a site. If CT conducted by a team of individuals, investigator is responsible leader, e.g., principal investigator

  - CT staff: Individuals responsible for study coordination, data collection and data management, e.g., mange participant recruitment and enrollment, maintain consistent study implementation, data management, ensure integrity and compliance with regulatory/reporting requirements; seek informed consent; enroll and meet with research participants; collect/record information from research participants

  - CT: Research study in which one or more human subjects are prospectively assigned to one or more interventions (including placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes

NIH GCP Training Policy

- GCP Training Requirements

  - **Content:** Principles of ICH GCP outlined In Section 2 ICH GCP (R2)

    - Acceptable GCP courses include the NIAID GCP Learning Center website (http://gcplearningcenter.niaid.nih.gov) and National Drug Abuse Treatment Clinical Trials Network (https://gcp.nihtraining.com/)

  - **Outcome:** Demonstrates individual have attained knowledge of CT quality standards for designing, conducting, recording and reporting trials that involve human research participants

  - **Effective Date**: January 1, 2017 to have either taken steps to meet the expectation, e.g., signed up to take a course, or have received training*

  - **Refresher**: Every 3 years

  - **Documentation**: Training recipients must retain documentation of training

Use of Electronic Informed Consent

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Use of Electronic Informed Consent – Qs and As

- Provides answers to 16 common questions about using electronic systems and processes that may employ multiple electronic media to obtain informed consent for both HHS-regulated human subject research and FDA-regulated clinical investigations of medical products, including human drug and biological products, medical devices, and combinations thereof
- Focuses on procedures to be followed when using electronic informed consent (eIC) to help:
  1. Ensure protection of the rights, safety and welfare of human subjects;
  2. Facilitate the subject's comprehension of the information presented;
  3. Ensure appropriate documentation is obtained when multiple electronic media are used; and
  4. Ensure the quality and integrity of eIC data included in FDA applications and made available to FDA during inspections.

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Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)

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Why Change?

- Amendments were needed to:
  - Encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording and reporting while continuing to ensure human subject protection and data integrity; and
  - Update standards regarding electronic records and essential documents standards in order to increase clinical trial quality and efficiency
- November 2016 - Adoption by the Regulatory Members of the ICH Assembly

Major Changes

- ALCOA"C" source document requirements
- Sponsor focused risk-based trial quality management guidance, including risk based monitoring (RBM)
- Investigator oversight responsibilities
- Sponsor oversight responsibilities regarding vendors
- Sponsor responsibilities regarding serious breaches
- Computer validation, electronic record and essential document standards

Source:
http://www.therqa.com/assets/js/tiny_mce/plugins/filemanager/files/Publications/Online_Articles/ICH_E6_re written_to_reflect_recent_GCP_findings.pdf

Clinical Trials Registration & Results Final Rule & NIH Complimentary Policy

Clinical Trials Registration and Results

- September 2016 HHS issued a final rule and NIH issued a new policy to increase the availability of information about clinical trials via ClinicalTrials.gov
  - HHS final rule describes requirements for registering and submitting summary results information for certain clinical trials to ClinicalTrials.gov.
  - NIH Complementary Policy expands the scope of the final rule to apply to *all* clinical trials funded by NIH, regardless of whether they are subject to the Final Rule
- Both initiatives aim to help ensure that information about clinical trials and their results are made publicly available in a timely manner

Clinical Trials Registration and Results (cont'd)

Element	HHS Final Rule	NIH Policy
Scope Applicability	Applies to applicable CTs of FDA-regulated drug, biological & device products & pediatric post-market surveillance studies of devices required by FDA Applicable CTs (1) CTs of drug and biological products that are controlled, clinical investigations, other than phase 1 investigations, of a product subject to FDA regulation; and (2) prospective clinical studies of health outcomes comparing an intervention with a device product against a control in humans (other than small feasibility studies) or any pediatric post-market surveillance studies required by FDA Does not apply to phase 1 trials or small feasibility device studies Applies to public and private sector sponsors and other entities who meet the definition of a responsible party	All NIH funded CTs including phase 1 CTs & trials that do not involve FDA regulated products, e.g., behavioral intervention trials Applies to NIH-funded CT applications or proposals received by NIH on or after effective date. Applies to NIH-conducted CTs initiated on or after policy effective date.
When register	NLT 21 days after enrollment of first participant	Same
Required registration data elements	Descriptive information, recruitment information, location & contact information, as well as administrative data.	Same

Clinical Trials Registration and Results (cont'd)

Element	HHS Final Rule	NIH Policy
Time trial results submitted	NLT 12 months after primary completion date; Possible delay of up to an additional 2 years for trials of unapproved products or of products when initial FDA marketing approval/clearance is sought or approval/clearance of a new use is sought.	Same
Results information elements submitted	Includes participant flow, demographic & baseline characteristics, outcomes & statistical analyses, adverse events, the protocol and statistical analysis plan & administrative information.	Same
Potential Non-compliance Consequences	Identify CT record as non-compliant in ClinicalTrials.gov Federal grant funding can be withheld if required reporting cannot be verified. Civil monetary penalties of up to $10,000/day (amount to be adjusted going forward)	Same May lead to suspension or termination of grant or contract funding Considered in future funding decisions
Effective Date	January 18, 2017	January 18, 2017

Revised Common Rule

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History

- **July 26, 2011 – HHS and OMB, Office of Science and Technology Policy (OSTP) issued an ANPRM in the *Federal Register***
  - Requested comment on how to modernize/revise Common Rule
  - Asked public to answer 74 questions
  - 1,051 comments received
- **September 8, 2015 – 16 Common Rule agencies published NPRM in *Federal Register***
  - Asked an additional 88 questions
  - Referenced multiple not yet developed decision tools, guidance documents, model agreements & document templates
  - Received 2,186 comments
- **January 19, 2017 – 16 Common Rule agencies published Final rule in *Federal Register***

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Revised Common Rule

- Compliance Dates
  - Cooperative Research/Single IRB – January 19, 2020
  - Research initially IRB approved, waived or deemed exempt before January 19, 2018 need not comply with New Common Rule; comply with the old Common Rule (Revised January 15, 2009)
  - Research initially IRB approved, waived or deemed exempt on or after January 19, 2018 shall comply with the new Common Rule (Revised January 19, 2017)

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Revised Common Rule Highlights

- Regulatory Oversight of IRBs Unaffiliated with Engaged Institutions
- Revised Exempt Categories
- Limited IRB Review
- New Approval Criteria
- Informed Consent
  - Broad Consent
  - Public Accessibility of Informed Consent Forms
  - Waiver of Informed Consent for Recruitment
- Changes to Continuing Review
- Single IRB Review of Multisite Research

National Academies of Sciences, Engineering and Medicine Report

Report Overview

- **Optimizing the Nation's Investment in Academic Research - A New Regulatory Framework for the 21st Century**

- Recommendations:
  - Congress authorize/President appoint independent national commission to examine and update the frameworks governing research involving human subjects (Belmont 2.0);
  - Withdraw NPRM Revising the Common Rule and not revise the Rule until a national commission issues recommendations and public has opportunity to comment;
  - Make changes to current regulations governing research involving select agents, export controls and intellectual property

The 21St Century Cures Act

"An innovation game-changer, a once-in-a-generation, transformational opportunity to change the way we treat disease"

21ST CENTURY CURES ACT

Expedites the DISCOVERY, DEVELOPMENT and DELIVERY of new treatments and cures and maintains America's global status as the leader in biomedical innovation

- **DISCOVERY**
  - Provides NIH with $4.8B in new research funding to:
    - ❖ Advance Precision Medicine Initiative ($1.5B)
    - ❖ Bolster "Cancer Moonshot" ($1.8B)
    - ❖ Invest in the BRAIN initiative to improve understanding of diseases like Alzheimer's

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21ST CENTURY CURES ACT

- **DEVELOPMENT**
  - Modernizes clinical trials and how safety and efficacy data is accumulated/analyzed;
  - Incorporates patient perspectives into drug development/regulatory review process;
  - Supports broader, more collaborative development and utilization of biomarkers, which help assess how therapy is working, earlier in the process;
  - Streamlines regulations and provides more clarity and consistency for innovators developing health software and mobile medical apps, combination products, vaccines, and regenerative medicine therapies;
  - Incentivizes development of drugs for pediatric diseases and medical countermeasures, and empowers FDA to utilize flexible approaches in reviewing medical devices that represent breakthrough technologies;
  - Provides FDA with $500m for regulatory modernization and gives the agency the ability to recruit and retain the best and brightest scientists, doctors, and engineers.

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21ST CENTURY CURES ACT

- **DELIVERY**
  - Improve delivery of new drugs and devices to the right patients at the right time by:
    - ❖ Ensuring electronic health record systems are interoperable for seamless patient care and help fully realize the benefits of a learning health care system; and
    - ❖ Improving education for health care providers and help facilitate seniors' access to the latest medical technology

2016 Legislative Actions to Reduce Research Regulatory Burden

Legislative Actions Taken to Reduce Research Regulatory Burden

Actions	21st Century Cures (Passed House and Senate. Signed into law Dec. 13) Link to PDF	American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16.) Link to PDF	National Defense Authorization Act (Passed House and Senate. Conference report language adopted by Senate on Dec. 8) Link to PDF
Research Policy Board A public-private entity recommended by the National Academies "to foster more effective conception, development and harmonization of research regulations." The NSB similarly recommended an interagency, intersector committee with stakeholder and OMB/OIRA representation.	Established by the Director of OMB. 10 or fewer federal members (OIRA, OSTP, HHS, NSF and others that support or regulate research). 9-12 representatives of academic or other non-profit research institutions or organizations with relevant expertise. Appointed through a formal process including nomination by members of the research community. The process would be established by the Secretary (in consultation with the Federal membership). This is likely in error, as in previous iterations the RPB was established by the HHS Secretary due to HELP jurisdiction, now the OMB Director. The board is charged with coordinating and improving regulations and policies; discussing policy and regulatory gaps and challenges; and ongoing assessment of regulatory burden. Expert subcommittees can be formed as needed. Not explicitly tasked with addressing prospective regulations and policies. Report to Congress and GAO evaluation. Sunsets 9/30/20.	Not addressed.	Not addressed.

Legislative Actions Taken to Reduce Research Regulatory Burden

Actions	21st Century Cures (Passed House and Senate. President Obama to sign.)	American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16)	National Defense Authorization Act (Passed House and Senate. Conference report language adopted by Senate on Dec. 8)
Interagency Working Group on Research Regulations	Not addressed.	To be established by OMB in coordination with OSTP. Charged with reviewing existing regulations and making recommendations for eliminating, streamlining or improving regulations and processes with the goal of reducing burden on researchers and IHEs. Directed to consult with stakeholders, an improvement over the existing research business models (interagency) working group. Requires a report to congressional committees annually for the first four years.	Not addressed.
Subrecipient Monitoring - reduce unnecessary or redundant oversight. Recommendations - National Academies - amend the UG to clarify applicability to IHEs only for project and performance monitoring. GAO - target higher risk subrecipients.	NIH Director directed to reduce administrative burden, including possible exemption where the subrecipient is subject to single audit and use of collaborative grant models or other structures allowing for multiple prime awardees.	Not addressed.	Not addressed.

Legislative Actions Taken to Reduce Research Regulatory Burden

Actions	21st Century Cures (Passed House and Senate. President Obama to sign.)	American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16)	National Defense Authorization Act (Passed House and Senate. Conference report language adopted by Senate on Dec. 8)
Micropurchase Threshold - Increase to $10,000 with the opportunity for higher thresholds. Recommendations - National Academies. GAO - target higher risk purchases.	Not addressed.	$10,000 or higher threshold as determined by the head of the relevant executive agency and consistent with audit findings, institutional risk assessment, or State law. Applicable only to NSF, NASA and NIST.	$10,000 or higher threshold as determined by the head of the relevant executive agency and consistent with clean audit findings, institutional risk assessment, or State law. Grants, cooperative agreements, and contracts for all federal agencies.
Review Financial Conflict of Interest Policies - harmonizing policies and reducing burden - Recommendations: National Academies - Federal-wide policy to be developed by Congress and OSTP; NSB and GAO - evaluation of the 2011 revisions to the PHS COI regulations.	Within two years of enactment. Led by the HHS Secretary. Review to include the minimum threshold for reporting and just-in-time reporting.	Not addressed.	Not addressed.
Evaluation of Financial Reporting Procedures and requirements with the goal of minimizing burden.	Specific to HHS/NIH. Avoid duplication between HHS and NIH and minimize burden.	Not addressed.	Not addressed.

Legislative Actions Taken to Reduce Research Regulatory Burden

Actions	21st Century Cures (Passed House and Senate. President Obama to sign.)	American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16)	National Defense Authorization Act (Passed House and Senate. Conference report language adopted by Senate on Dec. 8)
Review Animal Research Regulations - goal of reducing administrative burden. Recommendations - National Academies: OSTP to convene - goal of unified federal approach. NSB - engage all regulatory, independent and certification bodies.	Within two years of enactment. NIH, USDA and FDA are charged with identifying and eliminating inconsistent, overlapping or unecessarily duplicative regulations and policies and improving coordination.	Not addressed.	Not addressed.
Clarify or Affirm Alternatives to Effort Reporting - Recommendations - NSB: OMB issue a memo of clarification indicating that the payroll certification method is acceptable to the Federal Government. National Academies: OMB affirm that IHEs may take advantage of the flexibility of the UG for documentation of personnel expenses.	Directs the HHS Secretary to clarify applicability of the Uniform Guidance for management and certification systems, including those for documentation of personnel expenses. It would be our understanding that the intent is that the HHS Secretary affirm the flexibility under the UG in documenting personnel expenses.	Not addressed.	Not addressed.

Legislative Actions Taken to Reduce Research Regulatory Burden

Actions	21st Century Cures (Passed House and Senate. President Obama to sign.)	American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16)	National Defense Authorization Act (Passed House and Senate. Conference report language adopted by Senate on Dec. 8)
Unified Grant Format - Recommendations - National Academies	Not addressed.	Working group to consider a simplified, unified grant format for use by all agencies.	Not addressed.
Preliminary Proposals - Recommendations: NSB and GAO	Not addressed.	Consideration by interagency WG	Not addressed.
Simplified Budget Proposals - Recommendations - NSB; GAO	Not addressed.	Consideration by interagency WG	Not addressed.
Greater Use of Just-in-time - Recommendations - NSB and Academies reports	Not addressed.	Working Group to consider.	Not addressed.
Create a Centralized Researchers Profile Database - Recommendations - National Academies	Not addressed.	WG to establish a centralized database for biosketches, CVs, licenses, and related documents. Consider incorporating existing databases. To be utilized for all grant proposals "to the extent practicable."	Not addressed.

Legislative Actions Taken to Reduce Research Regulatory Burden

Actions	21st Century Cures (Passed House and Senate. President Obama to sign.)	American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16)	National Defense Authorization Act (Passed House and Senate. Conference report language adopted by Senate on Dec. 8)
Create a Centralized Assurances Repository - Recommendations - National Academies: "similar to the Single Audit Clearinghouse of the FDP."	Not addressed.	For all assurances required for federal grants.	Not addressed.
Review and Simplify Progress Reports - Recommendations - NSB, National Academies: single uniform format.	Not addressed.	Consider limiting reports to performance outcomes. The RBM working group has created the Research Performance Progress Report, a unified federal progress report. Potential for further simplification and limiting to performance outcomes.	Not addressed.

Reports cited include the National Science Board report "Reducing Investigators' Administrative Workload for Federally Funded Research," the National Academies Report "Optimizing the Nation's Investment in Academic Research;" and the GAO report "Federal Research Grants: Opportunities Remain for Agencies to Streamline Administrative Requirements"

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Human Research Subjects Protections Enforcement Actions

FDA and OHRP Enforcement Actions

Type of Action	FDA	OHRP
Inspections ■Conducted by FDA in FY2015 ■Opened by OHRP in FY2015	CI – 822 IRB – 138 Sponsor - 117	For cause – 7 Not for cause - 4
Noncompliance Letters Issued ■FDA Warning Letters (OAIs) ■OHRP Determination Letters (Noting Noncompliance)	CI – 6 IRB – 4 Sponsor - 2	FWA Holding Institution – 9
Disqualifications (CIs/IRBs/Sponsors)	1	0
Debarments (CIs/IRBs/Sponsors)	1	0
IRB Restrictions or Suspensions	0	0

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FDA Common Findings - CIs

- Failure to follow the investigational plan and/or regulations
- Protocol deviations
- Inadequate recordkeeping
- Inadequate accountability for the investigational product
- Inadequate communication with the IRB
- Inadequate subject protection – failure to report AEs and informed consent issues

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FDA Common Findings – IRBs [A4]

- Inadequate initial and/or continuing review
- Inadequate SOPs
- Inadequate membership rosters
- Inadequate meeting minutes
- Quorum issues
- Subpart D issues
- Inadequate communication with CI/institution
- Specific to devices – lack of or incorrect SR/NSR determination

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Slide 66

A4 Based on FY2014 Bimo stats; may need to revise when we get FY2015 Bimo stats.
Author, 11/23/2015

OHRP

Human Research Protections
OHRP Determination Letters

Date	Institution	Issue(s) Summary
10/13/15 2/2/16	San Diego State University	▪ Informed consent documents (i.e., telephone screening consent script and informed consent forms) failed to include basic elements ▪ Investigator implemented changes to research without prior IRB review ▪ IRB approved an advertisement that overpromised or gave a false impression of the likelihood of benefit in violation of 45 CFR 46.116(a)(3) ▪ IRB lacked sufficient information to make determinations required for approval of research, i.e., IRB conditionally approved a study when it should have deferred its approval
12/23/15	Oregon Health and Science University	▪ IRB lacked sufficient information to make determinations required for approval of research
1/7/16	Tulane University	▪ Informed consent document for one study did not include an adequate explanation of the purposes of the research in language understandable to the subject or representative ▪ Informed consent document for another study did not describe the risks of a research indicated biopsy
1/28/16	Baylor College of Medicine	▪ Informed consent documents for a study that were reviewed and approved by the IRB failed to include or adequately address certain applicable basic elements
2/23/16	University of Texas, San Antonio	▪ IRB lacked sufficient information to make determinations required for approval of research ▪ Research conducted without IRB review and approval ▪ Failure to report serious noncompliance to OHRP

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Human Research Protections
OHRP Determination Letters

Date	Institution	Issue(s) Summary
4/8/16	University of Virginia	▪ No findings of noncompliance
5/5/16	Suffolk University	▪ Institution did not have written IRB)procedures that adequately described certain activities
5/5/16	University of Nebraska Medical Center	▪ Failure of investigator to obtain the legally effective informed consent of subjects when the IRB did not waive obtaining informed consent ▪ Changes to research initiated without IRB review and approval
5/16/16	University of New Orleans	▪ No findings of noncompliance
7/14/16	Northwestern University	▪ No findings of noncompliance
9/27/16	George Washington University	▪ No findings of noncompliance
9/27/16	North Carolina, Chapel Hill	▪ IRB approved research contingent upon substantive modifications or clarifications directly relevant to IRB approval criteria without requiring additional review by the convened IRB
9/27/16	West Virginia School of Osteopathic Medicine	▪ No findings of noncompliance

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Human Research Protections
OHRP Investigations

Ongoing priorities for the OHRP's Division of Compliance Oversight

- **Findings in recent determination letters….**
  - Research conducted without IRB review and/or approval
  - Failure of IRB to review HHS grant applications
  - Lacking sufficient information to make determinations required for approval
  - Inadequate review at convened meetings
  - IRB members lacking expertise to make thoughtful determinations required for approval
  - Approval of research not approved by the IRB
  - Contingent approval of research with substantive changes expected, yet no additional review by convened IRB
  - Meetings convened without quorum (i.e., not enough members present, no non-scientist present, etc.)
  - Meeting convened by IRB members with a COI
  - Inadequate continuing review
  - Failure to conduct continuing review at least once a year
  - Inappropriate use of expedited review procedures
  - Failure to advise IRB members of expedited approvals
  - Expedited review conducted by someone other than an IRB member

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Human Research Protections
OHRP Investigations

Ongoing priorities for the OHRP's Division of Compliance Oversight

- **Findings in determination letters (cont.)**
  - Failure to report unanticipated problems, noncompliance, suspensions, terminations, etc. to IRB, IO, or OHRP
  - Changed to researcher initiated without IRB review and approval
  - Inappropriate application of exempt categories of research
  - Failure of Investigator to obtain legally effective and/or to document Informed Consent or of the IRB to waive requirements
  - Failure to provide a copy of the signed ICF to the subject (or their representative)
  - Inadequate ICF (e.g., lacks key elements, language too complex, exculpatory language, etc.)
  - IRB membership is not aligned with standards/rules/guidance
  - Poor documentation (minutes, records, files, retention of information)
  - Lack of appropriate written policies and SOPs
  - Lack of OHRP-approved FWA
  - IRB failure to determine that criteria for IRB approval are satisfied
  - Failure of IRB to make required findings when reviewing research involving children or prisoners.
  - Failure to notify Investigator / Institution of IRB actions
  - Failure of signatory official to fulfill obligations

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FDA

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Human Research Protections
FDA Warning Letters – Clinical Investigators

Date	Investigator	Issues(s) Summary
11/2/15	Thomas S. Tooma, M.D.	▪ Sponsor-investigator failed to submit an IND before conducting a clinical investigation involving an investigational new drug ▪ Sponsor-investigator failed to ensure proper monitoring of the clinical investigation ▪ Investigator failed to maintain adequate records of drug disposition, including dates, quantity and use by subjects
12/16/15	Gregory J. Tracey, M.D.	▪ Investigator failed to ensure that the investigation was conducted according to the investigational plan - enrolled a subject who did not meet eligibility criteria
2/19/16	Alexander Neumeister, M.D.	▪ Investigator failed to maintain adequate and accurate case histories ▪ Investigator failed to ensure that the investigation was conducted according to the investigational plan - enrolled subjects who did not meet eligibility criteria and did not complete a protocol specific test 24 hours after dosing
3/10/16	Cheta Nand, M.D.	▪ Investigator failed to ensure that the investigation was conducted according to the investigational plan - enrolled subjects who did not meet eligibility criteria
3/29/16	Benedict S. Liao, M.D.	▪ Investigator failed to ensure that the investigation was conducted according to the investigational plan - enrolled subjects who did not meet eligibility criteria and did not complete laboratory tests/imaging procedures at required time intervals ▪ Investigator failed to maintain adequate and accurate case histories ▪ Investigator failed to maintain adequate records of drug disposition, including dates, quantity and use by subjects

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Human Research Protections
FDA Warning Letters – Clinical Investigators

Date	Investigator	Issues(s) Summary
5/19/16	Jose Giron, M.D.	▪ Investigator failed to ensure that the investigation was conducted according to the investigational plan - failed to provide biological samples to central laboratory and failure to provide correct dose of investigational drug to subjects
6/28/16	John D. Gabriel, M.D.	▪ Investigator failed to ensure that the investigation was conducted according to the investigational plan – 25 subjects were randomized and received study drug prior to receipt of serum creatinine levels and investigator overdosed 2 subjects because investigator did not have the required test results at the time subjects were randomized and received study drug

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Human Research Protections
FDA Warning Letters – IRBs

Date	IRB	Issues(s) Summary
11/10/15	Monmouth Med Ctr IRB	▪ IRB failed to determine (and document) at time of initial review that studies involving children were in compliance with 21 CFR 50, subpart D ▪ IRB failed to review proposed research at convened meetings at which a majority of the members of the IRB were present, including at least one non-scientific member ▪ IRB failed to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings
2/24/16	Jamaica Hospital Med Ctr IRB	▪ IRB failed to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings and a list of IRB members
3/1/16	Pikeville Med Ctr IRB	▪ IRB failed to prepare, maintain and follow required written procedures governing functions and operations of the IRB ▪ IRB failed to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings ▪ IRB failed to review proposed research at convened meetings at which a majority of the members of the IRB were present, including at least one non-scientific member ▪ IRB failed to conduct continuing review of research not less than once per year
4/7/16	Oeyama-Moto Cancer Research Foundation IRB	▪ IRB failed to prepare, maintain and follow required written procedures governing functions and operations of the IRB ▪ IRB failed to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings ▪ IRB failed to notify investigators and the institution in writing of its decision to approve/disapprove research or of modifications required to secure IRB approval

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DOJ/HHS OIG Actions

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Lexington Couple Pleads Guilty to Grant Fraud

- 2/10/16: DOJ announces that a Lexington couple admitted in federal court that they submitted false claims related to federal grants from NIH and defrauded the government out of hundreds of thousands of dollars.
  - According to court documents, Ms. Brue certified on behalf of Telehealth Holdings, LLC, a company owned by Jerome Hahn, that company incurred expenses totaling $222,037 relating to two federal grants Telehealth received from NIH
  - Ms. Brue falsely certified that funds had been spent in accordance with grant rules and regulations
  - Ms. Brue plead guilty to making a false claim against the United States
  - Mr. Hahn plead guilty to conspiracy to defraud the Unities States
  - On March 30, 2016, U.S. District Judge sentenced Brue to seven months in prison, and an additional seven months on home detention. Brue was also ordered to pay $222,037 in restitution to NIH.
  - On June 13, 2016, U.S. District Judge sentenced Hahn to four months in prison and an additional six months on home detention. Hahn was also ordered to pay $222,037 in restitution to NIH.

Source: http://oig.hhs.gov/fraud/enforcement/criminal/index.asp

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U.S. District Court Orders $4.5M Civil Judgement Against Lexington Women and Her Medical Device Companies for Committing Grant Fraud

- 7/13/16: U.S. District Court enters a civil judgement against Vesta Brue and her companies, Life Techniques, Inc. and Care Team Solutions, LLC, to resolve False Claims Act allegations regarding defrauding NIH of millions of dollars over 8 years
  - NIH awarded Ms. Brue and her companies five (5) SBIR grants to support development of electronic pillboxes customized for specific patient populations
  - Ms. Brue acknowledged that they:
    - Made false statements in grant applications about company personnel, facilities and accounting systems;
    - Falsely stated on grant reports that they had spent grant funds for purposes of the grants and in compliance with grant regulations when in fact spent money on personnel expenses; and
    - Used grant money on business expenses not allowed under grant regulations, e.g., marketing and promotion expenses.
  - Government complained that Ms. Brue also falsified entries in her companies' accounting ledgers to conceal from NIH auditors that federal funds had been misspent.

Source: http://oig.hhs.gov/fraud/enforcement/criminal/index.asp

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Columbia University Agrees to Pay $9.5 Million to Settle Civil Fraud Allegations

- 7/14/16: DOJ and HHS OIG announces $9.5 Million settlement with Columbia University ("Columbia") for improperly seeking and receiving excessive cost recoveries in connection with research grants funded by NIH
  - The United States' Complaint alleged that from July 1, 2003, through June 30, 2015, Columbia impermissibly applied its "on-campus" indirect cost rate - instead of the much lower "off-campus" indirect cost rate - when seeking federal reimbursement for 423 NIH grants where the research was primarily performed at off-campus facilities owned and operated by the State of New York and New York City
  - The Complaint also alleged that Columbia failed to disclose to NIH that it did not own or operate these facilities and that Columbia did not pay for use of the space for most of the relevant period.
  - Columbia Admitted to Seeking and Receiving Cost Recoveries at the Higher "On-Campus" Rate for 423 Research Grants Even Though the Research Was Primarily Performed in Space Not Owned or Operated by Columbia

Source: http://oig.hhs.gov/fraud/enforcement/criminal/index.asp

Lexington KY Man and his Medical Device Company Sued for Grant Fraud

- 7/29/16: United States Government sued a Lexington man, Jerome Hahn, and the Lexington-based medical device company he owns, Telehealth Holdings, LLC, for violations of the False Claims Act alleging that they defrauded the government by submitting false claims in connection with federal grants.
  - According to the Complaint, Telehealth received three grants from the government worth over $600,000 to develop a sleep apnea monitoring system and for the development of pillboxes customized for specific patient populations.
  - The Complaint alleges Hahn and Telehealth did the following:
    - Made false statements in the grant applications about Telehealth's personnel, facilities and accounting systems;
    - Falsely stated on grant reports that they had spent grant funds for purposes of the grants and in compliance with grant regulations when in fact spent money on personnel expenses;
    - Used grant money on business expenses not allowed under grant regulations, e.g., marketing and promotion expenses;
    - Spent over $100,000 in grant funds for foreign goods and services, when grant regulations require recipients to use American goods/workers; and
    - Falsified accounting ledgers entries and created false invoices in order to conceal that federal funds had been misspent

Source: http://oig.hhs.gov/fraud/enforcement/criminal/index.asp

Research Misconduct

Recent ORI Administrative Actions

- **Andrew R. Cullinane, Ph.D., NIH:** ORI found that Dr. Cullinane, former postdoctoral fellow, Medical Genetics Branch, National Human Genome Research Institute ("NHGRI"), NIH, engaged in research misconduct ("RM") by knowingly reporting falsified and/or fabricated data and related images in two (2) publications and one (1) submitted manuscript by altering and/or reusing and/or relabeling experimental data.
- **Dr. Cullinane agreed for 3 years to:**
  - Have his research supervised and not participate in PHS-supported research until a supervision plan is submitted to/approved by ORI;
  - Have any institution employing him submit to ORI a certification that data provided by Dr. Cullinane is based on actual experiments and accurately reported; and
  - Be excluded from providing advisory services to PHS.
- Dr. Cullinane also agreed to retract or correct 2 of the publications.

Recent ORI Administrative Actions

- **Karen M. D'Souza, Ph.D., University of Chicago (UC):** ORI found that Dr. D'Souza, former Research Professional Associate, Department of Surgery, UC, engaged in RM in research supported by NHLBI, NIH grants K08 HL081472 and R01 HL107949 by including falsified and/or fabricated data in one (1) funded NIH grant, two (2) publications, two (2) posters, and one (1) presentation.

  Specifically, ORI found that Respondent reused and falsely relabeled and/or falsely spliced Western blot images, falsified the related densitometry measurements based on the falsified Western blots, and falsified and/or fabricated data for experiments that were not performed or from unrelated experiments.

Recent ORI Administrative Actions

- **Dr. D'Souza has agreed for 2 years to:**
  - Have her research supervised and not participate in any PHS-supported research until a supervision plan is submitted to/approved by ORI; supervision plan must ensure the scientific integrity of Dr. D'Souza's PHS-supported research contribution and include specific elements;
  - Have any institution employing her submit to ORI a certification that data provided by Dr. D'Souza is based on actual experiments and accurately reported; and
  - Be excluded from providing advisory services to PHS.
- Dr. D'Souza also agreed to retract 1 publication.

Recent ORI Administrative Actions

- **Meredyth M. Forbes, Albert Einstein College of Medicine:** ORI found that Ms. Meredyth M. Forbes, former Graduate Student, AECM, engaged in RM in research supported NIGMS, NIH grants R01 GM089979, T32 GM007491, R01 GM55101, and R01 GM88202 and NICHD, NIH grant T32 HD007502 by intentionally falsifying and/or fabricating data reported in the three (3) published papers and four (4) meeting presentations.

  ORI found that Ms. Forbes intentionally falsified and/or fabricated data for germ-cell development in zebrafish Dazap2 maternal-effect mutants (MDazap2) in one (1) paper and two (2) presentations when the mutants were not produced nor the data derived from them;

  ORI found that Ms. Forbes intentionally fabricated and/or falsified data for zebrafish embryogenesis and oocyte polarity in two (2) papers and two (2) presentations when the data were not obtained from actual experiments.

Recent ORI Administrative Actions

- **Ms. Forbes has agreed for 3 years to:**
  - Exclude herself from contracting/subcontracting with any US agency and from eligibility or involvement in US Government non-procurement programs;
  - Neither apply for nor permit her name to be used on any application, proposal, or other request for funds to the United States Government or any of its agencies
  - Neither receive nor be supported by funds of the United States Government made available through grants, subgrants, cooperative agreements, contracts, or subcontracts; and
  - Exclude herself from providing advisory services to PHS.

Recent ORI Administrative Actions

- **Zhiyu Li Ph.D., Mount Sinai School of Medicine**: ORI found that Dr. Zhiyu Li, former Postdoctoral Fellow, MSSM, engaged in RM in research that was supported by NCI, NIH grant R21 CA120017 by intentionally, knowingly, and recklessly including falsified and/or fabricated data in 10 published papers, submitted manuscript, poster presentation, and grant applications.

  ORI found that Dr. Zhiyu intentionally, knowingly, and recklessly claimed to have generated recombinant Clostridium perfringens (Cp) strains, Cp/sod-, Cp/sod-/PVL, and Cp/plc-/sod-/PVL, to depict the effects of recombinant Cp strains on their ability to destroy cancer cells in a murine model, when these bacterial strains were not produced nor the data derived from them, and by falsifying histopathological data reported in fifty-seven (57) images in two (2) published papers, one (1) submitted manuscript, two (2) poster presentations, and seven (7) of Respondent's supervisor's grant applications and fabricating the corresponding nineteen (19) summary bar graphs that were based on those false images.

Recent ORI Administrative Actions

- **ORI implemented the following administrative actions for a period of five (5) years:**
  - ORI debarred Dr. Zhiyu from contracting/subcontracting with any US Government Agency and from eligibility for, or involvement in, US Government Non-procurement Programs; and
  - ORI prohibited Dr. Zhiyu from providing advisory services to PHS.

Recent ORI Administrative Actions

- **Ricky Malhotra, Ph.D., University of Michigan and University of Chicago**: ORI found that Dr. Ricky Malhotra, former Research Assistant Professor, Department of Internal Medicine, UM, from 2005-2006, and Research Assistant Professor, Department of Surgery, UC, from 2007-2011, engaged in RM in research supported by NHLBI, NIH grants K08 HL081472 and R01 HL107949 by including falsified and/or fabricated data were included in three (3) NIH grant applications, one (1) NIH grant progress report, one (1) publication, seven (7) presentations, and one (1) image file by reusing and falsely relabeling Western blot gel images, falsifying the related densitometry measurements based on the falsified Western blots, and falsified and/or fabricated data for experiments that were not performed.
- Dr. Malhotra continued this falsification at UC, after the UM RM investigation was completed.

Recent ORI Administrative Actions

- **Dr. Malhotra agreed to the following administrative actions:**
  - If within five (5) years of the effective date of Agreement, Dr. Malhotra receives or applies for PHS support, he agreed to have research supervised for ten (10) years and to notify his employer/institution(s) of the terms of supervision; any supervision plan must be submitted to/approved by ORI; supervision plan must ensure the scientific integrity of Dr. Malhotra's PHS-supported research contribution and include specific elements;
  - If within five (5) years from the effective date of the Agreement, Dr. Malhotra receives or applies for PHS support, Dr. Malhotra agreed that for (10) years any institution employing him shall submit to ORI at six (6) month intervals certifications that data provided by Dr. Malhotra is based on actual experiments and accurately reported;
  - If no supervisory plan is provided to ORI, Dr. Malhotra agreed to provide certification to ORI on a quarterly basis for five (5) years that he has not engaged in, applied for, or had his name included on any application, proposal, or other request for PHS funds without prior notification to ORI.
  - For five years (5) exclude himself from providing advisory services to PHS.
- Dr. Malhotra also agreed to retract his publication.

Recent ORI Administrative Actions

- **John G. Pastorino, Ph.D., Rowan University School of Osteopathic Medicine**: ORI found that Dr. John G. Pastorino, Associate Professor, Department of Molecular Biology, RUSOM, engaged in RM in research supported by NIAAA, NIH grant R01 AA012897 and NCI, NIH grant R01 CA118356 by intentionally falsifying and/or fabricating data reported in eight (8) published papers, one (1) unpublished manuscript, and one (1) NIH grant application.

  Specifically, ORI found that he duplicated images, or trimmed and/or manipulated blot images from unrelated sources to obscure origin & relabeled them to represent different experimental results.

Recent ORI Administrative Actions

- **Dr. Pastorino has agreed for a period of five (5) years to:**
  - Exclude himself from contracting/subcontracting with any US Government Agency and from eligibility or involvement in US Government Non-procurement Programs;
  - Neither apply for nor permit his name to be used on any application, proposal, or other request for funds to the United States Government or any of its agencies;
  - Neither receive nor be supported by funds of the United States Government and its agencies; and
  - Exclude himself from providing advisory services to PHS.

Recent ORI Administrative Actions

- **Kenneth Walker, Ph.D., University of Pittsburgh**: Based on admission, ORI found that Dr. Kenneth Walker, former postdoctoral fellow, Department of Pediatrics, University of Pittsburgh (UP), engaged in RM in research supported by NIDDK, NIH grant R01 DK081128 by falsifying and/or fabricating data that were included in two (2) publications, one (1) submitted manuscript, and two (2) grant applications submitted to NIDDK, NIH.

  Specifically, ORI found that he falsified and/or fabricated quantitative real-time polymerase chain reaction (qPCR) data to demonstrate a statistically significant or "trend" of statistical difference in the expression of renal or bladder urothelium and muscle developmental markers between control and experimental (mutant) mice, when there was none.

Recent ORI Administrative Actions

- **Dr. Walker has agreed for 3 years to:**
  - Have his research supervised and not participate in PHS-supported research until a supervision plan is submitted to/approved by ORI;
  - Have any institution employing him submit to ORI a certification that data provided by Dr. Walker is based on actual experiments and accurately reported; and
  - Be excluded from providing advisory services to PHS.
- Dr. Walker also agreed to retract and/or correct two publications, as determined by the corresponding author.

RESEARCH MISCONDUCT RESOURCES

- **ORI website: http://ori.hhs.gov/**
- **Statutes and Regulations**
  - ORI Statutory Authority - 42 U.S.C. § 289b
  - Public Health Service (PHS) Policies on Research Misconduct – 42 CFR Part 93 – June 2005
  - HHS Debarment Regulations - 45 CFR Part 76
  - Federal Whistleblower Protection Act of 1989 - 5 U.S.C. § 1201
  - Freedom of Information Regulation - 45 CFR Part 5
  - Public Health Service Records Related to Inquiries and Investigations of Scientific Misconduct, HHS/OASH/ORI. 74 Fed. Reg. 44847 (2009)
- **ORI Sample Policy and Procedures for Responding to Research Misconduct Allegations**
- **ORI Guidelines for Institutions and Whistleblowers: Responding to Possible Retaliation Against Whistleblowers in Extramural Research**
- **ORI Handbook for Institutional Research Integrity Officers**

Removing Barriers to Clinical Research Act of 2016

Removing Barriers to Clinical Research Act of 2016

- **March 3rd, 2016: The House of Congress introduced a bill to amend title XVIII of the Social Security Act to ensure Medicare coverage of certain costs associated with FDA-approved clinical trials involving medical devices.**

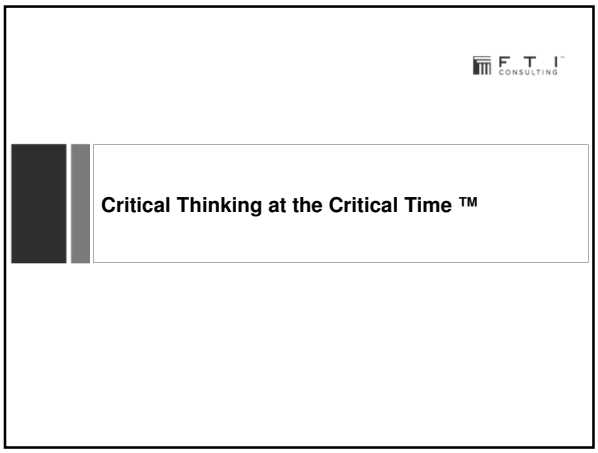
In summary, this Bill

- Clarifies Medicare Coverage of routine services and Category B devices
- Provides the industry with welcome guidance going forward

Removing Barriers to Clinical Research Act of 2016

- **The amendment clarifies the following points:**
  - Medicare coverage for clinical trials in which a Category A or Category B medical device is involved;
  - Which "routine costs" are covered for research using either a Category A or Category B medical device;
  - Assuming there is medical necessity and the use is consistent with routine standards, Category B devices are also covered; and
  - Clinical trials automatically meet the "Category A and Category B" definitions when the trial is conducted under an Investigation Device Exemption filing.

Questions?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