



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
 - 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





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:

- The number & nature of financial interests;
- How much Medicare paid for drugs and DMEPOS ordered by physicians who had financial relationships with manufacturers and group purchasing organizations; and
- 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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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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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:

- 2. Examine extent to which CDC ensures that sampled entities comply with annual internal inspection requirements & that identified observations are corrected. OlG 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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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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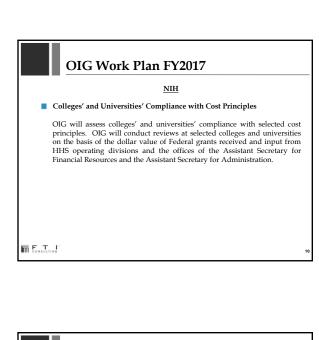
OIG Work Plan FY2017

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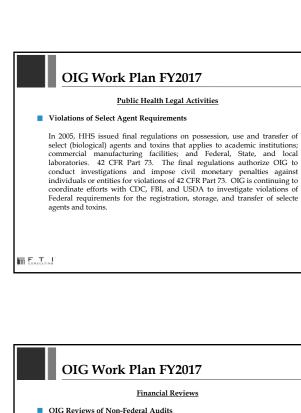
Review of NIEHS' Funding for Bisphenol A (BPA) Research

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.

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May want to add the OHRP audit initiative. I believe the audience would be interested in this topic. See **A**1 page Author, 12/1/2015



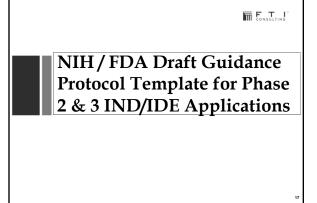
Pursuant to the Uniform Grant Guidance at 2 CFR Part 200, certain entities receiving Federal awards are required to have annual organization-wide audits of all Federal funds that they receive. OIG will continue to review the quality of audits conducted by non-Federal auditors, such as public accounting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

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

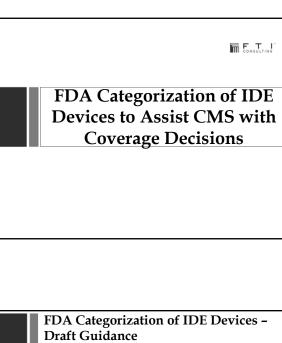
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| ı | 2016 Research Related Do | cume | nts |
|-------|---|---------------------|-------------------|
| Date | Title | Type of Document | Issuing Agency |
| 3/16 | NIH / FDA Draft Guidance Protocol Template for Phase 1 & 2 IND/IDE Applications | Draft 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 |
| 2/16 | 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 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

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- 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:
 - Schila seasoning 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;
- 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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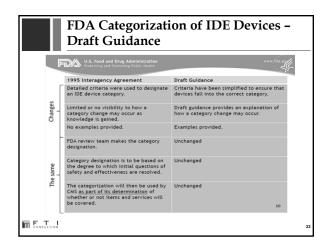


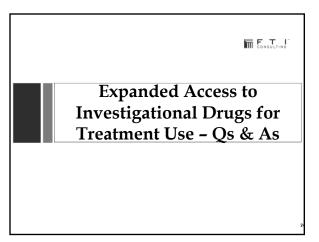
FDA Categorization of IDE Devices -**Draft Guidance**

- ■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:
- In No PMA approval, 510(k) clearance or de nov 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.
- 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 5&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.







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:
- Under FIAs regulations, time are tirree 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?

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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

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NIH Single IRB Policy

- June 21, 2016 NIH Single IRB (sIRB) Policy for multi-site research of nonexempt 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)

- - 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;

 - Roles and responsibilities of the sIKB 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 element with these involved.
- shared with those involved
- December 2016: NIH announced a revised effective date from May 25, 2017 to September 25, 2017





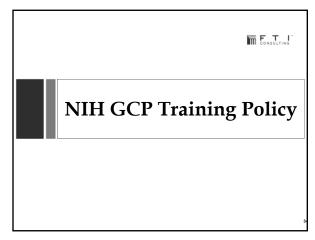
IRB Written Procedures



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;
- protected, and tan the Iko Operates in companied 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 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.

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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 integrily 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

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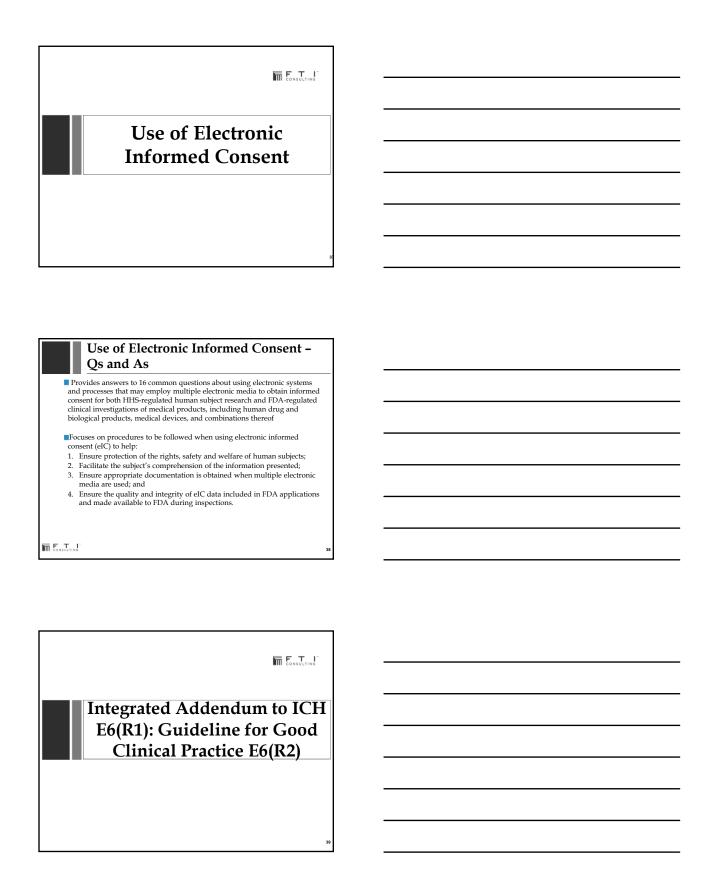


NIH GCP Training Policy

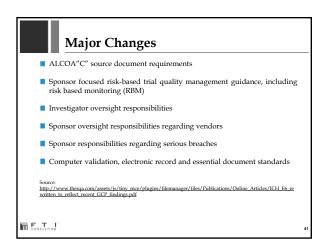
- GCP Training Requirements
- Content: Principles of ICH GCP outlined In Section 2 ICH GCP (R2)
- FAcceptable GCP courses include the NIAID GCP Learning Center website (http://gcplearningcenter.niaid.nih.gov) and National Drug Abuse Treatment Clinical Trials Network (https://gcp.nihtraining.com/)
- Outcome: 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

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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







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

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Clinical Trials Registration and Results (cont'd)

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

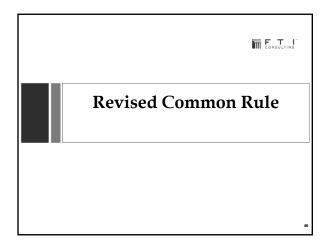
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Clinical Trials Registration and Results (cont'd)

| 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 | Identify CT record as non-compliant in ClinicalTrials.gov | Same |
| Consequences | 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 | May lead to suspension or termination of grant or contract funding |
| | going forward) | Considered in future funding decisions |
| Effective Date | January 18, 2017 | January 18, 2017 |

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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



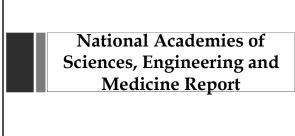


Revised Common Rule

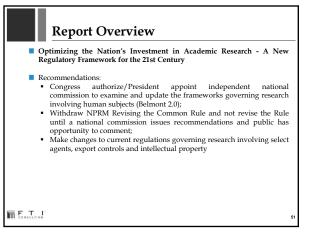
- ■Compliance Dates
 - Cooperative Research/Single IRB January 19, 2020
 - Research initially IRB approved, waived or deemed exempt before January 19, 2018 need not comply with New Common Rule; comply with the old Common Rule (Revised January 15, 2009)
 - Research initially IRB approved, waived or deemed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

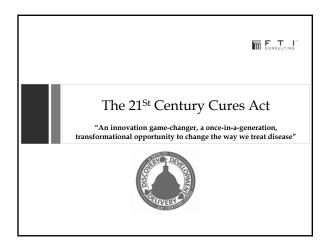
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| Revised Common Rule Highlights | |
|--|---|
| Regulatory Oversight of IRBs Unaffiliated with Engaged Institutions Revised Exempt Categories Limited IRB Review New Approval Criteria Informed Consent Broad Consent Public Accessibility of Informed Consent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

 - Advance Frecision medicine inhabity (\$1.50)
 Bolster "Cancer Moonshot" (\$1.8B)
 Invest in the BRAIN initiative to improve understanding of diseases

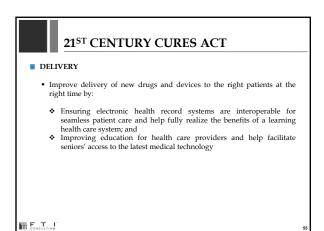
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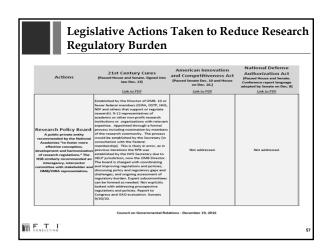
21ST CENTURY CURES ACT

■ 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, decrease and engineers.
- doctors, and engineers.



2016 Legislative Actions to Reduce Research Regulatory Burden



| 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 establishing regulations with reviewing establishing regulations and processes with the goal of reducing burden on researchers and RS. Directed to researchers and RS. Directed to researchers and RS. Directed to researchers and residence of the research business models (interagency) working group. Requires a report to congressional coremittes sensibly for the first four years. | Not addressed. | |
| Subrecipient Monitoring - reduce unecessary or redundant oversight. Reconvendations - lational Academies - amend the UG to clarify applicability to BES only for project and erformance monitoring. GAO arget 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. | |

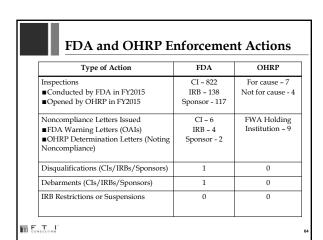
| Legislative Actions Taken to Reduce Research Regulatory Burden | | | | | |
|--|---|---|--|--|--|
| Actions | 21st Century Cures (Passed House and Senate, President Obama to sign.) | American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16) | National Defense Authorization 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 <u>slean</u> 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 bunden - Recommendations: National Academies - Federal-wide policy to be developed by Congress and STEP, NSB and GAO - evaluation of the 2011 revisions to the PHS COI regulations. | Within two years of anactment. Led by the 1945 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. | | |
| F T I | Council on Governmental Rel | ations - December 19, 2016 | | | |

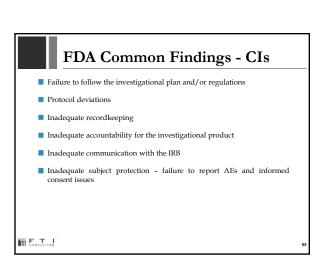
| Regulatory Burden | | | | |
|--|--|---|--|--|
| Actions | 21st Century Cures (Passed House and Senate, President Obama to sign.) | American Innovation and Competitiveness Act (Passed Senate Dec. 10 and House on Dec. 16) | National Defense Authorization Act (Passed House and Senate. Conference report 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 feature approach. NSB - engage all regulatory, independent and certification bodies. | Within two years of enactment. NH, 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 - Recommendation - 1958: OMB issue a memo of clarification indicating that the payroli certification method is acceptable to the Federal Government, National Academies OMB affirm that this may take advantage of the documentation of personnel expenses. | Directs the HHS Secretary to clarify applicability of the Uniform Outlainer for applicability of the Uniform Outlainer Service (Control of the Uniform Outla | Not addressed. | Not addressed. | |

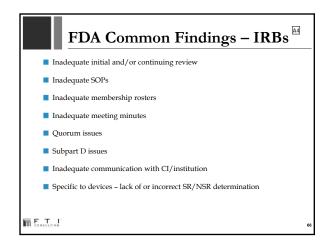
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|--|--|--|--|
| Jnified Grant Format - Recommendations - National Academies | Not addressed. | Working group to consider a simplified, unified grant format for use by all agencies. | Not addressed. |
| Preliminary Proposals - Recommendations: NSB and 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. |

| 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 - N5B. 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 National Nacidemia Research, academic Research, and the GAO report "Rederal Research Carsto: Opportunities Remain for Agencies to Streamline Administrative Regularements" | | | | |

| FONSULTING CONSULTING |
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| Human Research Subjects Protections Enforcement |
| Actions |
| |
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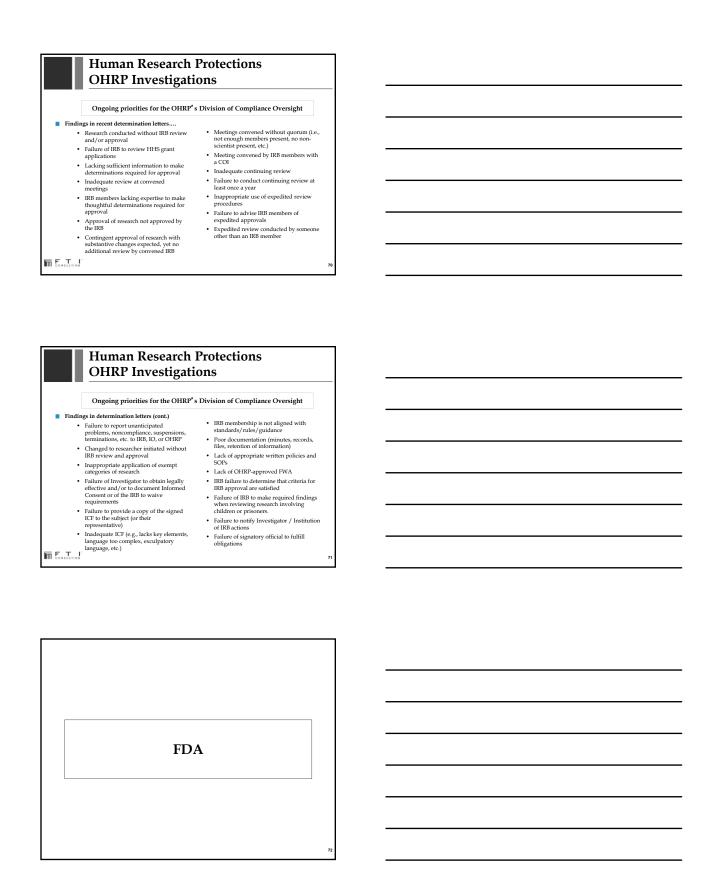
Based on FY2014 Bimo stats; may need to revise when we get FY2015 Bimo stats.

Author, 11/23/2015

| OHRP | |
|------|----|
| | _ |
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| Date | Institution | Issue(s) Summary | |
|--------------------|--|--|--|
| 10/13/15 2/2/16 | San Diego State University | Informed consent documents (i.e., belaphone screening consent script and informed consent form) lated 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 approof 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 | |

| 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 | 9/27/16 West Virginia School of Osteopathic Medicine West Virginia School of Osteopathic Medicine | | | |
| F. T. I | | | | |



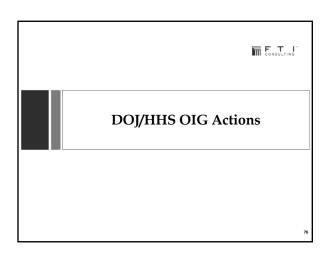
| Human Research Protections FDA Warning Letters - Clinical Investigators | | | |
|---|-------------------------------|--|--|
| Date | Investigator | Issues(s) Summary | |
| 11/2/15 | Thomas S. Tooma, M.D. | Sponsor-investigator failed to submit an IND before conducting a clinical investigation involving 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- emolded subjects who did not neet eligibility criteria and did not complete laboratory tests/imaging procedures at required time intervals Investigator failed to maintain adequate and accurate ace histories Investigator failed to maintain adequate and corrular 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 Investiga | | | | |
|--|--------------------------|--|--|--|
| 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 investigational plan – 25 subjects were randomized and received study drug praceipt of serum creatinine levels and investigator overdosed 2 subjects becaus investigator did not have the required test results at the time subjects were randomized and received study drug | | |

| Human Research Protections FDA Warning Letters - IRBs | | | |
|---|--|---|--|
| Date | IRB | Issues(s) Summary | |
| 11/10/15 | Monmouth Med Ctr IRB | IBB failed to determine (and document) at time of initial review that studies involvin children were in compliance with 2C FR 9th, subpart D IBB failed to review proposed research at convened meetings at which a majority of the members of the IBB were present, including at least one non-scientific member IBB 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 | RB failed to prepare, maintain and follow required written procedures governing functions and operations of the IRB RB failed to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings RB 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 RB failed to conduct continuing nerview 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. | |





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, 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.

F. T. I

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



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

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



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, 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.lshs.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
- and for the development of pillboxes customized for specials propulations.

 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





Research Misconduct



- Andrew R. Cullinane, Ph.D., NIH: ORI found that Dr. Cullinane, former ostdoctoral 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.

F. T. I



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.

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■ 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)

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.

F. T. I



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.

F. T. I



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.

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- ORI implemented the following administrative actions for a period of
- 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.

F. T. I



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 susported 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.

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Recent ORI Administrative Actions

- Dr. Malhotra agreed to the following administrative actions:
- Dr. Mainorta agreea 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.

E CONSULTING



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.

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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.

F. T. I

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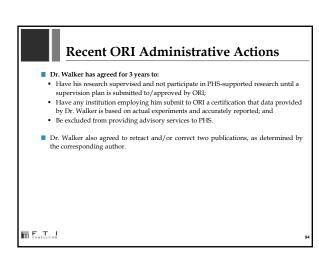
Recent ORI Administrative Actions

■ 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.

F. T. I

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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
- \blacksquare 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
- ■ORI Guidelines for Institutions and Whistleblowers: Responding to Possible Retaliation Against Whistleblowers in Extramural Research
- ORI Handbook for Institutional Research Integrity Officers





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| Critical Thinking at the Critical Time ™ | - | |
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