Ministry of Health and Sports

Research Misconduct

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Research Misconduct

Fabrication, Falsification and Plagiarism of data in either proposing, performing, reporting or review of data

The major forms of misconduct are:

Fabrication - making up data or results and recording or reporting them as though they were real. Creating data that were never obtained

Falsification - manipulating research materials, processes, or changing or omitting data or results such that the data do not represent what actually occurred

Plagiarism - appropriation of another person's ideas, processes, results, or words without giving proper credit including those obtained through confidential review of others' research proposals and manuscripts

Fraud

- Wrongful or criminal deception intended to result in financial or personal gain

- A person or thing intended to deceive others, typically by unjustifiably claiming or being credited with accomplishments or qualities

ARE FRAUD AND MISCONDUCT THE SAME?

- There is a gross distinction between the two.

- Fraud is an intentional deception made for personal gain or to damage another individual, for instance, intentionally falsifying and/or fabricating research data, and misleading reporting of the results.

- Misconduct may not be an intentional action, rather an act of poor management. It also includes failure to follow established protocols if this failure results in unreasonable risk or harm to humans

Misconduct in different stages of research

From research question- to-publication

Planning of the research:

- Presuming the research question is scientifically driven while it is actually based on commercial or political interests, namely the interests of those granting the study
- Using other people's ideas in research proposals and applications for funding without permission and/or citation
- Making up data or pilot data for research proposals and applications for funding

Research practice (methodology) misconduct

- Poor research design
- Experimental, analytical, computational errors
- Violation of human subject protocols
- Abuse of laboratory animals

Data-related misconduct

- Fabrication and falsification of data
- Wholly or partly failing to observe the inclusion and exclusion criteria in the protocol
- Infringing the privacy of persons
- Bad data management, storage

Analysis

- Manipulating data to produce better results; adding and discarding data
- Improper use of statistical techniques to produce more desirable conclusions
- Distorted interpretation of data or distorted conclusions

Reporting

- Incorrect or distorted representation of other people's findings (misquotation)
- Intentional and unjustifiable referencing
- Failing to acknowledge other people's original observations (under-citation)
- Exaggerated self-citation to inflate one's own citation index

Plagiarism

- Plagiarism (copying of sentences without referencing)
- Appropriation of another person's ideas, processes, results, or words without giving proper credit including those obtained through confidential review of others' research proposals and manuscripts

Submission for publication

- Claiming undeserved authorship
- Denying authorship to contributors
- Artificially proliferating publications
- Unreported conflict of interest

Financial and other misconduct

- Misuse of research funds for unauthorised purchases or for personal gain
- Peer review abuse e.g., unfairly holding up a rival's publication
- Making an unsubstantiated or malicious misconduct allegation

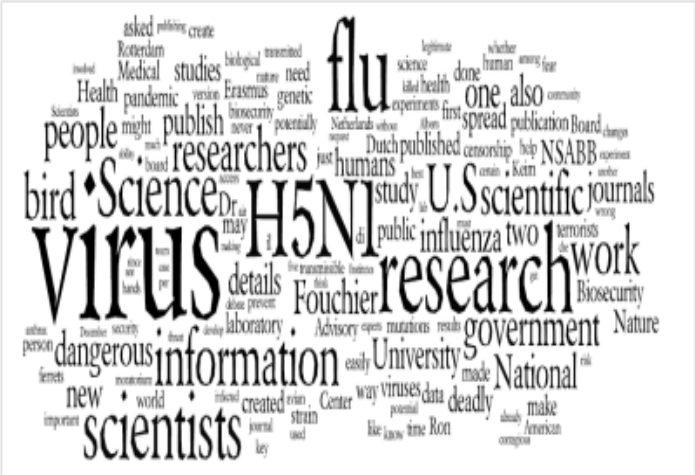
Examples of Fraud in Clincal trials

- Tampering with eligibility criteria for inclusion
- Pt. entered several times
- Pts. enrolled in other concurrent studies
- Forged Consent Forms
- Falsifying Ethics Committee approval
- Fabricating lab results

Responsible Life Science and Dual Use Research

Dual-Use Research (DUR) is legitimate life sciences research that is intended for benefit, developed for beneficial purposes, but which might yield information and/or technology that can easily be misapplied for malevolent purposes.

(Talk on RCR: Biosafety/Biosecurity of Emerging Pathogens at 47th Myanmar Health Research Congress, January, 2019)



Criteria for Research misconduct

- RM must be committed intentionally or knowingly, or recklessly
- Research misconduct does NOT include honest error
- Thorough investigation of an allegation is vital
- Allegation must be proven by sufficient evidence

What are the consequences?

Consequences of misconduct and fraud

Actions may include, but are not limited to:

- Debarment from eligibility to receive funds for grants & contracts (Ineligibility to apply for grants for years)
- Prohibition from service on advisory committees, peer review committees, or as consultants
- Stopping mentorship program

Consequences of misconduct and fraud (cont..)

- Withdrawal or correction of all pending and published papers & abstracts affected by misconduct
- Reprimand, removal from project
- Rank & salary reduction
- Reassignment of position
- Loss of employment

Action taken may be time limited or permanent

Consequences of misconduct and fraud (cont..)

- Harm to individuals and to society, if fraudulent research results in the release of an unsafe product or process (e.g., a drug or a therapy). Society may be harmed if false results become widely known and believed
- Direct damage to science itself, by creating false leads for other scientists to follow, and/or forcing others to waste time, effort and money to reproduce fraudulent results

Consequences of misconduct and fraud (cont..)

- The degradation of relations among scientists, between senior researchers and students and between researchers and programme managers

- Damage the reputation of the institution

Misconduct studies

- In a 2002 survey in Nature of 3,600 mid-career scientists and 4,160 postdocs, NIH researchers
- 33% of respondents admitted punishable misbehavior in the previous 3 years, including:

  - falsifying or fabricating data

  - not disclosing conflicts of interest

  - using others' ideas without credit

  - failing to present data that contradict one's previously published research

Case Studies

Dr Robert Fiddes (1997)

Director of Southern California Research Institute, USA

Lead investigator in clinical trials for pharmaceutical company sponsors

- Fictitious patients enrolled
- Paid 25 USD per urine sample to employee with proteinuria (inclusion criteria for clinical trial) as it were from patient
- Lab data altered
- Blood pressure, EKG results fabricated

Whistleblower contacted FDA to do investigation
Fraud over a decade
Sentenced to 15 months in prison

Dr Werner Beswoda (1999)

Professor and chair of Department of Haematology and Oncology, University of Witwatersrand, South Africa

In 1999 at the ASCO (American Association of Clinical Oncology) meeting positive (statistically significant) favouring the use of high-dose chemotherapy and stem cell rescue in treatment of breast cancer

The NCI (National Cancer Institute) hired independent audit team –

- No medical records available for patients
- No evidence of informed consent
- No approval by human research oversight committee

Removed from position after admitting to misconduct

Dr Eric Poehlman (2005)

An expert on ageing and metabolism, at University of Vermont College of Medicine, USA

Falsifying data in 15 federal grant applications & 10 published articles

Grant funds - 3 million USD (NIH)

One year in jail & $250,000 fine and has been barred for life from receiving any U.S. research funding

Dr Jon Sudbo (2005)

Norwegian physician and researcher

Published in *The Lancet* a paper on NSAID and the risk of oral cancer

Case control study of 908 subjects (454 oral cancer patients and 454 matched controls) with findings-
“ Long term use of NSAIDs associated with reduced incidence of oral cancer but increased risk of death due to cardiovascular disease”

On investigation-

- All 908 patients fictitious (complete fabrication) (records showed 250 subjects had same birthday)
- Previous papers (including doctoral dissertation contained fabricated data)

Banned from practicing medicine and conducting medical research

Dr Scott Reuben (2010)

Anesthesiologist-Chief of acute pain clinic, Massachusetts, USA

Clinical trial of Celebrex and Vioxx for post operative pain management-

- said to enroll 200 patients
- 100 cases and 100 controls
- not enrolled in reality

Six months in prison and > $300,000 fine to pharmaceutical company

Dr Haruko Obokata (2014), Riken Institute, Kobe, Japan

Major ground breaking "STAP" cells (Stimulus Triggered Acquisition Pleuropotential cells)- published in the journal "Nature"

-Methods not reproducible (10 stem cell labs)

-Images manipulated (splicing from other experiments)

-Cell lines incorrect

-Methods copied from others without citation (Plagiarism)

-Article retracted from journal

-Dr Obokata removed from her job

-Whole institution under investigation

Dr He Jiankui (2018), Southern University of Science and Technology, Shenzhen, China

- In Nov 2018, Dr. He Jiankui claimed to have genetically edited twin babies to reduce HIV risk (Edited CCR5 gene)
- High-risk research – CRISPR technology is not ready to be tested in humans

Nature Research Co. & JKin Cheung/AP/Shutterstock

Human genome editing: CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)

1. Faked ethics approval documents and informed consent
2. Lack of background research data
3. Technical errors
4. Non-transparancy of results

Fired from his University, sentenced to three years in prison and fined $ 430,000

Why does research misconduct happen?

- Publish or Perish Pressure
- Desire to “get ahead” (highly competitive)
- Dependent on scarce resources (cut corners, speed things up)
- Personal problems

Agencies relevant to research fraud

Office for human research protections*	www.hhs.gov/ohrp/
Office of research integrity*	http://ori.dhhs.gov
US food and drug administration	www.fda.gov
Office of human subjects research, national Institutes of health	see http://ohsr.od.nih.gov/ guidelines for regulations and ethics) guidelines
Association for the accreditation of human research protection programs, Inc. (private accrediting agency)	www.aahrpp.org
Association of American universities#	www.aau.edu
Association of American medical colleges#	www.aamc.org

*Part of the US department of health and human service, #Provides guidelines for research conduct

Gupta A, Perspect Clin Res. 2013:4: 144-147

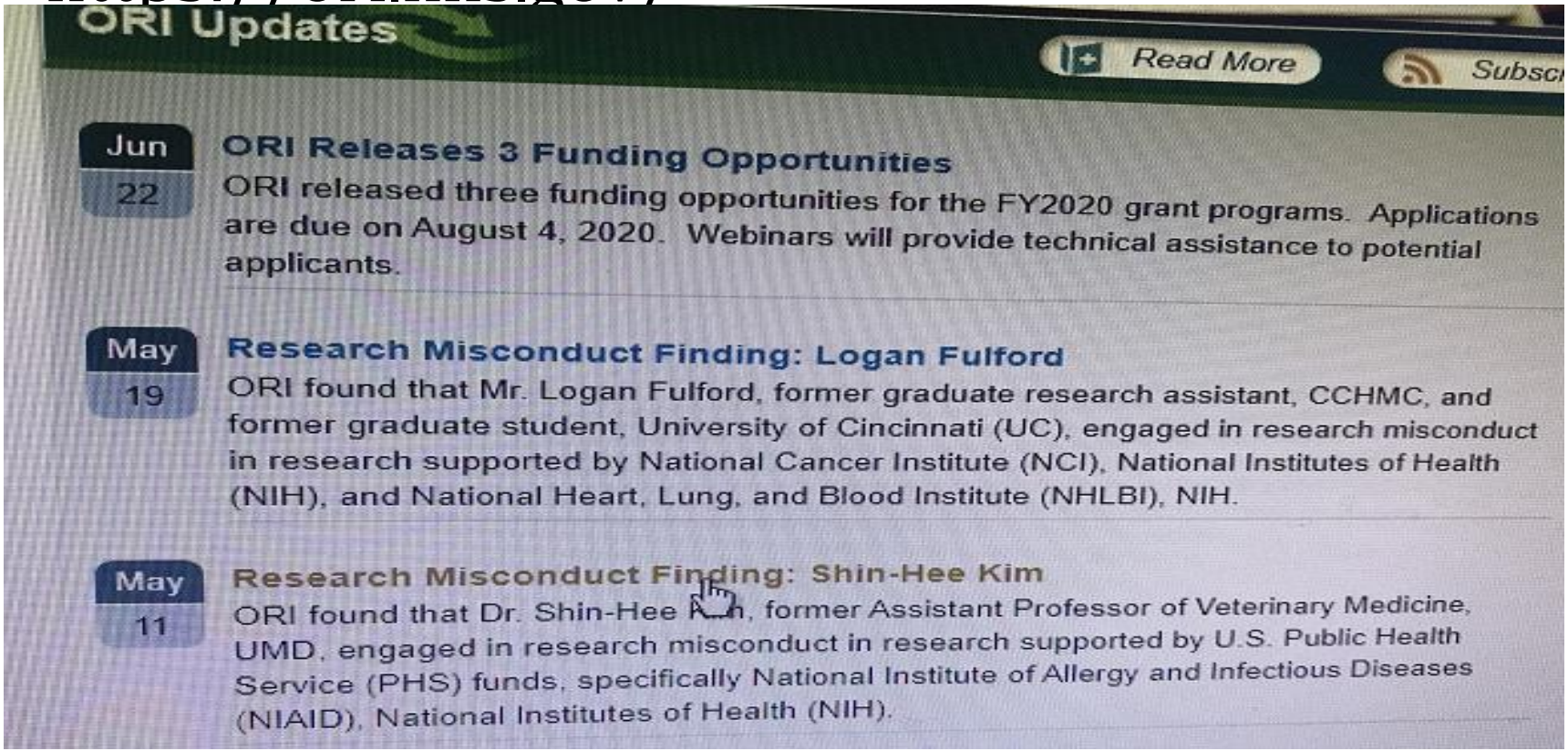
ORI carries out its responsibility by-

•Developing policies, procedures and regulations related to the detection, investigation, and prevention of research misconduct and the responsible conduct of research;

•Reviewing and monitoring research misconduct

•Implementing activities and programs to teach the responsible conduct of research, promote research integrity, prevent research misconduct, and improve the handling of allegations of research misconduct;

Check the ORI website- https://ori.hhs.gov/



Office of Research Integrity recommendations to reduce Research Misconduct

- **Adopt zero tolerance**
- **Clarify how to report RM**
- **Properly train the Mentors**
- **Promoting model ethical behavior**
- **Protect both whistleblowers & the accused until a determination is made**

The need for building Research Culture

- Research Misconduct can occur especially where there lack of an effective mechanism / organization for detection , investigation and prosecution of misconduct in most countries

- Thus, critical to develop a good “research culture” developed within the system based on fundamentals such as “integrity”

The pursuit of scientific investigation with “**integrity**”-

Responsible Conduct of Research (RCR)

The general principles of integrity include:

- honesty
- trust
- fairness
- respect
- responsibility

What can be done to Promote Research Integrity in your institution?

- Know and understand your institution's standards, vision, missions and expectations on research
- Endeavor to uphold the shared values in your work and in your conduct- honesty, accuracy, efficiency and objectivity

Building Research Culture

•Every organization involved in research should have and implement clear policies and Standard Operating Procedures (SOPs)

•Open communication amongst the research groups on this important aspect of Responsible Conduct of Research (RCR) in addition to discussion on ongoing projects and practices may help reduce the incidence of fraud if not completely prevent it

• Finally, the emphasis should be more on quality rather than quantity of research

CONCLUSION

In essence, there should be a system of shared responsibilities between-

- **Researchers**
- **Sponsors/ Funding agencies**
- **Ethics Review Committees/IRBs as well as**
- **Monitoring and regulatory bodies all working together to preserve the integrity of research!**

Information Sources

•Bhatt A. Quality of clinical trials: A moving target. Perspect Clin Res. 2011;2:124–8.

•Gupta A. Fraud and misconduct in clinical research: A concern. Perspect Clin Res. 2013:4: 144-147

• Jessen J, Robinson E, Bigaj S, Popiolek S, Goldfarb NM. Unreported clinical research fraud and misconduct. J Clin Res Best Pract. 2007;3:1–5.

• Office of Research Integrity http://ori.dhhs.gov/

• Polanin-Huk J, Huk J, Filip R. Fraud and misconduct in clinical research.2010; 2:158-160

Information Sources

- Sheehan JG. Fraud, conflict of interest, and other enforcement issues in clinical research. Cleve Clin J Med. 2007;74:S63–7.
- Steneck, Nicholas H. (2007) ORI: Introduction to the Responsible Conduct of Research.
- Titus SL, Wells JA, Rhoades LJ. Repairing research integrity. Nature. 2008;453:980–2.
- Workshop on Responsible Conduct of Research and Research Ethics, Department of Medical Research (POLB), April 2019, Pyin Oo Lwin.

Thank you
for your kind attention!