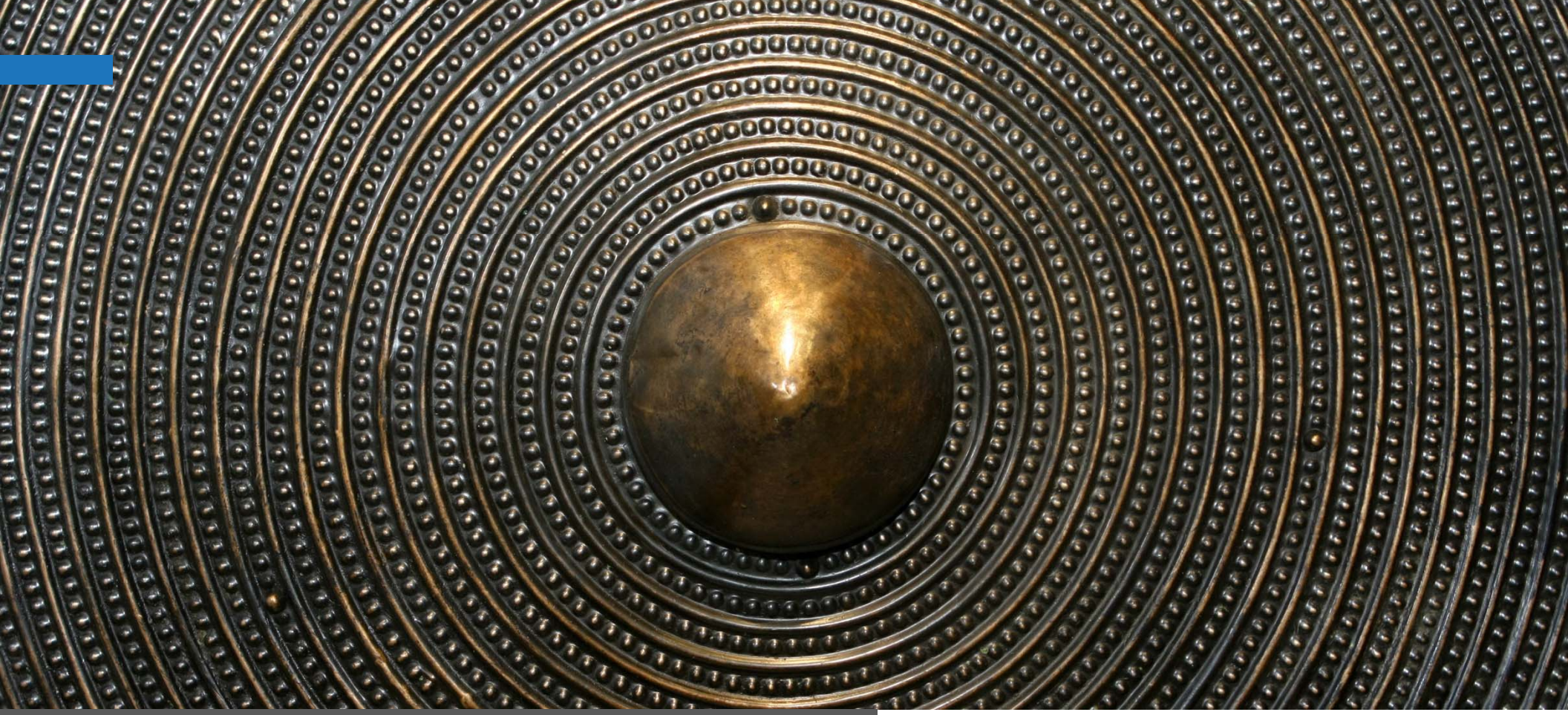

2018-2019 Research Year-in- Review

February 26, 2019

ankura

Your Host

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RESEARCH CONSULTING, COMPLIANCE, INVESTIGATIONS & PROCESS IMPROVEMENT

- JD
- Certifications: CHC, CHRC
- More than 30 years of healthcare, research, fraud and abuse, HIPAA privacy, and compliance experience.
- Provided operational and compliance consulting services to life sciences organizations, research sites, CROs, and investigators across the globe.
- Served as in-house counsel to two nationwide healthcare organizations and as chief compliance officer for both an insurer and an university and its health system.

Table of Contents

2018 Research Year in Review

FDA REGULATORY UPDATE

2018 FDA Updates

The Revised "Common Rule" and FDA Regulated Clinical Trials

- On Jan. 19, 2017, HHS revised its version of the Common Rule; the revised version went into effect January 21, 2019.
- When a clinical study is conducted or supported by HHS *and* involves an FDA regulated product, then both HHS and FDA rules apply.
- Because FDA has not yet harmonized its version of the Common Rule with HHS, FDA issued a Guidance on October 11, 2018 to "reduce confusion and burden":
  - Informed Consent: the new informed consent requirements (e.g., content, process, additional elements) "…are not inconsistent with FDA's current policies and guidance."
  - Expedited Review and Continuing Review: IRBs must continue to follow FDA rules as written.
- On Nov. 15, 2018, FDA published its Proposed Rule for harmonization that may be finalized this year. (see next slide)

https://www.govinfo.gov/content/pkg/FR-2017-01-19/pdf/2017-01058.pdf

2018 FDA Updates - Continued

FDA Proposes to Implement Cures Act

- On Nov. 15, 2018 FDA published a Proposed Rule for implementing the Cures Act (2016).

- The Proposed Rule, if finalized, permits an IRB to waive the requirement to obtain informed consent for some minimal risk clinical investigations.

- Under the proposed exception, an IRB may waive informed consent when:

  - The clinical investigation involves no more than minimal risk to the subjects;
  - The waiver of informed consent will not adversely affect the rights and welfare of the subjects;
  - The clinical investigation could not be carried out without the waiver; and
  - The subjects are provided with additional "pertinent" information after participating in the study.

https://www.govinfo.gov/content/pkg/FR-2018-11-15/pdf/2018-24822.pdf

2018 FDA Updates - Continued

Civil Money Penalties Relating to ClinicalTrials.gov Data Bank

- On Sept. 20, 2018 FDA issued a draft Guidance describing its current thinking on civil money penalties (CMPs) for parties that fail to submit data or submit false or misleading data to the ClinicalTrials.gov data bank.

- FDA will utilize a "risk-based approach" to decide when to issue a Pre-Notice Letter and will focus enforcement on:

    - Parties that fail to submit data;
    - Parties having pattern of previous non-compliance; and
    - Clinical trials with multiple issues of statutory and/or regulatory non-compliance.

- Parties are given 30 days to remedy non-compliance.

- Parties may be assessed a CMP of $10,000 per violation and $10,000 for each day the non-compliance is not remedied.

https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM607698.pdf

2018 FDA Updates - Continued

Acceptance of Clinical Data Obtained Outside the U.S.

- On Feb. 21, 2018 FDA published a Final Rule updating its standards for accepting clinical data from investigations conducted outside the U.S when submitted to support an IDE or a device marketing application.

- Final Rule does not apply to clinical data from investigations conducted outside the U.S. and submitted for other purposes.

- Submitted data is subject to the reporting requirements found at 21 CFR 812.28(b), *viz*. names and qualifications of the investigators, summary of the protocol, results, how informed consent was obtained, and any incentives offered to subjects.

- Sponsors may request FDA to waive these requirements after explaining why compliance with the requirements is unnecessary or cannot be achieved.

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=812.28

2018 FDA Updates - Continued

Proposed Rule to Amend Public Info Regulations

- On Sept. 13, 2018 FDA published a Proposed Rule to incorporate changes to FOIA by the OPEN Government and FOIA Improvement Acts; would amend 21 CFR part 20.
- Amendments would require FDA to withhold information only if FDA reasonably foresees that disclosure would:
  - Harm an interest protected by an exemption; or
  - The disclosure is prohibited by law.
- FDA would also be required to establish procedures for identifying records that are appropriate for public disclosure and making those records publicly available.

https://www.govinfo.gov/content/pkg/FR-2018-09-13/pdf/2018-19864.pdf

NIH REGULATORY UPDATE

NIH Single IRB (sIRB) Policy

- Effective Date: January 25, 2018
- NIH-funded multi-site domestic studies involving non-exempt human subjects research are expected to use a single IRB
- Policy does not apply to:
  - Foreign sites
  - Career development (K), institutional training (T), and fellowship awards (F)
  - Current awards
- Exceptions:
  - Policy-based Exceptions: when Federal, State, Tribal, local laws/regulations/policies require local review
  - Time Limited Exceptions: When ancillary studies are part of ongoing studies or parent studies
  - Compelling Justification or Other Exceptions: When there is a compelling justification for local IRB review

https://grants.nih.gov/sites/default/files/Single%20IRB%20%26%20Exceptions%20Process%20Webinar%20October%2018%202017.pdf

OHRP UPDATES

OHRP Updates

The Revised Common Rule

FINAL REVISIONS TO THE COMMON RULE WENT INTO EFFECT ON JANUARY 21, 2019

Major areas of change are related to:

- Definitions [§46.102]
- Informed consent requirements [§46.116]
- Single IRB Review [§46.114]
- Continuing Review [§46.109]
- Exempt Categories [§46.104]

https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html

OHRP Updates

Institutional Review Board Written Procedures: Guidance for Institutions and IRBs (As stated under FDA Updates, effective May 2018)

- Replaces OHRP'S July 1, 2011 guidance titled, "Guidance on Written IRB Procedures."
- Goal: to assist Institutional and IRB staff in preparing/maintaining written procedures
- Includes written procedure checklist incorporating HHS and FDA regulatory requirements for written procedures, operational recommendations and topics for consideration when developing P&P.

https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm512761.pdf

OIG UPDATES

OIG Advisory Opinion No. 18-13

- Charitable trust suggested making a significant donation to a Research Institute partnered with a health care system.
  - The Research Institute does not bill Federal health care programs – the health care system does.
  - The trustees have ownership/financial interests in long-term care facilities that have long-standing business relationships with the health care system.
- Anti-kickback Statute implications - affiliation with health care system can generate business for trustee's long term care facilities
  - Knowing and willful offense to offer, pay, solicit or receive any remuneration to induce/reward referrals of items/services
  - Potential self-dealing: the trustees want to donate (remuneration) to an entity that could indirectly generate business (financial relationship) for the trustee's business.
- Conclusion: low risk under AKS

https://oig.hhs.gov/fraud/docs/advisoryopinions/2018/AdvOpn18-13.pdf

OIG Advisory Opinion No. 19-02

- Pharmaceutical manufacturer's proposal to loan limited-function iphone to financially needy patients lacking the technology necessary to receive data from sensor embedded in digital medication (DM).
  - Patch records patient ingestion of drug and indicators of patient rest patterns/activity, which must be accessed through smartphone.

- Beneficiary Inducement Implications of Civil Monetary Penalties Law: would remuneration (loaner device) likely influence beneficiary to select provider/practitioner/supplier (prescriber/pharmacy)?
  - Yes-prescriber completes paperwork for patient to obtain device → patient could believe that he/she must continue receiving care from provider while using loaner device.
  - Meets Access to Care Exception: 1) promotes access to care and 2) low risk of harm.

- AKS Implications: would remuneration influence beneficiary to select item/service reimbursable by Fed. health care programs?
  - Device integral to and only available (temporarily) to those needing the drug and would otherwise unable to use the drug without the technology.
  - Not advertised → patients unlikely to suggest DM solely to receive device
  - No imposition AKS sanctions (no requisite intent to induce referrals)

https://oig.hhs.gov/fraud/docs/advisoryopinions/2019/AdvOpn19-02.pdf

OIG Active Work Plan Items

NIH's Implementation of Financial Conflict of Interest Regulations

- Extramural grants to researchers working at universities/institutions comprise more than 80% ($37 billion) of NIH budget.
- Grantee institutions required to safeguard IP from NIH-funded research by managing financial COI and reporting significant conflicts to NIH.
- OIG directed to examine grantees' compliance with NIH policies (including NIH efforts to ensure integrity grant application/selection processes and effectiveness of efforts to protect IP derived from NIH-supported research).
- This review to assess whether NIH has P&P and controls in place to ensure foreign and domestic grantees disclose all sources research support, financial interests, and affiliations.

https://oig.hhs.gov/reports-and-publications/workplan/updates.asp

OIG Active Work Plan Items - Continued

NIH Monitoring of Extramural Researchers' Financial Conflicts of Interest

- Extramural grants to researchers working at universities/institutions comprise more than 80% ($37 billion) of NIH budget.
- Grantee institutions protect U.S. biomedical research by managing researchers' COI and reporting conflicts to NIH.
- NIH Director: Concerns of increased risks to security IP in biomedical research enterprise.
- NIH addressing by accurate reporting financial interests. Grantee institutions must submit sufficient info enabling NIH understand nature and extent COI and assess appropriateness of institutional COI management plan.
- OIG directed to examine oversight grantees' compliance with NIH policies (including NIH efforts to ensure integrity of grant application/selection process)

https://oig.hhs.gov/reports-and-publications/workplan/updates.asp

OIG Active Work Plan Items - Continued

NIH's Pre-Award Process for Assessing Risk for Grant Applicants and Post-Award Process for Oversight of Grantees

- Extramural grants to researchers working at universities/institutions comprise more than 80% ($37 billion) of NIH budget.
- Prior to making Federal award, NIH required to determine whether part eligible to receive Federal funds. Even if eligible, party may still be subject to certain conditions due to risks associated with Federal award.
- OIG required to examine NIH oversight of grantees' compliance with NIH policies (including NIH efforts ensuring integrity of application/selection process). OIG to conduct audits to review pre-award process to ass risk of potential recipients of Federal funds and post-award process to oversee/monitor grantees on risks identified during pre-award process.

https://oig.hhs.gov/reports-and-publications/workplan/updates.asp

OIG Active Work Plan Items - Continued

NIH's Peer Review Process for Evaluating Grants

- NIH strives to eliminate bias in its funding of extramural research grant-making process.
- Initial Review by Scientific Review Group (SRG)-peer reviewers with subject matter expertise. NIH officials within relevant Institute or Center (IC) rank and package the applications for Second level review by Advisory Council.
- NIH Director: Concerns over increased risks to integrity peer review (peer reviewers attempting to influence funding decisions).
- OIG to examine NIH efforts to ensure integrity of its grant evaluation/selection process (a key component of this is peer review).
- OIG to determine extent to which ICs follow grant application process with respect to SRGs. OIG to determine how staff and directors of ICs review results of SRGs to develop funding recommendations for advisory council.

https://oig.hhs.gov/reports-and-publications/workplan/updates.asp

OCR UPDATES

OCR Updates

ALJ Rules in Favor of OCR – MD Anderson to pay $4.3 million in penalties for HIPAA violations

- 3 separate OCR investigations in 2012-2013 involving the theft of an unencrypted laptop from the residence of a MD Anderson employee and the loss of two unencrypted thumb drives containing ePHI 33,500 individuals.

- Investigation showed that MD Anderson had written encryption policies and that MD Anderson's own risk analyses identified high-risk in the lack of device-level encryption. MD Anderson eventually adopted a device-level encryption solution, but it failed to encrypt the entire inventory of devices.

- ALJ upheld penalties for each day of MD Anderson's non-compliance with HIPAA and for each record breached.

- MD Anderson claimed that the ePHI at issue was for "research" and thus not subject to HIPAA's nondisclosure requirements. ALJ objected; nothing in regulations supports argument and argument ignores fact that there is mechanism to separate research function from clinical function.

https://www.hhs.gov/sites/default/files/alj-cr5111.pdf

ENFORCEMENT UPDATES

Recent DOJ Cases

Texas A&M Research Foundation Pays $750,000 to Settle Claims Alleging Improper Charges to Federal Grants

- The settlement is the result of an investigation that began after a *qui tam*, or whistleblower, lawsuit was filed under seal on June 6, 2013. The whistleblowers are employed by TAMRF and alleged that during their employment they witnessed TAMRF allow personnel to ignore federal restrictions and permitted the overcharging of salaries, which inflated grant expenses. The whistleblowers also alleged TAMRF engaged in cost shifting; allowed academic employees to wrongfully receive longevity pay; violated salary caps; and improperly charged grants for expenses not incurred or not covered.
- The United States also concluded that TAMRF improperly charged various federal grants for expenses not properly allocable to them, including salaries and wages for individuals not working on the grants and supplies and equipment unrelated to the grants. TAMRF also improperly charged various federal grants for unallowable costs such as travel expenses unrelated to the objectives of the grants or for unaffiliated parties not working on the grants.

https://www.justice.gov/usao/pressreleases

Recent DOJ Cases

Drug Maker Pfizer Agrees to Pay $23.85 Million to Resolve False Claims Act Liability for Paying Kickbacks

- Pharmaceutical company Pfizer, Inc. (Pfizer) agreed to pay $23.85 million to resolve claims that it used a foundation as a conduit to pay the copays of Medicare patients taking three Pfizer drugs, in violation of the False Claims Act.
- Under the Anti-Kickback Statute, a pharmaceutical company is prohibited from offering, directly or indirectly, any remuneration—which includes paying patients' copay obligations—to induce Medicare patients to purchase the company's drugs.
- The government alleged that Pfizer used a foundation as a conduit to pay the copay obligations of Medicare patients taking three Pfizer drugs: Sutent and Inlyta, which both treat renal cell carcinoma, and Tikosyn, which treats arrhythmia in patients with atrial fibrillation or atrial flutter. The government alleged that, in order to generate revenue, and instead of giving Sutent and Inlyta to Medicare patients who met the financial qualifications of Pfizer's existing free drug program, Pfizer used a third-party specialty pharmacy to transition certain patients to the foundation, which covered the patients' Medicare copays.

https://www.justice.gov/usao/pressreleases

Recent DOJ Cases

Advanced Thermal Technologies and CEO Agree to Pay $100,000 for Failing to Account for Federal Research Funds

- Advanced Thermal Technologies, LLC (ATT), and its President and Chief Operating Officer, James W. Connell, of Upton, Mass., agreed today to pay $100,000 to resolve allegations that they failed to account for a portion of federal research grants they received and that they used a portion of the funds unlawfully.
- The government's complaint alleges that on multiple occasions from 2007 to 2016, Connell personally certified to NSF and DOE that: (1) ATT maintained an adequate financial system to account for the award funds as required by regulations, (2) ATT would comply with the award terms and conditions, and (3) ATT spent the award funds and performed the research in accordance with the terms and conditions. The complaint alleges that these certifications were often false because ATT and Connell failed to prepare and maintain documentation substantiating that they used the funds for the awarded research projects, and, on occasion, that they claimed and received funds for NSF projects that were already completed.

https://www.justice.gov/usao/pressreleases

Recent DOJ Cases

University of Pittsburgh Professor Pays $132,000 and Agrees to Exclusion to Resolve Allegations of False Claims for Federal Research Grants

- Christian Schunn, Ph.D., a professor at the University of Pittsburgh since 2001, has agreed to pay the United States $132,027 to resolve allegations that he violated the False Claims Act by submitting false documents to the National Science Foundation (NSF) in order to obtain federal grants to fund his research.
- From 2006-2016, Schunn allegedly created false IRB approvals and submitted them to NSF in connection with multiple proposals for NSF funding totaling more than $2.3 million.
  - NSF awarded funding to the University of Pittsburgh (Schunn as Principal Investigator) and award funds were drawn down.
  - Schunn then allegedly made, or caused others to make, false claims for payment by certifying that the drawdowns were in accordance with the terms and conditions of the awards (when no proper IRB approval had been in place).
  - The United States contended that Schunn also made false certifications in connection with annual and project reports associated with these awards.

https://www.justice.gov/usao/pressreleases

Recent Cases

University of North Texas Health Science Center to Pay $13 Million to Settle Claims Related to Federal Grants

- UNTHSC has agreed to pay the United States $13,073,000 to settle claims that it inaccurately measured, tracked and paid researchers for effort spent on certain NIH-sponsored research grants.

Memorial Sloan Kettering Cancer Center: Conflict of Interest

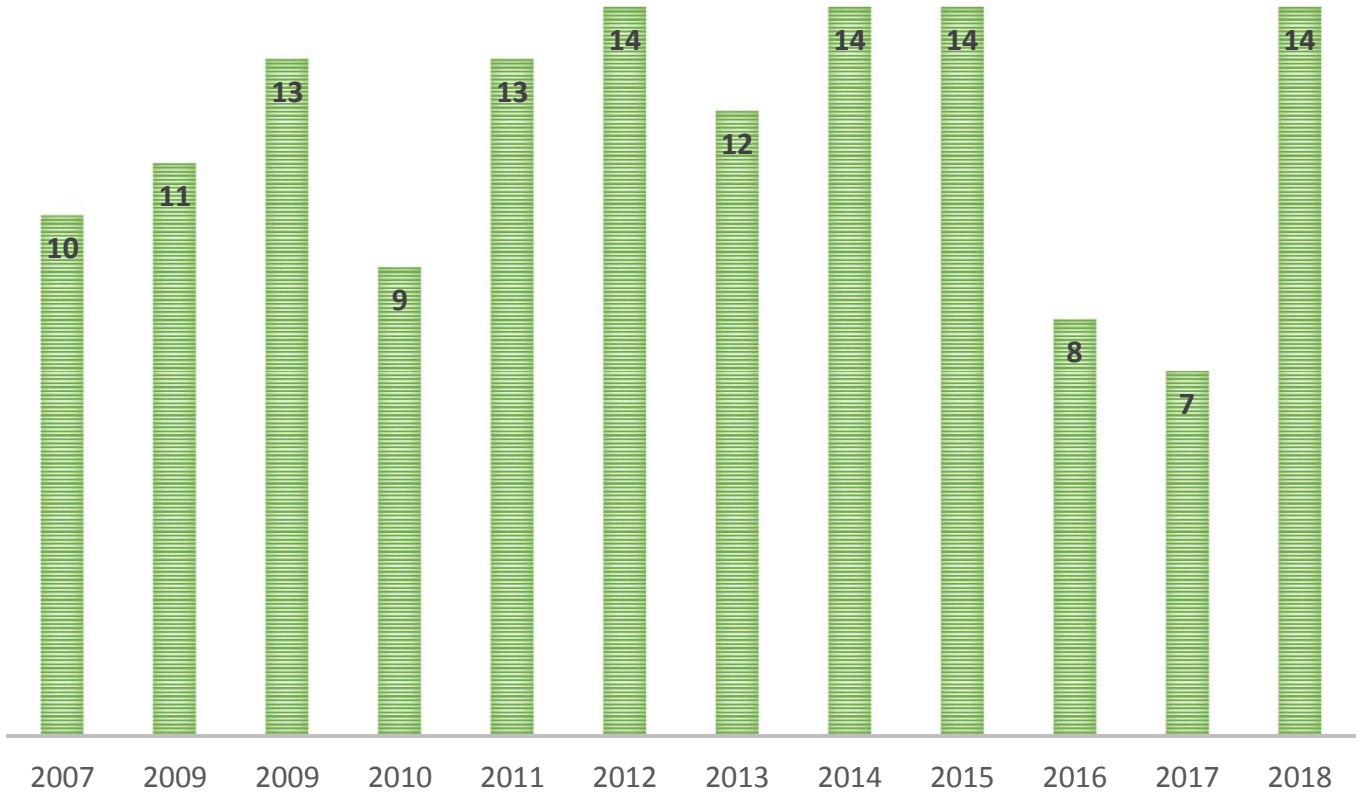
- In September 2018, it was reported that the MSKCC Chief Medical Officer (Jose Baselga, M.D., PhD) failed to report "significant industry relationships" to medical journal editors in over 100 papers published in prestigious medical journals including *The New England Journal of Medicine*.

https://www.justice.gov/usao/pressreleases

ORI UPDATES

Cases with Research Misconduct by ORI

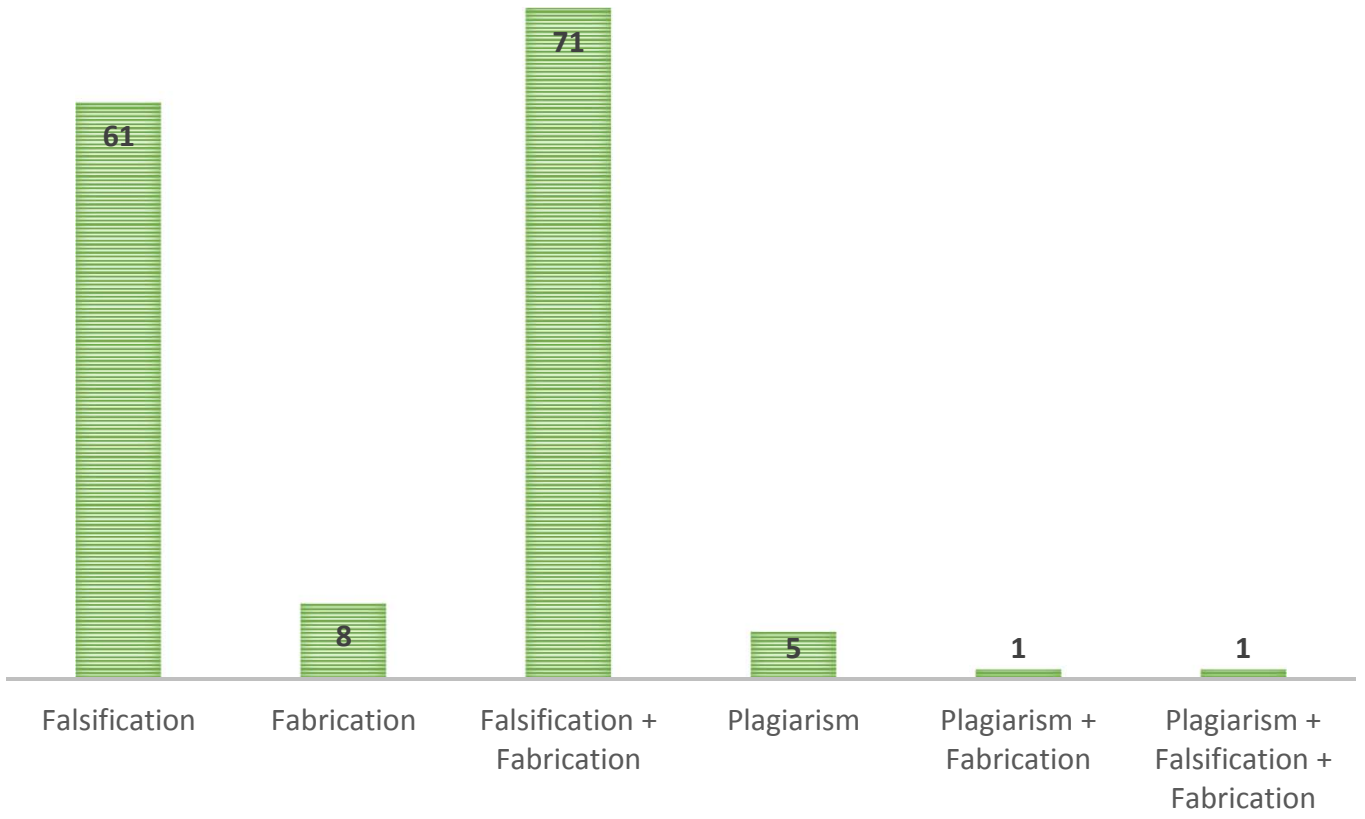
Updated through 2018



https://ori.hhs.gov/case_summary

Types of Misconduct

Updated Through 2018



https://ori.hhs.gov/case_summary

Cases with Research Misconduct by ORI

Srivastava, Rakesh: Plagiarism

- Procedure:
  - ORI issued charge letter, Respondent requested hearing before ALJ to dispute findings, ORI moved for summary judgement in favor of ORI and ALJ granted summary judgement and issued recommended decision.

- ORI found that Respondent, as PI, intentionally committed research misconduct by including plagiarized words in the submission of a grant application to NIH.

- Final notice Issued-Administrative Action:
  - Two year debarment from contracting or subcontracting with any agency of US Government and eligibility/involvement in non-procurement programs of the US government; and
  - Two year prohibition from serving in any advisory capacity to PHS.

https://ori.hhs.gov/case_summary

Cases with Research Misconduct by ORI

Murthy, Krishna H.M.: Falsification/ Fabrication

- Former Research Associate Professor, University of Alabama at Birmingham, committed research misconduct in research supported by PHS grant by:
  - Intentionally, knowingly, or recklessly engaging in research misconduct by falsifying and/or fabricating X-ray crystallographic data for 11 protein structures and falsely reporting them as experimentally derived from X-ray diffraction experiments in 9 publications and in 12 deposits in the PDB.
  - Intentionally, knowingly, or recklessly falsifying and/or fabricating the PDB coordinate files deposited for all of the 11 and the X-ray diffraction data (structure factors) corresponding to 6 of the 11 structures.
- Respondent disputed findings before an Administrative Law Judge (ALJ).
- ALJ issued a recommended decision in favor of ORI:
  - Debarment for 10 years from eligibility for any contracting or subcontracting with any agency of the U.S. Government and from eligibility for or involvement in non-procurement programs of the U.S. Government.
  - Prohibited from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for a period of ten (10) years; and
  - Notice to journals requiring correction/retraction.

https://ori.hhs.gov/case_summary

Cases with Research Misconduct by ORI

Elqutub, Maria Cristina Miron: Falsification/Fabrication

- Respondent engaged in research misconduct by intentionally and knowingly falsifying and/or fabricating data by recording dates and providing her own blood samples to cause samples to be falsely labeled as samples from 98 study subjects that were included in the following two (2) published papers and two (2) grant progress reports submitted to NIDCR.
- Voluntary Settlement Agreement-Respondent agreed:
  - to have her research supervised for a period of 3 years;
  - to certify to ORI (employer to certify for Respondent involvement in any funded study) that the data provided by Respondent are based on actual experiments;
  - if no supervisory plan is provided to ORI, to provide certification to ORI on an annual basis that she has not engaged in, applied for, or had her name included on any application, proposal, or other request for PHS funds without prior notification to ORI;
  - to exclude herself voluntarily from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for a period of 3 years; and
  - to the correction or retraction of PLoS One 10(6):e0128753, 2015 Jun 2.

https://ori.hhs.gov/case_summary

Cases with Research Misconduct by ORI

Baughman, Brandi M., Ph.D.: Falsification

- Based on a UNC review, Respondent's admission, and ORI Review, ORI found that Dr. Baughman, postdoctoral, University of North Carolina Chapel Hill, engaged in research misconduct by falsely reusing and relabeling 14 individual Western blot images from an unrelated experiment conducted in September 2013 showing pulldown with biotin-UNC1215 using 0401 and HeLa overexpressed FL L3MBTL3 lysates (hereafter referred to as the "9/13 experiment") to falsely represent Western blot analysis of GFP.Flag co-IP experiments in GFP-WT lysates in Figure 3 of the Manuscript and a supplementary analysis of co-IPs with FullL-D274A in Figure 6 of ASC 2016.

- Dr. Baughman entered into a Voluntary Exclusion Agreement in which she agreed:
  - to exclude herself voluntarily from any contracting or subcontracting with any agency of the U.S. Government and from eligibility or involvement in non-procurement programs of the U.S. Government and
  - to exclude herself voluntarily from serving in any advisory capacity to the U.S. Public Health Service (PHS) including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

https://ori.hhs.gov/case_summary

Follow-up

QUESTIONS? complianceroundup@ankura.com

NEXT ROUND-UP WEBINAR: April 22, 2019

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QUESTIONS

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