2019-2020 Research Year-in-Review

June 1, 2020

Created by Christopher Cuña,
Senior Associate at Ankura Consulting

ankura
COLLABORATION DRIVES RESULTS

1

Lisa Murtha
Senior Managing Director
Philadelphia

lisa.murtha@ankura.com
+1.267.386.4980 Direct

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.

2

Table of Contents

3

FDA Updates

4

FDA Updates

Update to Proposed Rule: IRB Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations

- Published in November 15, 2018.
- The proposed rule, if finalized would allow an exception from the requirement to obtain informed consent when a clinical investigation is no more than minimal risk to human subjects and includes the appropriate safeguards to protect the rights, safety and welfare of human subjects.
- The Institutional Review Board ("IRB") would be permitted to waive certain informed consent elements or to waive obtaining informed consent under limited conditions for certain Food and Drug Administration ("FDA") regulated minimal risk clinical investigations.
- The comment period was reopened by the FDA in February 13, 2019.
- The FDA took action by reopening the comment period to allow interested individuals additional time to submit comments due to technical issues with the Federal eRulemaking Portal.
- Electronic and written comments were allowable until March 7, 2019.

ankura

https://www.govinfo.gov/content/pkg/FR-2019-02-25/html/2019-03195.htm

5

5

FDA Updates

Humanitarian Device Exemption (HDE) Program

- Finalized on September 6, 2019.
- This guidance concerns the humanitarian device exemption ("HDE") program as a whole and explains the criteria that the FDA uses to determine if "probable benefit" has been demonstrated as part of the FDA's decision-making process when marketing authorization for a humanitarian use device ("HUD").
- The guidance also includes recent amendments to the Federal Food, Drug, and Cosmetic Act ("FD&C Act") that affect the HDE program. The answers to common questions asked about the program are also included within this guidance.
- The FD&C Act are a set of laws that allow the FDA to oversee the safety of food, drugs, medical devices and cosmetics.
- The guidance reflects the following recent amendments that impact the program:
  - A modification to number of eligible patients that a HUD is designed to treat or diagnose (no more than 8,000 individuals in the United States).
  - The removal of a requirement which required only local institutional review committees and IRBs to approve and supervise clinical testing of HUDs.
  - The use of a device under an HDE at a facility may now be approved by an appropriate local committee or an IRB. Prior to this, only an IRB was able to perform this function.

ankura

https://www.federalregister.gov/documents/2019/09/06/2019-19290/humanitarian-device-exemption-program-guidance-for-industry-and-food-and-drug-administration-staff

6

6

FDA Updates

Enrichment Strategies for Clinical Trials To Support Demonstration of Effectiveness of Human Drugs and Biological Products

- Finalized on March 3, 2019.
- The purpose of this guidance is to assist industry in developing enrichment strategies that can be used in clinical investigations intended to demonstrate effectiveness (and in some cases safety) of human drugs and biological products.
- This guidance defines several types of enrichment strategies, provides examples of potential clinical trial designs, and discusses potential regulatory considerations when using enrichment strategies in clinical trials.
- Changes made to the guidance took into consideration comments received related to discussions of study design and analysis, specific patient populations to be studied, and genomic strategy considerations. In addition, editorial changes were made, primarily, for clarification and elimination of redundancies.

ankura

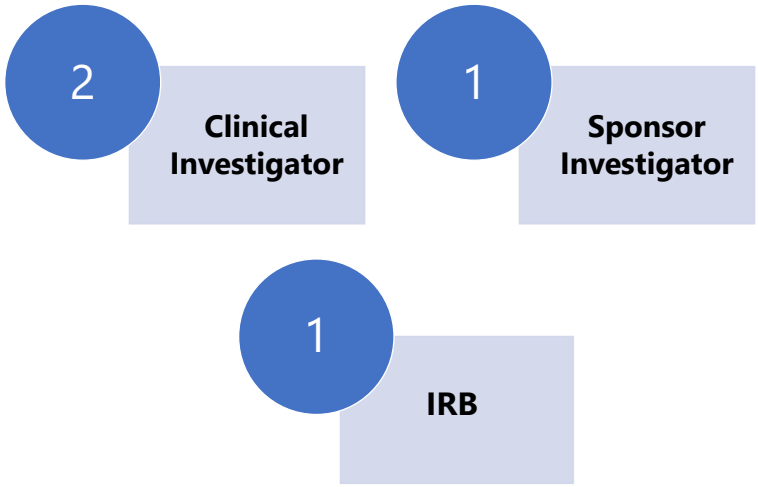
https://www.federalregister.gov/documents/2019/03/15/2019-04815/enrichment-strategies-for-clinical-trials-to-support-demonstration-of-effectiveness-of-human-drugs

7

7

FDA Updates

2019 FDA Warning Letters



All issued by the Center for Drug Evaluation and Research

ankura

https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126500.pdf

8

8

2019 FDA Warning Letters

Balamurali K. Ambati, M.D. 09/03/2019

- Failed to submit an investigational new drug ("IND") for the conduct of clinical investigations with an IND that is subject to 21 CFR 312.2(a) [21 CFR 312.20(a) and 312.40(a)].
- Failed to submit an IND before conducting a clinical investigation under Protocol. The FDA inspected 12 human subjects were enrolled and treated with the unapproved drug from April 2017 to December 2018.

Susan P. King-Harris, D.P.M. 09/09/2019

- Failed to ensure that the investigation was conducted according to the investigational plan [21 CFR 312.60].
- The inclusion and exclusion criteria for their protocol required enrolled subjects to have a bunion severity determined by the intermetatarsal angle ("IMA") between 10 and 15 degrees.
- FDA inspected that the IMA measurements were not performed for 14 subjects between 2008 and 2014.
- Resulted in failure to fully evaluate and ensure subjects' eligibility before enrollment.

Lymol Medical Corp 01/08/2019

- Failed to comply with the milestone date in the timetable for completion of a postmarketing requirement ("PMR") for Sterile Talc Powder under New Drug Application ("NDA") 21388.
- Failure to comply with PMR milestone dates without demonstrating good cause for noncompliance is a violation of section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act.

Chris Christensen III, DO 06/24/2019

- Failure to review proposed research at convened meetings at which a majority of members of the IRB are present, including at least one member whose primary concerns are in non-scientific areas.
- Failure to prepare and maintain adequate documentation of IRB activities. Minutes from an IRB meeting contained discrepancies with membership rosters. Minutes from another IRB meeting did not document the IRB's approval of a study.

ankura https://www.fda.gov/drugs/warning-letters-and-notice-violation-letters-pharmaceutical-companies/warning-letters-2019

9

NIH Updates

ankura

10

Foreign Interference in NIH Research

- Media reports and congressional hearings have addressed the issue of foreign interference occurring within research that is funded by the National Institutes of Health ("NIH"). A NIH investigation with the Federal Bureau of Investigation ("FBI"), found numerous violations of laws and policies with:
  - Scientists improperly sharing details of research proposals with foreign entities within the peer review process.
  - Scientists failing to disclose foreign ties or funding from foreign governments.
  - Scientists involved in research fraud by signing employment contracts and earning salary from both U.S. and foreign institutions.
- Research institutions and scientists must comply with NIH grant policies based on:
  - Financial conflicts of interest ("FCOI").
  - Research misconduct.
  - Reporting of any other research support.
  - Peer reviewers agreeing to keep research proposals confidential.
- NIH grants are strictly awarded to institutions and not to researchers, which leaves institutions primarily responsible for compliance.

11

Foreign Interference in NIH Research (continued)

- The Department of Health and Human Services ("HHS") Office of the Inspector General ("OIG") issued reports in 2019 related to foreign interference at NIH. Two reports in September 2019 regarding FCOIs recommended that NIH:
  - Ensure that grantee institutions have publicly available FCOI policies.
  - Enhance agency monitoring of institutions' FCOI policies.
  - Perform periodic quality assurance reviews of FCOIs reported by institutions.
  - Use information already collected to decide to revise the FCOI review process.
- The Senate Committee on Homeland Security and Governmental Affairs ("HSGAC") has recommended that all federal agencies develop policies related to foreign interference (including the NIH). The HSGAC specifically recommends that all federal agencies include:
  - A comprehensive strategy against foreign interference.
  - Harmonize conflict of interest and foreign support disclosure requirements.
  - Promote best practices for international collaboration.
  - Bar awards to participants within foreign talent programs absent full disclosure of terms and conditions of such programs.

12

Case Study in Review Integrity: Asking for Favorable Treatment

- Dr. Miller was a newly appointed reviewer to the NIH study section. He had received an email from a former lab colleague, Dr. Johnson. They had not kept in touch and it had been many years since the two have interacted. Dr. Johnson was a PI on one of the applications that Dr. Miller was currently reviewing.
- Dr. Johnson began to ask if other applications contained any members from the "old gang" and if those applications could receive favorable consideration from Miller and other reviewers. Dr. Miller did not know how to respond and said that he could not help. Dr. Miller responded with "It's not wrong, it's how we help each other. And I remember, I know a lot of people".
- Dr. Miller felt unsettled with this response as Dr. Johnson was looking for favorable treatment. Dr. Johnson's response also posed as a threat by knowing "a lot of people". It implied that Dr. Johnson knew powerful people in the field that could go against Dr. Miller if the study outcomes were not favorable.
- Dr. Miller forwarded the emails to the NIH scientific reviewer officer ('SRO") who was running the NIH study section he was in. The email exchange was forwarded to the NIH Office of Extramural Research ("OER"). The NIH terminated Dr. Johnson's service in NIH peer review and the application that contained Dr. Johnson as the PI was deferred to another study section for review.
- The Vice President for Research at Dr. Johnson's institution took the appropriate steps to address the violation. The Vice President sent a formal letter to NIH leadership confirming that an investigation was completed by the institution.

13

Case Study in Review Integrity: Asking for Favorable Treatment (continued)

- The investigation done by the University confirmed that Dr. Johnson had improper communications with an individual serving on an NIH section study. Dr. Johnson was to be:
  - Prohibited by the institution from submitting any applications or receiving any support from the NIH for at least 2 years.
  - Prohibited by the institution from serving on an NIH or other federally chartered study section for at least 3 years.
  - Required by the institution to complete a course in responsible conduct or research.
  - Subject to administrative penalties at the institution.
- Dr. Johnson's institution is planning on enhancing its existing faculty training to include a module that is focused on peer review integrity.

14

OHRP Updates

15

Background on Common Rule and Required Use of a Single IRB on HHS Cooperative Research

- In a final rule published on January 19, 2017, the Department of Health and Human Services ("HHS") and other Federal departments and agencies revised the Federal Policy for the Protection of Human Subjects (the "Common Rule"), codified with respect to HHS at subpart A of 45 CFR part 46.
- The Common Rule is followed by 19 other Federal departments and agencies, either as Common Rule signatories, or as required by Executive Order or statute. The revised Common Rule, including amendments made by a January 22, 2018 interim final rule (83 FR 2885) and June 19, 2018 final rule (83 FR 28497) (also referred to as the "2018 Requirements"), became effective on July 19, 2018.
- The revised Common Rule requires that U.S. institutions engaged in cooperative research must rely on a single institutional review board ('IRB") to review and approve the portion of the research conducted at domestic sites. The compliance date for the single IRB requirement is January 20, 2020. The revised Common Rule applies to all research initially approved by an IRB on or after January 21, 2019.
- As of January 20, 2020, the compliance date for the single IRB requirement, all cooperative research subject to the revised Common Rule will be required to use a single IRB, whether the research was initially 3 approved by a single IRB or multiple IRBs.

https://s3.amazonaws.com/public-inspection.federalregister.gov/2019-25358.pdf

16

Determination of Exception to the Required Use of a Single IRB for Certain HHS Cooperative Research

- The Office for Human Research Protections ("OHRP") and the Office of the Assistant Secretary for Health of the Department of Health and Human Services (HHS) announced its determination of exception for two categories of research from the required use of a single institutional review board (IRB) to review cooperative research under the HHS regulations for the protection of human subjects. The exception was issued in November 2019.

- OHRP determined that for HHS cooperative research subject to the revised Common Rule (also referred to as the 2018 Requirements), and for purposes of 45 CFR 46.114(b)(2)(ii), an institution may continue to use multiple IRBs, in lieu of a single IRB, for the following research:

  - (1) Cooperative research conducted or supported by HHS agencies other than the National Institutes of Health (NIH), if an IRB initially approved the research before January 20, 2020.

  - (2) Cooperative research conducted or supported by NIH if either:

    a. the NIH single IRB policy does not apply, and the research was initially approved by an IRB before January 20, 2020, or

    b. NIH excepted the research from its single IRB policy before January 20, 2020.

    - Note that this determination is only made for purposes of section 46.114(b)(2)(ii) – namely, for determining whether certain cooperative research may be excepted from the single IRB mandate.

17

OIG Updates

18

OIG Work Plan Items

Announced/ Revised	Report No.	Agency	Title	Summary	Impact
Jan-20	A-06-16-02002; A-09-16-02034; W-00-20-35726	CMS	Selected Independent Clinical Laboratory Billing Requirements	Medicare covers diagnostic clinical laboratory services that are ordered by a physician who is treating a beneficiary and who uses the results in the management of the beneficiary's specific medical problem (42 CFR 410.32(a)). Previous OIG audits, investigations, and inspections have identified areas of billing for clinical laboratory services that are at risk for noncompliance with Medicare billing requirements. Payments to service providers are precluded unless the provider furnishes on request the information necessary to determine the amounts due (the Social Security Act § 1833(e)). We will review Medicare payments for clinical laboratory services to determine laboratories' compliance with selected billing requirements. We will focus on claims for clinical laboratory services that may be at risk for overpayments.	Medicare overpayments for clinical lab services will be under scrutiny. Ensure that your organizations methodology for billing to Medicare for clinical lab services is compliant with Medicare's regulatory requirements.
Jan-20	A-18-19-06003; W-00-19-42020	NIH	Audit of National Institutes of Health's Compliance With Information Technology Controls Within the Electronic Health Records System	The National Institutes of Health (NIH) comprises 27 separate Institutes and Centers and is the primary Federal agency for conducting and supporting biomedical research to enhance health, lengthen life, and reduce illness and disability. Within NIH, certain Institutes and Centers provide direct patient care. NIH uses an electronic health records (EHR) system to help facilitate effective care. The Departments of Defense and Labor, Health and Human Services, and Education Appropriations Act, 2019 and Continuing Appropriations Act, 2019 (Public Law No. 115-245) and its Accompanying Report directed that OIG examine operations of NIH. We will determine whether select EHR system controls are in place in accordance with Federal requirements and assess EHR interoperability challenges.	Electronic health record systems will be under increased scrutiny. Ensure that your organizations methodology for the use of EHRs are compliant with Federal requirements.

19

OIG Work Plan Items (continued)

Announced /Revised	Report No.	Agency	Title	Summary	Impact
Jun-19	W-00-19-50000	FDA	Review of the Food and Drug Administration's Foreign Drug Inspection Process	FDA estimates that nearly 40 percent of finished drugs and approximately 80 percent of active pharmaceutical ingredients are manufactured in registered establishments in more than 150 countries. To ensure that drugs are manufactured in compliance with current good manufacturing practice regulations, FDA conducts inspections of foreign facilities that manufacture drugs for the U.S. market. FDA may take additional actions to ensure that the violations are corrected. FDA's major programmatic changes included a structural realignment of its Office of Regulatory Affairs (ORA) and an agreement between FDA's Center for Drug Evaluation and Research and ORA that aligns and coordinates FDA's field professionals who conduct inspections and its review staff who evaluate drug products. Recently, Congress raised concerns about the safety of certain drugs manufactured overseas and the challenges that FDA faces with its foreign drug inspection process. Our review will determine whether recent programmatic changes have improved FDA's foreign drug inspection process.	The FDA will be inspecting foreign drug facilities with greater scrutiny. Foreign drug facilities should ensure that drugs are manufactured in compliance with good manufacturing practice regulations.
Oct-19	OEI-01-19-00470	FDA	An Assessment of the U.S. Food and Drug Administration's Postmarket Surveillance of Medical Devices	As the information that the U.S. Food and Drug Administration (FDA) receives about medical device safety and effectiveness is increasingly gathered in the postmarket setting, it is more important than ever that FDA's postmarket safety surveillance system can effectively identify and act on safety signals. We will assess and describe how FDA's established passive postmarket surveillance system identifies and tracks safety concerns and assess FDA's response to those concerns. We will also describe how elements of FDA's newer surveillance system initiatives, such as the Unique Device Identification system, are being integrated into the passive postmarket surveillance system. In addition, we will describe how FDA plans to integrate these initiatives into the National Evaluation System for health Technology, its in-development active postmarket surveillance system.	The safety and effectiveness of postmarket medical devices will be under scrutiny. Ensure that your organization is identifying and appropriately documenting safety concerns with postmarket medical devices.

20

OIG Work Plan Items (continued)

Announced /Revised	Report No.	Agency	Title	Summary	Impact
May 20	W-00-20-59445	NIH	Review of Institutions of Higher Education Grantees Receiving National Institutes of Health Awards	OIG has identified areas of potential risk at institutions of higher education receiving NIH awards such as inappropriate or unsupported charges to Federal awards, lack of financial conflict-of-interest polices, and deficiencies in internal control related to the financial management system. In addition, Congress, NIH, and Federal intelligence agencies have raised concerns about foreign threats to the integrity of U.S. medical research and intellectual property at institutions of higher education. Our objective will be to determine whether institutions of higher education (1) managed NIH awards to ensure allowability of costs in accordance with Federal and award requirements, and (2) met Federal conflict-of-interest requirements.	Office of Audit Services will conduct audits of research universities throughout 2020-2021.

https://oig.hhs.gov/reports-and-publications/workplan/active-item-table.asp

OCR Updates

OCR Secures $2.175 Million HIPAA Settlement after Hospitals Failed to Properly Notify HHS of a Breach of Unsecured Protected Health Information

- In an agreement with the Office for Civil Rights ("OCR") at the U.S Department of Health and Human Services (HHS), Sentara Hospitals (Sentara) have agreed to take corrective actions and pay $2.175 million to settle potential violations of the Health Insurance Portability and Accountability Act ("HIPAA") Breach Notification and Privacy Rules. Sentara is made of 12 acute care hospitals with over 300 sites throughout Virginia and North Carolina.
- In April 2017, HHS had received a compliant regarding Sentara sending a bill to an individual containing another patient's protected health information ("PHI"). OCR opened an investigation, which determined that Sentara had mailed 577 patients' PHI to wrong addresses which included patient names, account numbers and dates of services. Sentara reported this incident as a breach to only 8 individuals since the disclosure did not include patient diagnosis, treatment information and other medical information. Sentara incorrectly persisted its refusal to properly report the breach after being advised to do so by OCR for the remaining individuals affected. OCR also found that Sentara failed to have a business associate agreement in place with Sentara Healthcare which is an entity that performed business associate services for Sentara.
- "HIPAA compliance depends on accurate and timely self-reporting of breaches because patients and the public have a right to know when sensitive information has been exposed." said Roger Severino, OCR Director. "When health care providers blatantly fail to report breaches as required by law, they should expect vigorous enforcement action by OCR."
- In November 2019, Sentara agreed to settle the HIPAA settlement with OCR for $2.175 million along with undertaking a corrective action plan that involves 2 years of monitoring.

ankura

https://www.hhs.gov/about/news/2019/11/27/ocr-secures-2.175-million-dollars-hipaa-settlement-breach-notification-and-privacy-rules.html

DOJ Updates

ankura

Recent DOJ Cases

5/2020 - Pennsylvania State University to Pay $151,000 to Resolve Potential False Claims Liability

- The United States Attorney's Office for the Middle District of Pennsylvania announced that Pennsylvania State University has agreed to pay the United States $151,000 to resolve potential liability under the False Claims Act.
- According to U.S. Attorney David J. Freed, the investigation arose from alleged mischarges to various grants and contracts from the National Science Foundation, the Department of the Navy, the National Aeronautics and Space Administration, and the Air Force. The grants and contracts were awarded to Penn State in 2012-2017 and the isolated alleged mischarges identified occurred in 2013-2016.
- "Part of the important work that takes place at such institutions involves appropriate management of federal grants and contracts. When mischarges occur, investigative arms of federal grant-making entities have a responsibility to act to on behalf of the taxpayers. In this matter, a cooperative investigation among all parties has resulted in a fair settlement and appropriate policy changes to prevent a reoccurrence of such mischarges," said U.S. Attorney Freed.
- "The integrity of the DoD grant and contracting process is a top priority for the Defense Criminal Investigative Service (DCIS)," stated Special Agent in Charge Leigh-Alistair Barzey, DCIS Northeast Field Office. "The settlement agreement announced today is the result of a joint investigative effort and demonstrates the DCIS' commitment to work with the USAO-MDPA and its law enforcement partners to ensure that claims submitted to the U.S. Department of Defense by academic institutions are reasonable, allocable, allowable and supported by adequate documentation."
- Pennsylvania State University cooperated with the investigation and has implemented policy changes to prevent mischarges in the future. The settlement agreement is not an admission of liability by Penn State.

25

Recent DOJ Cases

4/2020 - Harvard University Agrees to Pay Over $1.3 Million to Resolve Allegations of Overcharging NIH Grants

- Harvard University has agreed to pay $1,359,791 to resolve allegations that Harvard's T.H. Chan School of Public Health (HSPH) overcharged certain grants funded by the National Institutes of Health (NIH) and the Health Resources & Services Administration (HRSA). This settlement resulted from Harvard's self-disclosure of issues that it identified on NIH and HRSA grants by a particular professor and her team between at least 2009 and 2014.
- The government alleges that Professor Donna Spiegelman and her team inappropriately charged their time and effort by evenly distributing their time across all grants for which they provided statistical support, without accurately accounting for the time they actually spent on particular grants. The government further alleges that Professor Spiegelman overstated a portion of her time and effort on a HRSA-funded President's Emergency Plan for AIDS Relief ("PEPFAR") grant, on which she was key personnel. As a result, between 2009 and 2014, Professor Spiegelman and her team allegedly overcharged certain NIH and HRSA grants by approximately $1,359,791.
- "As this resolution shows, this Office will continue to examine whether colleges and universities, and their professors, are appropriately using government funding," said United States Attorney Andrew E. Lelling. "Grant fraud wastes scarce government resources and limits the availability of funding for other research. We commend Harvard for itself disclosing the alleged overcharges at the School of Public Health and for taking steps to prevent future recurrences."
- Since Harvard disclosed these potential overcharges to NIH and the U.S. Attorney's Office in 2016, it investigated the potential overcharges by the professor and others at HSPH, disclosed its findings, and worked cooperatively to explain the overcharges. In addition, Harvard has put in place additional internal controls and safeguards aimed at preventing overcharges from occurring in the future.

26

Recent DOJ Cases

4/2020 - Rice University Pays to Resolve Claims it Defrauded Federal Grant Program

- William Marsh Rice University has paid the United States more than $3.7 million to resolve claims it engaged in a pattern and practice of improperly charging National Science Foundation (NSF) research and development awards, announced U.S. Attorney Ryan K. Patrick.
- In 2016, authorities began an investigation of Rice's suspected misuse of NSF grant funds. Specifically, Rice allegedly budgeted for graduate student stipends in its research grant proposals but then used a portion of the money to pay the students to perform teaching duties unrelated to the NSF awards. As an NSF grant awardee, Rice falsely certified on each proposal, and each time it requested a payment under the grant, that it was complying with NSF award terms and conditions. Those terms and other applicable regulations require each grant recipient adhere to specific federal cost principles which state that costs must be necessary, reasonable and allocable to be properly charged to an award. Rice knowingly failed to follow these requirements.
- From Nov. 18, 2006, through Sept. 30, 2018, Rice knowingly engaged in a pattern and practice of improperly charging graduate students' stipends, tuition remission and related facilities and administrative charges to NSF awards. These charges were used in part for time the graduate students spent performing teaching duties unrelated to Rice's NSF research and development awards. The activities were not specifically incurred for the research awards, did not benefit those awards and otherwise were not allowable or allocable to the NSF awards, in violation of NSF award terms and conditions and the False Claims Act.
- To settle the allegations, Rice has agreed to pay $3,754,186– double the loss to the United States. The settlement resolved the claims without a determination of liability.

27

Recent DOJ Cases

1/2020 - Harvard University Professor and Two Chinese Nationals Charged in Three Separate China Related Cases

- According to court documents, since 2008, Dr. Lieber who has served as the Principal Investigator of the Lieber Research Group at Harvard University, which specialized in the area of nanoscience, has received more than $15,000,000 in grant funding from the National Institutes of Health (NIH) and Department of Defense ("DOD"). These grants require the disclosure of significant foreign financial conflicts of interest, including financial support from foreign governments or foreign entities. Unbeknownst to Harvard University, beginning in 2011, Lieber became a "Strategic Scientist" at Wuhan University of Technology (WUT) in China and was a contractual participant in China's Thousand Talents Plan from in or about 2012 to 2017.
- China's Thousand Talents Plan is one of the most prominent Chinese Talent recruitment plans that are designed to attract, recruit, and cultivate high-level scientific talent in furtherance of China's scientific development, economic prosperity and national security. These talent programs seek to lure Chinese overseas talent and foreign experts to bring their knowledge and experience to China and reward individuals for stealing proprietary information.
- In November 2018, NIH inquired of Harvard whether Lieber had failed to disclose his then-suspected relationship with WUT and China's Thousand Talents Plan. Lieber caused Harvard to falsely tell NIH that Lieber "had no formal association with WUT" after 2012, that "WUT continued to falsely exaggerate" his involvement with WUT in subsequent years, and that Lieber "is not and has never been a participant in" China's Thousand Talents Plan.

28

Recent DOJ Cases

1/2020 - Former Stony Brook University Professor Pleads Guilty to Stealing Cancer Research Funds

- Geoffrey Girnun, a former Associate Professor in the Department of Pathology and Director of Cancer Metabolomics at the Renaissance School of Medicine at Stony Brook University (SBU), pleaded guilty to theft of government funds from cancer-related research grants issued by the National Institutes of Health (NIH).
- "With today's guilty plea, Girnun has been held accountable for his unconscionable scheme to embezzle for his personal use hundreds of thousands of dollars in government funds that were intended to help find a cure for cancer," stated United States Attorney Donoghue.
- Between December 2013 and December 2017, Girnun stole approximately $78,000 in NIH funds that were earmarked for cancer research. He then used those funds to pay for personal expenses, including payments on his home mortgage. At his guilty plea proceeding today, Girnun agreed to pay restitution in the amount of $225,000, which includes the NIH funds and approximately $147,000 from SBU's foundation and state-sponsored grants.

Recent DOJ Cases

12/2019 - Department Of Justice Reaches $5.5 Million Settlement With Van Andel Research Institute To Resolve Allegations Of Undisclosed Chinese Grants To Two Researchers

- The Department of Justice announced that Van Andel Research Institute ("VARI") has agreed to pay $5,500,000.00 to resolve allegations that it violated the False Claims Act by submitting federal grant applications and progress reports to the National Institutes of Health (NIH) in which VARI failed to disclose Chinese government grants that funded two VARI researchers.
- The government alleged that in applying for the NIH grants, and in submitting claims for federal grant funds, VARI did not disclose any foreign research funding for those researchers or any foreign components of their NIH-sponsored research. The government specifically alleged that between Jan. 2012 and Dec. 2018, a professor received grants and research support from a variety of Chinese sources, including the People's Republic of China's Thousand Talents Program.
- U.S. Attorney Birge added that institutions concerned about a prior statement on a grant application should know that it is Department of Justice policy that entities or individuals that make "proactive, timely, and voluntary self-disclosures to the Department about misconduct will receive credit during the resolution of a False Claims Act case."

Recent DOJ Cases

11/2019 - Business Owner Found Guilty of Committing Fraud Regarding Human Clinical Research Trials

- Richland –William D. Hyslop, United States Attorney for the Eastern District of Washington, announced that Sami Anwar, 42, of Richland, WA, was found guilty late Friday of Conspiracy to Commit Wire Fraud, Conspiracy to Commit Mail Fraud, and 45 additional charged crimes including Wire Fraud, Mail Fraud, Obtaining Controlled Substances Through Fraud, and Furnishing False Information to the Drug Enforcement Administration ("DEA").
- According to the Superseding Indictment on which Sami Anwar was found guilty of all counts, and the evidence presented during the three-week long trial, between 2013 and 2018 Sami Anwar headed a conspiracy to have his companies fraudulently pose as legitimate human clinical research trial sites and provided mountains of false clinical research trial data regarding drug safety and drug efficacy to dozens of drug companies and, through them, the Food and Drug Administration (FDA).
- The false clinical research data that Sami Anwar injected into the public health system included safety data on dozens of different drugs and medicines designed to treat a wide variety of diseases and conditions including, but not limited to, heart disease, diabetes, asthma, pediatric illnesses, adolescent smoking, cirrhosis, scabies, depression, and opioid addiction to name just a few, according the evidence presented at trial. The evidence at trial indicated that Sami Anwar and his companies received over $5.6 million dollars from the fraud.

Recent DOJ Cases

10/2019 - Research Scientist Admits Making False Statements in Connection with NIH Grants

- Gerwin Schalk, age 48, of Albany, pled guilty to making false statements on conflict of interest certifications he submitted in connection with National Institutes of Health (NIH) grants. In pleading guilty, Schalk admitted that he knowingly and repeatedly lied about, and failed to disclose, payments he was receiving from a company whose products Schalk regularly purchased and used in connection with his research. Schalk admitted that the company paid him at least $70,000, from July 2013 to April 10, 2019, and that he signed at least 15 conflict of interest forms during that time, never once disclosing a payment from the company as he was required to do.

10/2019 - Professor Pleads Guilty to A Scheme to Defraud the National Science Foundation

- Dr. Han, a Purdue University professor and the Director of its Center for Materials Processing Research, devised a scheme to defraud the National Science Foundation ("NSF") into giving Hans Tech over $1.3 million in research grants through its Small Business Innovation Research ("SBIR") and Small Business Technology Transfer ("STTR") programs by making materially false and fraudulent pretenses, representations, promises and material omissions. In pleading guilty, Dr. Han, individually, and Ms. Shao on behalf of Hans Tech, acknowledged that the purpose of the scheme was to obtain grant funds allocated for research and to use some or all of those funds for other purposes, including to pay personal expenses or for the enrichment of Dr. Han, Ms. Shao, or their children.

8/2019 - University of Kansas Researcher Indicted for Fraud for Failing to Disclose Conflict of Interest with Chinese University

- Feng "Franklin" Tao, 47, of Lawrence, Kansas, an associate professor at KU's Center for Environmentally Beneficial Catalysis (CEBC), is charged with one count of wire fraud and three counts of program fraud. "Tao is alleged to have defrauded the U.S. government by unlawfully receiving federal grant money at the same time that he was employed and paid by a Chinese research university — a fact that he hid from his university and federal agencies," said Assistant Attorney General Demers for National Security.

Recent DOJ Cases

3/2019 - University to Pay $1.5 Million to Settle False Claims Act Allegations

- Scott C. Blader, United States Attorney for the Western District of Wisconsin, announced that the Board of Regents of the University of Wisconsin System, acting through the University of Wisconsin-Madison ("University"), agreed to pay $1.5 million to the United States to settle the claims that it violated the False Claims Act by failing to properly account for rebates and credits to reduce costs allocable to federal grants and awards ("Federal Awards").

3/2019 - Duke University Agrees to Pay U.S. $112.5 Million to Settle False Claims Act Allegations Related to Scientific Research Misconduct

- Duke University has agreed to pay the government $112.5 million to resolve allegations that it violated the False Claims Act by submitting applications and progress reports that contained falsified research on federal grants to the National Institutes of Health (NIH) and to the Environmental Protection Agency (EPA), the Justice Department announced today.

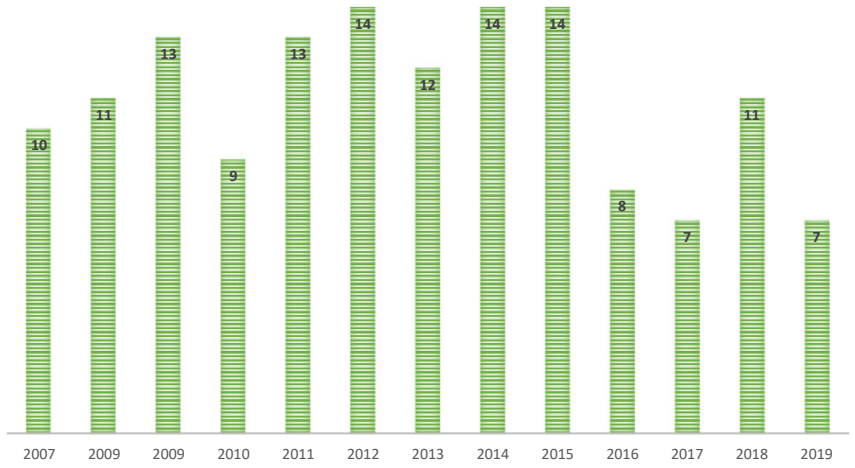
2/2019 - Former Virginia Tech Professor Found Guilty of Grant Fraud, False Statements, Obstruction

- According to evidence presented at trial, Yiheng Percival Zhang, who at the time of the offenses was a biological systems engineering professor at Virginia Tech, founded Cell-Free Bioinnovations, Inc. ("CFB"), a research firm located in Blacksburg, Virginia. CFB relied exclusively on federal grants for funding its research activities. Zhang began working as a paid researcher for the Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences by, at least, 2014. In 2015, Zhang caused fraudulent grant proposals to be submitted to the NSF. Evidence presented at trial indicated grant funds obtained would be used for research Zhang knew had already been done in China. Zhang intended to use the grant funds for other CFB projects rather than for the projects for which the funds were requested. To obstruct the investigation, Zhang submitted falsified timesheets to government investigators.

ORI Updates

ORI Updates

Cases with Research Misconduct by ORI



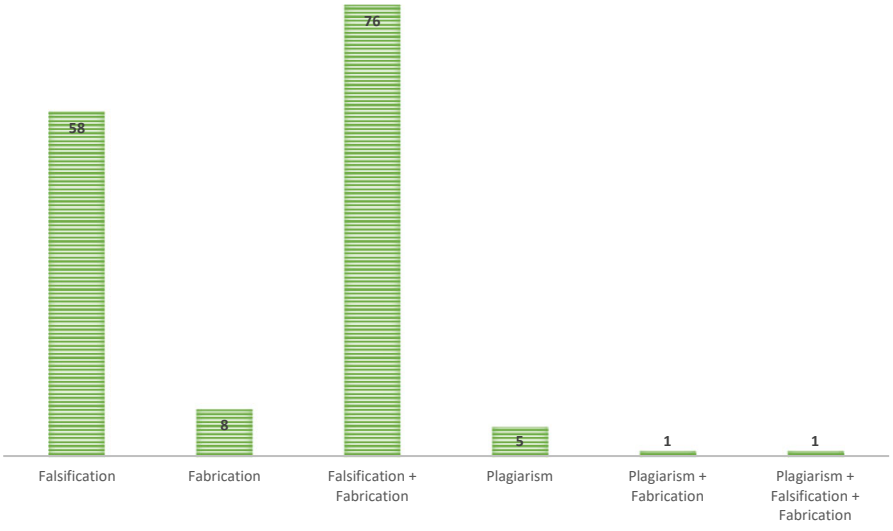
https://ori.hhs.gov/case_summary

35

35

ORI Updates

Types of Misconduct 2007 - 2019



36

36

Cases with Research Misconduct by ORI

2020 : Ozgur Tataroglu, Ph.D.: Falsification/ Fabrication

University of Massachusetts Medical School: ORI found that Dr. Ozgur Tataroglu, former postdoctoral fellow, Department of Neurobiology, UMMS, engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Institute of General Medical Sciences (NIGMS), and National Institutes of Health.

- Specifically, ORI found that Respondent engaged in research misconduct by knowingly, intentionally, and/or recklessly falsifying data in bar graphs representing phase shift of circadian clock activity between Drosophila without and with heat pulse (HP) treatment and in two (2) figures recorded in his unpublished data files, by selectively altering the original Drosophila behavior locomotor data in his primary data files.
- Dr. Tataroglu entered into an Agreement and voluntarily agreed:
  - To have his research supervised for a period of three (3) years beginning on December 30, 2019. Respondent agreed that prior to the submission of an application for PHS support for a research project.
  - A supervision plan with a committee of 2-3 senior faculty members at the institution who are familiar with Respondent's field of research, but not including Respondent's supervisor or collaborators, will provide oversight and guidance for three (3) years.
  - That for a period of three (3) years beginning on December 30, 2019, any institution employing him shall submit, in conjunction with each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved.
  - To exclude himself 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 three (3) years beginning on December 30, 2019.

37

Cases with Research Misconduct by ORI

2019 : Alexander Neumeister, M.D.: Falsification/ Fabrication

New York University School of Medicine, Langone Medical Center: ORI found that Alexander Neumeister, M.D. (Respondent), who was a Professor of Psychiatry and Radiology, Department of Psychiatry, New York University School of Medicine, Langone Medical Center (NYUSOM). Dr. Neumeister engaged in research misconduct in psychiatric clinical research supported by National Institute of Mental Health (NIMH), National Institutes of Health (NIH).

- ORI found that Respondent engaged in research misconduct by intentionally, knowingly, and/or recklessly falsifying and/or fabricating data in the clinical records of research supported by six (6) NIMH grants, resulting in the inclusion of falsified and/or fabricated research methods and results in four (4) published papers.
- This resulted in the inclusion of subjects in experimental and control groups who did not meet the criteria for entry, as specified in the protocols of the Respondent's funded grants, rendering the data and/or published results invalid in the four (4) papers.
- Dr. Neumeister entered into an Agreement and agreed:
  - To exclude himself voluntarily for a period of two (2) years, beginning on December 13, 2019, from any contracting or subcontracting with any agency of the United States Government and from eligibility for or involvement in nonprocurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension.
  - To exclude himself 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 four (4) years.
  - As a condition of the Agreement, Respondent will utilize information provided by ORI to request that the following papers be corrected or retracted in accordance with 42 C.F.R.§ 93.407(a)(1).

38

Cases with Research Misconduct by ORI

2019 : Erin N. Potts Kant: Falsification/ Fabrication

Duke University School of Medicine: ORI found that Erin N. Potts Kant engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), National Institute on Environmental Health Sciences (NIEHS), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Cancer Institute (NCI), National Center for Research Resources (NCRR), and National Institute of Child Health and Human Development (NICHD) grants.

- ORI found that Respondent engaged in research misconduct by knowingly and intentionally falsifying and fabricating research data included in one hundred and seventeen (117) figures and two (2) tables in thirty-nine (39) published papers, three (3) manuscripts, and two (2) research records, fabricating data and analyses in a manuscript submitted to *Nature*, which was subsequently voluntarily withdrawn. These fabricated data and analyses also appear in Figure 1 of grant progress report R01 CA193649-02. Respondent stated during the inquiry that two abstracts that appear in *Cancer Research* are based on the fabricated data and analyses.
- Ms. Potts Kant entered into a Voluntary Exclusion Agreement (Agreement) and voluntarily agreed, beginning on October 1, 2019:
  - To exclude herself permanently from any contracting or subcontracting with any agency of the United States Government and from eligibility for or involvement in nonprocurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation (2 C.F.R. Part 376) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension, 2 C.F.R. Part 180 (collectively the "Debarment Regulations").
  - To exclude herself permanently 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.

39

Cases with Research Misconduct by ORI

2019 : Deepti Malhotra: Falsification/ Fabrication

Ph.D., Johns Hopkins Bloomberg School of Public Health: ORI found that Deepti Malhotra, Ph.D. (Respondent), former Doctoral Student and Postdoctoral Fellow, Department of Environmental Health Sciences, JHSPH, engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Heart, Lung, and Blood Institute (NHLBI), and National Institutes of Health (NIH) grants.

- ORI found that Respondent engaged in research misconduct by knowingly, intentionally, and/or recklessly falsifying and/or fabricating data included in the following four (4) published papers and her Ph.D. Thesis.
- Respondent knowingly, intentionally, and/or recklessly falsified and/or fabricated Western blot data for protein expression in cultured cell lines and/or alveolar macrophages of patients with chronic obstructive pulmonary disease (COPD), reusing and relabeling them to represent Western blot data for unrelated experiments in seventeen (17) figures included in four (4) published papers and twelve (12) figures included in her Ph.D. Thesis.
- Dr. Malhotra entered into a Voluntary Exclusion Agreement (Agreement) and agreed for a period of four (4) years, beginning on October 1, 2019:
  - To exclude herself voluntarily from any contracting or subcontracting with any agency of the United States Government and from eligibility for or involvement in nonprocurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation (2 C.F.R. Part 376) of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension, 2 C.F.R. Part 180 (collectively the "Debarment Regulations").
  - 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.

40

Cases with Research Misconduct by ORI

2019 : Dr. Sudhakar Yakkanti: Falsification/ Fabrication

Boys Town National Research Hospital: ORI found that Dr. Sudhakar Yakkanti (Respondent), former staff scientist and Director of the Cell Signaling, Retinal & Tumor Angiogenesis Laboratory, BTNRH, engaged in research misconduct in research supported by PHS funds, specifically, NCI and NIH grants.

- ORI found by a preponderance of the evidence that Respondent intentionally, knowingly, or recklessly falsified and/or fabricated figures in the following eight (8) unfunded NIH grant applications, one (1) funded NIH grant application, seven (7) publications, and two (2) unpublished manuscripts.
- The following administrative actions have been implemented, beginning on August 24, 2019:
  - Respondent is debarred for a period of five (5) years from eligibility for any contracting or subcontracting with any agency of the United States Government and from eligibility for, or involvement in, nonprocurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation (2 C.F.R. Part 376 *et seq*) of Office of Management and Budget (OMB) Guidelines to Agencies on Governmentwide Debarment and Suspension, 2 C.F.R. Part 180 (collectively the "Debarment Regulations").
  - Respondent is 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 five (5) years.
  - In accordance with 42 C.F.R. 93 §§ 93.407(a)(1) and 93.411(b), HHS will send a notice of the findings and of the need for correction or retraction to the pertinent journals.

41

Cases with Research Misconduct by ORI

2019 : Dr. Rahul Agrawal: Falsification/ Fabrication

National Institutes of Health: Based on Respondent's admission, an assessment conducted by the National Institutes of Health (NIH), and additional analysis conducted by the Office of Research Integrity (ORI) in its oversight review, ORI found that:

- Dr. Rahul Agrawal (Respondent), former visiting fellow at the Center for Cancer Research, Laboratory of Pathology, Cancer Molecular Pathology Section, National Cancer Institute (NCI), NIH, engaged in research misconduct in research supported by the Intramural Research Program of NCI, NIH.
- ORI found that Respondent engaged in research misconduct by intentionally, knowingly, and/or recklessly falsifying and/or fabricating data in the unpublished research record by the alteration, reuse, and/or relabeling of quantitative real-time polymerase chain reaction (qRT-PCR) data and colony forming cell (CFC) and focus formation (FF) assay images to represent experiments that measured microRNA expression levels and the effect of long intergenic non-protein coding (LINC) RNAs in human cancer cell lines that were not conducted.
- ORI found that Respondent knowingly, intentionally, and/or recklessly falsified and/or fabricated: qRT-PCR data in fifty-nine (59) Excel files by:
  - Conceiving Cycle Threshold (CT) values and PCR machine run identification numbers and run dates for fifty-nine (59) experiments that were not conducted.
  - Inserting falsified and/or fabricated CT values in fifty-four (54) files that originated from one (1) Excel template with a single file creation date to represent distinct experimental runs with different experimental dates in exported Excel files from the PCR machine.
  - Utilizing an earlier PCR machine calibration date in four (4) Excel files to represent experiments completed at a later date.
- Dr. Agrawal entered into a Voluntary Settlement Agreement (Agreement) and voluntarily agreed:
  - To have his research supervised for a period of one (1) year beginning on August 8, 2019. Respondent agreed that prior to the submission of an application for U.S. Public Health Service (PHS) support for a research project on which Respondent's participation is proposed and prior to Respondent's participation in any capacity on PHS-supported research.

42

Cases with Research Misconduct by ORI

2019 : William W. Cruikshank: Falsification/ Fabrication

Ph.D., Boston University School of Medicine: Based on an investigation conducted by Boston University (BU) and analysis conducted by the Office of Research Integrity (ORI) in its oversight review, ORI found that William W. Cruikshank, Ph.D. (Respondent), former Professor of Medicine, Pulmonary Center, BU School of Medicine engaged in research misconduct in research supported by National Cancer Institute (NCI) and National Institutes of Health (NIH) grants.

- ORI found that Respondent engaged in research misconduct by knowingly, intentionally, and/or recklessly falsifying and/or fabricating data included in the following published paper, an earlier version of the submitted manuscript, a seminar presentation, and two grant applications submitted to NCI and NIH.
- Respondent knowingly, intentionally, and recklessly falsified and/or fabricated Western blot data for protein expression in primary CD4+ T cells from patients with advanced T-cell acute lymphocytic leukemia (T-ALL) or cutaneous T-cell lymphomas (CTCL), by copying blot band images from unrelated sources, manipulating to disguise their origin, and combining multiple images to generate new figures to falsely represent results using sixty-four (64) such band images in the following sixteen (16) figures and related text included in one (1) manuscript, one (1) published paper, two (2) grant applications, and a seminar presentation.
- Dr. Cruikshank entered into a Voluntary Exclusion Agreement (Agreement) and voluntarily agreed for a period of five (5) years, beginning on May 13, 2019:
  - To exclude himself from any contracting or subcontracting with any agency of the United States Government.
  - To exclude himself 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.

43

Cases with Research Misconduct by ORI

2019 : Edward J. Fox, Ph.D.: Falsification/ Fabrication

University of Washington: Based on Respondent's admission, an inquiry conducted by the University of Washington (UW), and additional analysis conducted by the Office of Research Integrity (ORI) in its oversight review, ORI found that Edward J. Fox, Ph.D. (Respondent), former Acting Assistant Professor in the Department of Pathology, UW, engaged in research misconduct in research supported by National Cancer Institute (NCI) and National Institutes of Health (NIH) grants.

- ORI found that Respondent engaged in research misconduct by intentionally, knowingly, or recklessly:
  - Fabricating data and analyses in a manuscript submitted to *Nature*,[1] which was subsequently voluntarily withdrawn. These fabricated data and analyses also appear in Figure 1 of grant progress report R01 CA193649-02.[2] Respondent stated during the inquiry that two abstracts that appear in *Cancer Research*[3] are based on the fabricated data and analyses.
  - Fabricating or falsifying data and analyses in the preliminary results section of grant application R01 CA193649-01A1, section C.1.a(iv).
  - Presented data-based explanations that are fabricated or falsified because some of them were based on the fabricated or falsified data.
- Respondent and ORI desire to close this matter without further expense of time and other resources and thus have entered into a Voluntary Settlement Agreement (Agreement). With respect to grant application R01 CA193649-01A1, Respondent acknowledges that his research records were poorly maintained and lacked the documentation necessary to support the reported preliminary results.
- Dr. Fox entered into an Agreement and voluntarily agreed:
  - To have his research supervised for a period of one (1) year beginning on March 18, 2019. Respondent agreed that prior to submission of an application for U.S. Public Health Service (PHS) support for a research project.

44

Sources

- https://www.govinfo.gov/content/pkg/FR-2019-02-25/html/2019-03195.htm
- https://www.federalregister.gov/documents/2019/09/06/2019-19290/humanitarian-device-exemption-program-guidance-for-industry-and-food-and-drug-administration-staff
- https://www.federalregister.gov/documents/2019/03/15/2019-04815/enrichment-strategies-for-clinical-trials-to-support-demonstration-of-effectiveness-of-human-drugs
- https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126500.pdf
- https://crsreports.congress.gov/product/pdf/IN/IN11207
- https://nexus.od.nih.gov/all/2020/01/10/case-study-in-review-integrity-asking-for-favorable-treatment/
- https://oig.hhs.gov/fraud/docs/advisoryopinions/2019/AdvOpn19-03.pdf
- https://oig.hhs.gov/fraud/docs/advisoryopinions/2019/AdvOpn19-04.pdf
- https://oig.hhs.gov/reports-and-publications/workplan/active-item-table.asp
- https://www.hhs.gov/about/news/2019/11/27/ocr-secures-2.175-million-dollars-hipaa-settlement-breach-notification-and-privacy-rules.html
- https://www.justice.gov/usao/pressreleases
- https://ori.hhs.gov/case_summary

45

QUESTIONS

F. Lisa Murtha: lisa.murtha@ankura.com Or (215) 801-7824

46