BANGKOK HOSPITAL

ที่ พร 62 / 2561

ใบเรียน
วันที่ 4 มิ.ย.61
เวลา 16.54น.

คณะแพทยศาสตร์
จุฬาลงกรณ์มหาวิทยาลัย
056421/3561
6 มิ.ย.61 11.00

คณะกรรมการจริยธรรมการวิจัยในคน รพ.กรุงเทพ สนง.ใหญ่

30 พฤษภาคม 2561

เรื่อง ขอเรียนเชิญ ศาสตราจารย์กิตติคุณ แพทย์หญิงชาดา สืบหลินวงศ์ เป็นวิทยากร
เรียน คณบดี คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
สิ่งที่ส่งมาด้วย กำหนดการจัดประชุมวิชาการ

ด้วยคณะกรรมการจริยธรรมการวิจัยในคน โรงพยาบาลกรุงเทพ สำนักงานใหญ่ จะได้จัดการอบรม "จริยธรรมการวิจัยในคน 2018" **ในวันศุกร์ที่ 5 ตุลาคม พ.ศ. 2561** เวลา 08.30 – 16.00 น. ณ ห้องประชุม 7R1 อาคาร R (Rehabilitation) ชั้น 7 โรงพยาบาลกรุงเทพ สำนักงานใหญ่ ซอยสุขุมวิท 3 โดยมีวัตถุประสงค์เพื่อให้บุคลากรและผู้วิจัยได้รับความรู้เกี่ยวกับจริยธรรมการวิจัยในคน เพื่อให้สามารถดูแลและให้การปกป้องผู้เข้าร่วมโครงการวิจัยอย่างถูกต้อง

ในการนี้คณะกรรมการจริยธรรมการวิจัยในคน โรงพยาบาลกรุงเทพ สำนักงานใหญ่ มีความเห็นว่า ศาสตราจารย์กิตติคุณ แพทย์หญิงชาดา สืบหลินวงศ์ เป็นผู้มีความรู้ ความสามารถและประสบการณ์ที่จะให้ความรู้แก่ผู้เข้ารับการอบรมครั้งนี้ได้เป็นอย่างดี จึงขออนุญาตเรียนเชิญศาสตราจารย์กิตติคุณ แพทย์หญิงชาดา สืบหลินวงศ์ เป็นวิทยากรบรรยาย ซึ่งมีรายละเอียด ดังนี้

08:45-10:30	**แนวคิดหลักการทั่วไปของจริยธรรมการวิจัยในคน และประเด็นที่สำคัญ** c History of ethics in human subjects research c International and national regulation including Good Research Practice c Principles of human subjects research o Respect for person: Informed consent process / Confidentiality / Privacy o Beneficence: Risk vs benefit / Scientific Integrity o Justice: Inclusion and exclusion criteria / Number of research participants o Vulnerable subjects o Research involving vulnerable subjects o Requirements when children are research participants o Broad consent

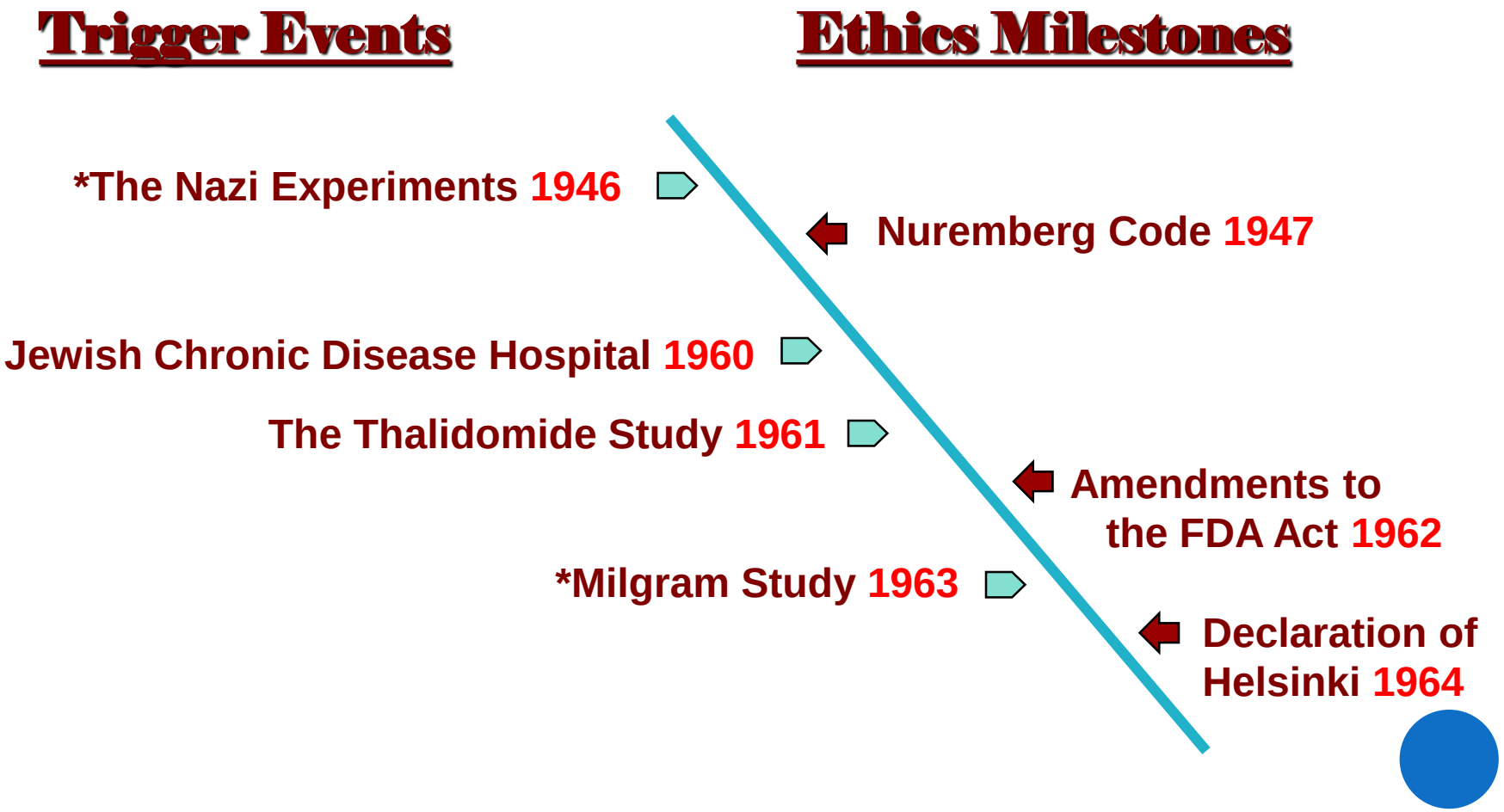
08:45-10:30	**แนวคิดหลักการทั่วไปของจริยธรรมการวิจัยในคน และประเด็นที่สาคัญ** o History of ethics in human subjects research o International and national regulation including Good Research Practice o Principles of human subjects research o Respect for person: Informed consent process / Confidentiality / Privacy o Beneficence: Risk vs benefit / Scientific Integrity o Justice: Inclusion and exclusion criteria / Number of research participants o Vulnerable subjects o Research involving vulnerable subjects o Requirements when children are research participants o Broad consent

Research Ethics on Human participants

Tada Sueblinvong

5 October,2018

Research Ethics Milestones



*From "Protecting Study Volunteers in Research" Dunn & Chadwick

Research Ethics Milestones

Trigger Events

*The Beecher Article 1966

Willowbrook 1972

*The Syphilis Study

(1932-1972)

Ethics Milestones

US Federal Regulations

The Belmont Report 1979

Consolidated HHS/FDA Regulations 1981

CIOMS Guidelines 1982

ICH GCP 1996

National Bio Ethics Advisory Committee

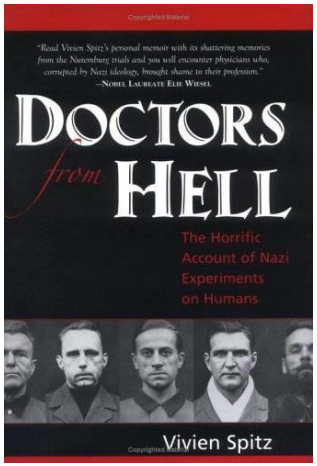
Declaration of Helsinki 2013

During World War II

- แพทย์ชาวนาซีทำการทดลองในค่ายกักกันเชลยศึก
- ไม่มีการขอคำยินยอม
- ผลการทดลองมีผู้เสียชีวิตหรือพิการเป็นจำนวนมาก

The Nuremberg Military Tribunals in 1946

- แพทย์ชาวเยอรมัน 23 คน
- ทำการทดลองที่ผิดมนุษยธรรมภายในค่ายกักกันเชลยศึกโดยปราศจากความปรานี ไร้ศีลธรรม
- 16 คนมีความผิดจริงตามข้อกล่าวหา
- 7 คนถูกตัดสินประหารชีวิต



The Nuremberg Code (1947)

As part of the verdict, the Court enumerated some rules for "Permissible Medical Experiments", now known as the “Nuremberg Code”. These rules include:

- หลักการของการขอคำยินยอม
- สัดส่วนความเสี่ยงและประโยชน์ที่จะได้รับ
- ความสามารถหรือสิทธิของอาสาสมัครในการออกจากการเป็นส่วนหนึ่งของงานวิจัย

http://www.hhs.gov/ohrp/references/nurcode.htm

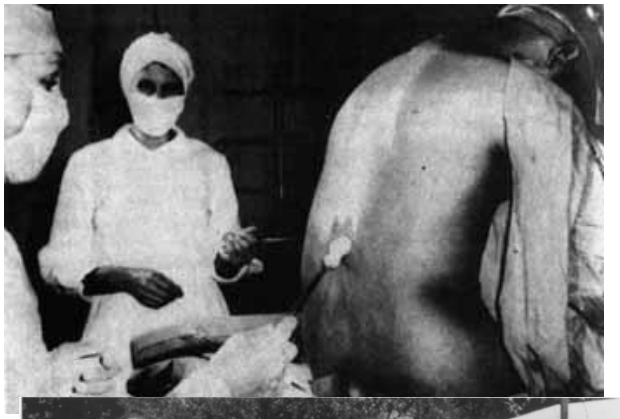
Tuskegee Syphilis Experiment

(1932-1972)

- โครงการได้รับการสนับสนุนจากรัฐบาลสหรัฐ
- คนผิวดำ 399 ที่ป่วยเป็นโรคซิฟิลิสถูกชักชวนเข้าร่วมโครงการ
- ไม่ได้รับการชี้แจงว่าเข้าร่วมโครงการอะไร ตัวเองป่วยเป็นอะไร
- ประโยชน์คือได้รับอาหารกลางวันฟรี ค่าเดินทางฟรี ตรวจร่างกายฟรี
- **ไม่ได้รับการรักษา**

SECOND PHASE BEGAN IN 1933

- โครงการเพิ่มกลุ่มควบคุม 201 คน
- ทั้งหมดเป็นคนผิวดำ
- ประโยชน์คือได้รับการตรวจศพ ฟรี
- ไม่ชี้แจงรายละเอียดเกี่ยวกับการวิจัย
- บอกเพียง เป็นการทดลองเกี่ยวกับเลือดเสีย **Bad Blood**



New York Times Reported Tuskegee case in (1972)

- หนังสือพิมพ์ลงข่าว
- นำเข้าสู่สภา ในปี 1973
- รัฐบาลต้องสั่งระงับการทดลอง
- รัฐบาลจ่ายค่าชดเชยให้ผู้เสียชีวิตและครอบครัว

The New York Times

Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HELLER
The Associated Press

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its late effects, even though an effective therapy was eventually discovered.

The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

Doctors in the service say they are now rendering whatever other medical services they can give to the survivors while the study of the disease's effects continues.

Dr. Merlin K. DuVal, Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men,

Kenneth John Ryan, Chair

The Commission

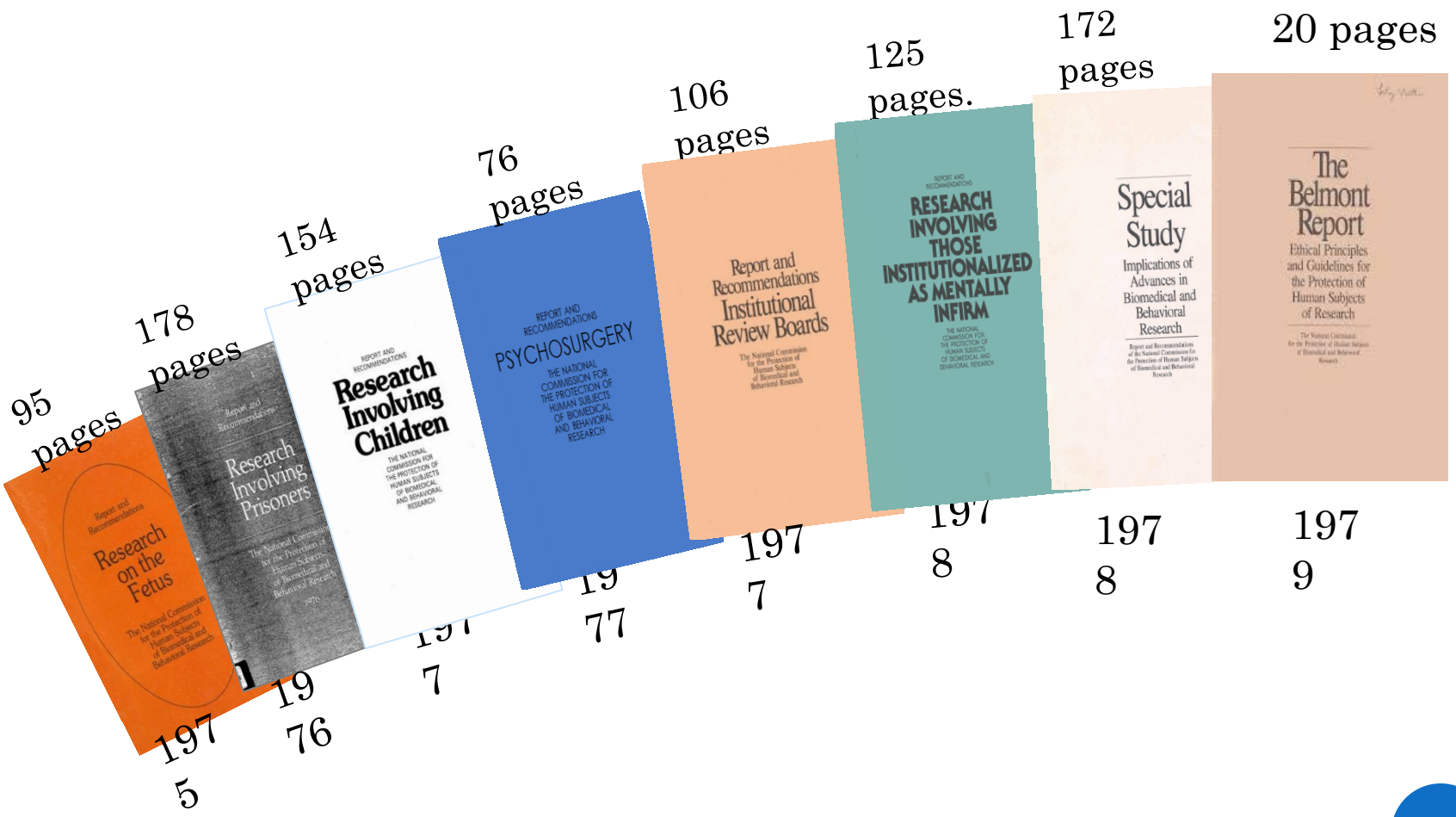
- 3 MDs
- 4 PhDs
  - 1=ethics,
  - 1=psychologist
- 3 Lawyers
- 1 Lay person

period of discussions at the Smithsonian Institution's **Belmont Conference**

Monthly deliberations- 4 years

Does **not** make specific recommendations for administrative action

Reports and recommendations



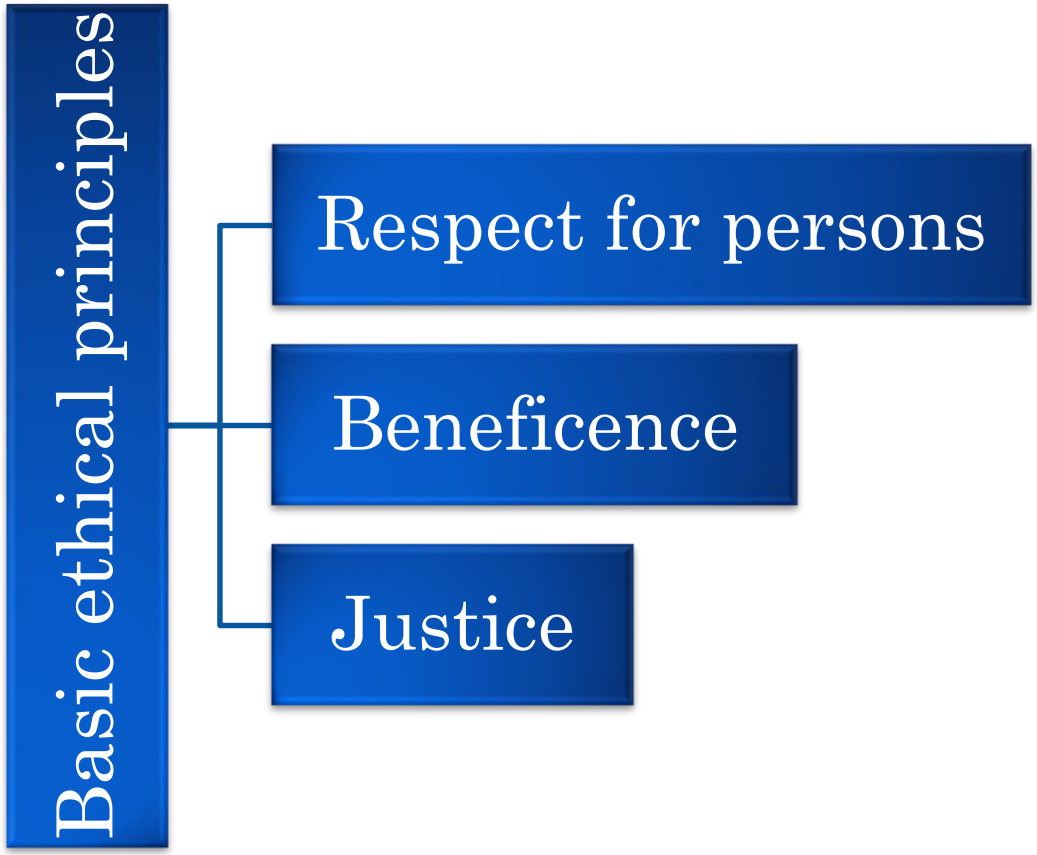
http://en.wikipedia.org/wiki/National_Commission_for_the_Protection_of_Human_Subjects_of_Biomedical_and_Behavioral_Research

The Belmont Report

PART A: BOUNDARIES BETWEEN PRACTICE & RESEARCH

- "**Practice**" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success.
- "**Research**' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships).

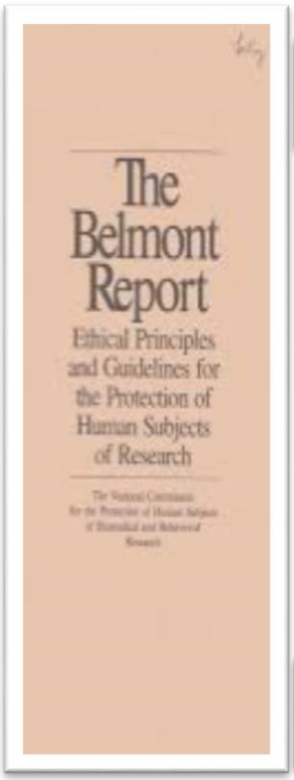
PART B: BASIC ETHICAL PRINCIPLES

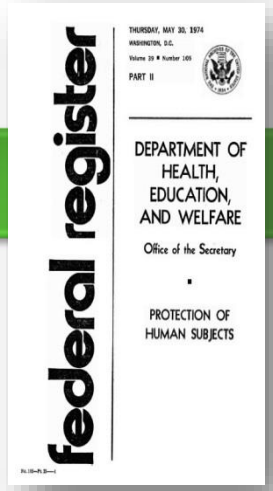


INFLUENCES

1991-Common rule

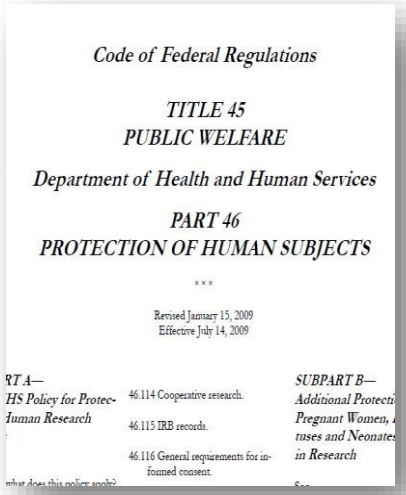
1974





- 7 CFR Part 1c - Department of Agriculture
- 34 CFR Part 97 – Department of Education
- 49 CFR Part 11 - Department of Transportation

2009



1981

http://www.hhs.gov/ohrp/humansubjects/

21 CFR part 50 "Protection of human subjects," issued in 1980, amended in 1981, 1989, 1990, 1991, 1996, 1997, 1999, 2006, and 2011,
Subpart D added.

DECLARATION OF HELSINKI (1964)

- เขียนโดยแพทยสมาคมโลก
- การวิจัยทางการแพทย์ที่เกี่ยวข้องกับมนุษย์หมายรวมถึงการศึกษาตัวอย่างหรือข้อมูลที่สามารถบ่งชี้ตัวผู้ป่วยด้วย
- การวิจัยที่เกี่ยวข้องกับมนุษย์ต้องผ่านความเห็นชอบจากคณะกรรมการจริยธรรมการวิจัยที่เป็นอิสระ
- สวัสดิภาพผู้เข้าร่วมการวิจัยเป็นสิ่งพึงคำนึงก่อนประโยชน์ต่อวิชาการและสังคม
- ต้องมีการขอคำยินยอมเป็นลายลักษณ์อักษร
- การทดสอบวิธีใหม่ต้องเทียบกับวิธีที่ดีที่สุดเท่าที่มีอยู่ในปัจจุบัน

DECLARATION OF HELSINKI (2013)

- Declaration of Helsinki ฉบับ 2013 ประกาศในที่ประชุม 64th WMA General Assembly, Fortaleza, Brazil, October 2013 เป็นฉบับล่าสุด มีแก้ไข 7 paragraphs จากฉบับ 2008
- Declaration of Helsinki ฉบับ 2008 ประกาศในที่ประชุม 59th WMA General Assembly, Seoul, Republic of Korea,October 2008.

Pankae Mahaisavariya “Changes in Declaration of Helsinki 2013”

DECLARATION OF HELSINKI (2013)

15. Adequate compensation and treatment for subjects who are harmed as a result of participating in the research must be ensured.

- New paragraph. It reflects the obligation to ensure that subjects who are harmed will receive compensation and treatment.

  (The Belmont report --non maleficence)

DECLARATION OF HELSINKI (2013)

17. All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

- **Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.**

- Second part is new. Addresses the issue of risk minimization and monitoring during the trial. (The Belmont report - non maleficence)

Declaration of Helsinki (2013)

23……. At the end of the study, the investigators must submit a final report to the committee containing a summary of the study's findings and conclusions.

- Clarifies what should occur at the end of the study.

DECLARATION OF HELSINKI (2013)

26. In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post- study provisions and any other relevant aspects of the study.

All subjects should be given the option of being informed about the general outcome and results of the study

- Add more information about post-trial provision and research results (The Belmont Report – respect for person, beneficence)

DECLARATION OF HELSINKI (2013)

34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information should also be disclosed to participants during the informed consent process.

- Clarifies and strengthens post-trial access issue (The Belmont Report – respect for person, beneficence)

DECLARATION OF HELSINKI (2013)

35. Every research involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

- Change form “clinical trial” to research involving human subjects to expand the scope of research registration (The Belmont Report – beneficence)

DECLARATION OF HELSINKI (2013)

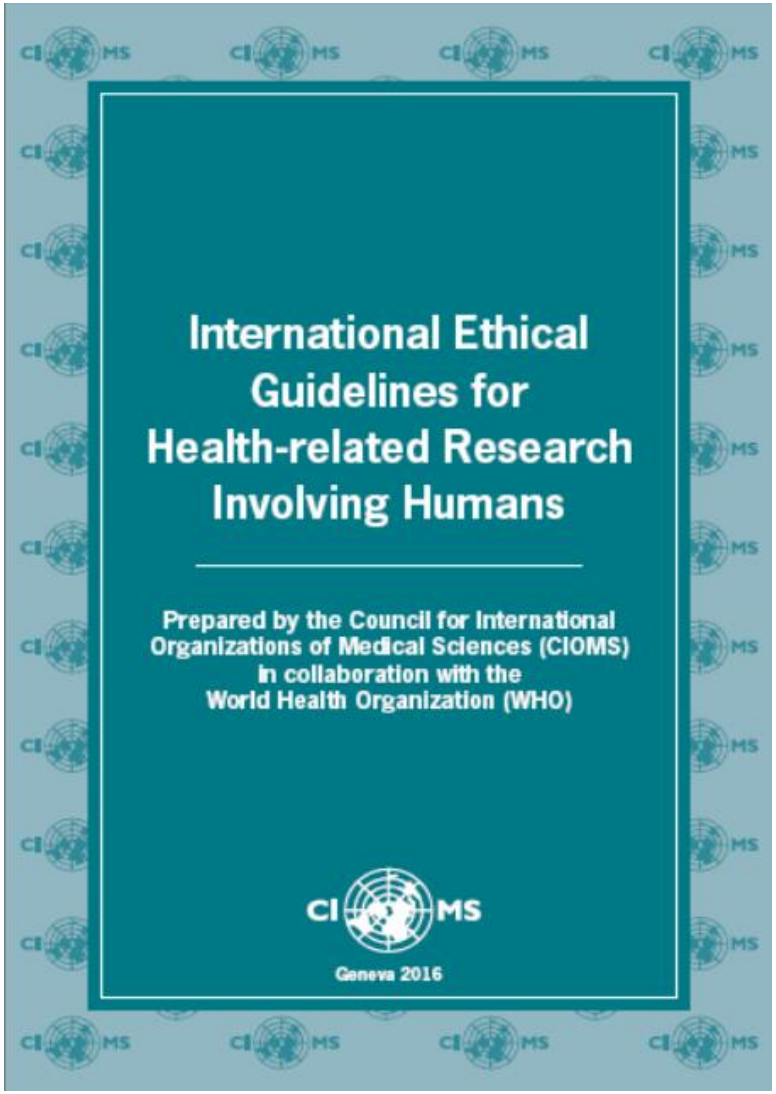
37. In the treatment of an individual patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.

- Strengthens requirement to make the intervention the object of subsequent research – compassionate use of ZMAPP in Ebola outbreak

The Council for International Organization of Medical sciences

- 1982 First version of CIOMS Guidelines on ethics in biomedical research.
- 1993 Second version of CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects.
- 2002 Third version of CIOMS Guidelines on ethics in biomedical research.
- 2016 The Fourth version of CIOMS, International Ethical Guidelines for Health-related Research Involving Humans

2016 The Fourth version of CIOMS



Guideline 1: Scientific and Social value and respect for right

☞ Ensure the proposed study are scientifically sound, build on an adequate prior knowledge base, and are likely to generate valuable information.

☞ Ensure all researches uphold human rights, respect, protect, and are fair to study participants and the communities.

Social value → Importance of information

↓

Direct relevance to a significant health problem

↓

Expected contribution to promote individual or public health

No scientific value → No social value

Scientific integrity & dissemination of results
+
Relevance to health need & contribution to individual & public health

No social value → No ethical acceptability

Scientific & social value
+
respect rights & welfare of individual participant and communities
+
fairness across different classes or groups (in both burdens and benefits)

Guideline 11 biospecimen & related data VS 12 Data in health-related research institutions must have a governance system to obtain authorization for future use of these data

- When specimens are collected for research purposes, either specific informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the person from whom the material originally is obtained.
- When human biological materials are left over after clinical diagnosis or treatment (so-called “residual tissue”) and are stored for future research, a specific or broad informed consent may be used or may be substituted by an informed opt-out procedure.

- When data are collected and stored for research purposes, either specific informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the person from whom the data were originally obtained.
- When data are used that were collected in the context of routine clinical care, an informed opt-out procedure must be used.
- This means that the data may be stored and used for research unless a person explicitly objects.
- However, a person’s objection is not applicable when it is mandatory to include data in population-based registries.

Pankae Mahaisavariya “CIOMS guidelines 2016 VS. WHO Standard & Operational Guidance 2011 VS. The Common Rule 2017”

GUIDELINE 11: COLLECTION, STORAGE AND USE OF BIOLOGIC MATERIAL AND RELATED DATA

- When specimens are collected for research purposes, either specific informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the person from whom the material originally is obtained.
- When human biological materials are left over after clinical diagnosis or treatment (so-called “residual tissue”) and are stored for future research, a specific or broad informed consent may be used or may be substituted by an informed opt-out procedure.
- The informed opt-out procedure must fulfil the following conditions:
  - 1) patients need to be aware of its existence;
  - 2) sufficient information needs to be provided;
  - 3) patients need to be told that they can withdraw their data;
  - 4) a genuine possibility to object has to be offered.

Same as guideline 12 collect, store & use data

COMMENTARY ON GUIDELINE 11

- Human biological materials may include:
  - tissues, organs,
  - blood, plasma, serum,
  - DNA, RNA, proteins,
  - cells, hair, nail clippings, skin,
  - urine, saliva, or other bodily fluids
- Source
  - diagnostic or therapeutic procedures,
  - autopsy specimens,
  - donations of organs or tissue from living or dead humans,
  - bodily wastes or abandoned tissue

COMMENTARY ON GUIDELINE 11

- Since the precise nature of the research is typically unknown, it is impossible to obtain specific informed consent at the time the material is collected.
- The broad informed consent for future use is an acceptable alternative to specific informed consent.
- Broad informed consent requires proper governance and management of the biobank.

Pankae Mahaisavariya “CIOMS guidelines 2016 VS. WHO Standard & Operational Guidance 2011 VS. The Common Rule 2017”

Broad consent: Biospecimen VS. Data

- Broad informed consent is not blanket consent that would allow future use of bodily material without any restriction.
- On the contrary, broad informed consent places certain limitations on the future use of bodily materials.

- Secondary use of stored data: collected in databanks, during research or during other activities (for example, clinical practice, health insurance)
- Typically the precise research questions will be unknown at the time of data collection.
- In those cases, it is acceptable to use the data for secondary analysis when the intended use falls within the scope of the original (broad) informed consent

Broad consent: Biospecimen VS. Data

Biospecimen

- the purpose of the biobank;
- the conditions and duration of storage;
- the rules of access to the biobank;
- the ways in which the donor can contact the biobank custodian and remain informed about future use;
- the foreseeable uses of the materials, whether limited to an already fully defined study or extending to a number of wholly or partially undefined studies;
- the intended goal of such use, whether only for basic or applied research , or also for commercial purposes; and
- the possibility of unsolicited findings and how they will be dealt with

Data

- the purpose of the databank;
- the conditions and duration of storage;
- the rules of access to the databank,
- the ways in which the donor can contact the databank custodian and remain informed about future use;
- the foreseeable uses of the data, whether limited to an already fully defined study or extending to a number of wholly or partially undefined studies;
- who will manage access to the data;
- the intended goal of such use, whether only for basic or applied research, or also for commercial purposes;
- the possibility of unsolicited findings and how they will be dealt with.

Vulnerable Subjects

- Guideline 15 : Research involving vulnerable persons and Groups

" When vulnerable individuals and groups are considered for recruitment in research, researchers and research ethics committees must ensure that specific protections are in place to safeguard the rights and welfare of these individuals and groups in the conduct of the research"

-one widely accepted criterion of vulnerability is limited capacity to consent or decline to consent to research participation.

-Special protections include : allowing no more than minimal risk procedures with no potential individual benefits for participants; supplementing the participant's agreement by the permission of family members, legal guardians or other appropriate representatives, etc.,

Vulnerable Subjects

Guideline 16 : Research Involving Adults Incapable of Giving Informed Consent

"Adults who are not capable of giving informed consent must be included in health-related research unless a good scientific reason justified their exclusion. As adults who are not capable of giving informed consent have distinctive physiologies and health needs, they merit special consideration by researchers and research ethics committees. At the same time, they may not be able to protect their own interests due to their lack of capacity to provide informed consent. Specific protections to safeguard the rights and welfare of these persons in research are therefore necessary"

Vulnerable Subjects

Guideline 17 : Research Involving Children and Adolescents

“ Children and adolescents must be included in health-related research unless a good scientific reason justifies their exclusion. As children and adolescents have distinctive physiologies and health needs, they merit special consideration by researchers and research ethics committees. However, their distinctive physiologies and emotional development may also place children and adolescents at increased risk of being harmed in the conduct of research. Moreover, without appropriate support, they may not be able to protect their own interests due to their evolving capacity to give informed consent. Specific protections to safeguard children’s rights and welfare in the research are therefore necessary”

Vulnerable Subjects

Guideline 18 : Women As Research Participants

"Women must be included in health-related research unless a good scientific reason justifies their exclusion. Women have been excludes from much health-related research because of their child-bearing potential. As women have distinctive physiologies and health needs, they merit special consideration by researchers and research ethics committees. Only the informed consent of the woman herself should be required for her research participation. Since some societies lack respect for women's autonomy, in no case must the permission of another person replace the requirement of individual informed consent by woman.

Women of child-bearing potential must be informed in advance of the possibility of risks to the fetus should they become pregnant during their research participation. When participation in research might be hazardous to a fetus or a woman if she becomes pregnant, sponsors and researchers must guarantee access to pregnancy tests, effective contraceptive methods before and during the research and to safe, legal abortion"

Vulnerable Subjects

Guideline 19 : Pregnant and Breastfeeding Women as Research Participants

“ Pregnant and breastfeeding women have distinctive physiologies and health needs. Research designed to obtain knowledge relevant to the health needs of the pregnant and breastfeeding woman must be promoted. Research in pregnant women must be initiated only after careful consideration of the best available relevant data.

In no case must the permission of another person replace the requirement of individual informed consent by the pregnant or breastfeeding woman.

For research interventions or procedures that have the potential to benefit either pregnant or breastfeeding women or their fetus or infant, risk must be minimized and outweighed by the prospect of potential individual benefit.

Vulnerable Subjects

Guideline 19 : Pregnant and Breastfeeding Women as Research Participants (cont.)

For research interventions or procedures that have no potential individual benefits for pregnant and breastfeeding women :

- ☛ the risk must be minimized and no more than minimal; and
- ☛ the purpose of the research must be to obtain knowledge relevant to the particular health needs of pregnant or breastfeeding women or their fetuses or infants.

When the social value of the research for pregnant or breastfeeding women or their fetus or infant is compelling, and the research cannot be conducted in non-pregnant or non-breastfeeding women, a research ethics committee may permit a minor increase above minimal risk.

Vulnerable Subjects

Guideline 19 : Pregnant and Breastfeeding Women as Research Participants (cont.)

Short-term and long-term follow-up of the fetus and the child may be required in research involving pregnant and breastfeeding women depending upon the study intervention and its potential risks.

As a general rule, health-related research involving pregnant women that has the potential for harm to the fetus should be conducted only in settings where women can be guaranteed access to a safe, timely and legal abortion in the event that participation in the research makes the pregnancy unwanted.

"Federalwide Assurance" (FWA)
= a statement that the institution will comply with the requirements of the Common Rule

- Since the 1970s, federal regulation of research involving human participants has been limited to two categories:
  (1) research conducted or supported by various agencies of the federal government and
  (2) research subject to regulation by the U.S. Food and Drug Administration (FDA).
- Furthermore, OHRP asks institutions to include in their FWA a statement that they will extend their application of Common Rule requirements to all research conducted within the institution without regard to source of funding.

1981

- 45 CFR § 46 – first published

1991

- Department of Health and Human Service (DHHS) Issuing Subpart A as the Common Rule

2011

- an Advance Notice of Proposed Rulemaking (ANPRM) published a plan for the first general revision of 45 CFR § 46

2017

- The Common Rule
- Department of Health & Human Service (DHHS), USA

how updated human subjects protections regulations can effectively respond to current research contexts and methods

HHS.gov

U.S. Department of Health & Human Services

Office for Human Research Protections

Final Revisions to the Common Rule

The U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies have issued final revisions to the Federal Policy for the Protections of Human Subjects (the Common Rule). The Final Rule was published in the Federal Register on January 19. 2017. It implements new steps to better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators.

~ HHS.gov website

Final revision available at: https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf

Key Changes

- **Eliminates continuing review** for most minimal risk research
- **Expands exemption categories** and changes the review processes
- **Reframes informed consent information** and adds required elements
- **Requires single IRB review** of research involving external collaborators

Cindy Shindledecker “Key Changes to the Common Rule – Regulations for the Protection of Human Subjects 45 CFR 46” Health Sciences & Behavioral Sciences IRB, University of Michigan.

Exemption Changes

Changes to Exemption Review Processes

New processes

- **Self-determination** – smart form questions will allow the investigator to issue a self-determination letter for some exempt projects

  Note – a quality assurance process to validate a sample of self-determinations will be implemented

- **Submit to IRB –**
  - Exemption with **"limited IRB review"** (new regulatory category)
    - For projects collecting sensitive, identifiable data, the IRB must review privacy/confidentiality protections (review an IRB member)
  - Standard **exempt review by IRB staff** member for certain types of exemptions or by investigator choice

Exemption 1 – Educational Exemption

What's new?

- Now must consider "adverse affects" on student learning of required educational content or on assessment of educators
- Self-exemption permitted, except where research involves access to student education records under FERPA

▪ **Family Educational Rights and Privacy Act** of 1974(**FERPA** or the **Buckley Amendment**) is a United States federal law that governs the access of educational information and records to public entities such as potential employers, publicly funded educational institutions, and foreign governments.

Exemption 2 – Surveys/Interviews/Educational Tests/Public Observation ONLY

What's new?

- Projects collecting **sensitive** and **identifiable** data may be exempt after "limited IRB review" (for privacy/confidentiality protections)
- Clarifies that the exemption **does not apply** to projects involving:
  - Interventions
  - Collection of biospecimens
  - Linking to additional personally-identifiable data
  - Children (except for educational tests or some public observations)
- Self-exemption is permitted if information is not identifiable or not sensitive

Exemption 3 – Benign Behavioral Interventions

What's new?

- This exemption is completely new – similar to Michigan Exemption 2a but more complex!
- Limited to research with adults

What is a benign behavioral intervention?

- Brief in duration
- Harmless and painless
- Not physically invasive
- Not likely to have a significant adverse impact on subjects
- Not offensive or embarrassing

Exemption 3 – Benign Behavioral Interventions

- Information is collected via
  - Verbal or written responses (surveys/interviews)
  - Data entry
  - Observation of subject (including audiovisual recording)
- Does not permit data collection via physical procedures
  - Physical sensors (e.g. blood pressure monitors, EEG, FitBits)
  - Minimally invasive procedures (e.g. blood draw or saliva collection)

Exemption 3 – Benign Behavioral Interventions

- Must obtain “prospective agreement to the intervention and information collection”
- **No deception**, except where the subject is told that they will be unaware or misled about the nature or purposes of the research and they agree
  - Debriefing still encouraged
- Self-exemption permitted for projects that do not involve deception and where information collected is not identifiable or not sensitive
- “Limited IRB Review” required for projects collecting sensitive and identifiable data

Exemption 4 – Secondary Research Uses of Identifiable Private Information or Identifiable Biospecimens

What's new?

- No longer limited to retrospective data review
- Permits secondary use of identifiable protected health information (PHI) (with HIPAA privacy board review)
- No self-exemptions

Exemption 5-Public Benefit/Service Program Research (Federal Demonstration Projects)

What's New :

- A new eligibility criterion for this interaction / exemption will be that the project must be published on a federal website.

Review Path :

- An IRB Determination is required.

Exemption 6 – Taste/Food Quality evaluation & Consumer acceptance

What's New : Unchanged
Review Oath : An IRB Determination is required.

Exemptions 7 & 8 – Storage and Secondary Use of Data/Biospecimens

- Related new exemptions
- Exemption 7 covers the storage and maintenance of identifiable data and/or biospecimens for future research collected under broad consent (i.e. creation of a repository). More on broad consent later…
  - "Limited IRB review" required to assess the terms of the broad consent
- Exemption 8 covers the use of data or biospecimens collected under broad consent
  - "Limited IRB review" required to confirm that the proposed use is consistent with the broad consent and that privacy of subjects and confidentiality of data is appropriate

The Common Rule 2017

- Newly defined categories of exempt or excluded research studies based on the level of risk posed to study participants
- Does not require consent for secondary uses of nonidentifiable biospecimens
- Explicitly excludes public health surveillance from human subject research
- Allows investigators to obtain broad consent for use of identifiable biospecimens in future unspecified research studies
- Generally requires the use of a single IRB for multi-institutional studies within the United States

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH Harmonised Tripartite Guideline

Guideline for Good Clinical Practice (ICH-GCP)

Step 4 of the ICH Process
on 1 May 1996

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

ICH Harmonised Guideline

Integrated Addendum to ICH E6 (R1) :
Guideline for Good clinical Practice (ICH-GCP)
E6(R2)

Step 4 version
dated 9 November 2016

The Principles of ICH-GCP

2.1 Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

2.2 Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.

2.3 The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

2.4 The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.

2.5 Clinical trials should be scientifically sound, and described in a clear, detailed protocol.

The Principles of ICH-GCP

2.6 A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.

2.7 The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

2.8 Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).

2.9 Freely given informed consent should be obtained from every subject prior to clinical trial participation.

2.10 All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

The Principles of ICH-GCP

2016 ADDENDUM

This principle applies to all records referenced in this guideline, irrespective of the type of media used.

2.11 The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

2.12 Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

2.13 Systems with procedures that assure the quality of every aspect of the trial should be implemented.

2016 ADDENDUM

Aspects of the trial that are essential to ensure human subject protection and reliability of trial results should be the focus of such systems.

Good Research Practice

Principles

Good research practices are based on fundamental principles of research integrity. They guide researchers in their work as well as in their engagement with the practical, ethical and intellectual challenges inherent in research.

These principles are:

- ***Reliability in ensuring the quality*** of research, reflected in the design, the methodology, the analysis and the use of resources.
- ***Honesty in developing, undertaking,*** reviewing, reporting and communicating research in a transparent, fair, full and unbiased way.
- ***Respect for colleagues, research*** participants, society, ecosystems, cultural heritage and the environment.
- ***Accountability for the research from*** idea to publication, for its management and organisation, for training, supervision and mentoring, and for its wider impacts.

Good Research Practice

Research Integrity

Research integrity may be defined as active adherence to the ethical principles and professional standards essential for the responsible practice of research.

By active adherence we mean adoption of the principles and practices as a personal credo, not simply accepting them as impositions by rulemakers.

By ethical principles we mean honesty, the golden rule, trustworthiness, and high regard for the scientific record.

https://ori.hhs.gov/education/products/ucla/chapter1/page02.htm

Good Research Practice

NAS report definition

"For individuals research integrity is an aspect of moral character and experience. It involves above all a commitment to intellectual honesty and personal responsibility for ones actions and to a range of practices that characterize responsible research conduct." These practices include:

- Honesty and fairness in proposing, performing, and reporting research;
- Accuracy and fairness in representing contributions to research proposals and reports;
- Proficiency and fairness in peer review;
- Collegiality in scientific interactions, communications and sharing of resources;
- Disclosure of conflicts of interest;
- Protection of human subjects in the conduct of research;
- Humane care of animals in the conduct of research;
- Adherence to the mutual responsibilities of mentors and trainees."

https://ori.hhs.gov/education/products/ucla/chapter1/page02.htm

Good Research Practice

Research Misconduct

Research misconduct is traditionally defined as fabrication, falsification, or plagiarism (the so-called FFP categorisation) in proposing, performing, or reviewing research, or in reporting research results:

- ***Fabrication is making up results and*** recording them as if they were real.

- ***Falsification is manipulating research*** materials, equipment or processes or changing, omitting or suppressing data or results without justification.

- ***Plagiarism is using other people's work*** and ideas without giving proper credit to the original source, thus violating the rights of the original author(s) to their intellectual outputs

The European Code of Conduct for Research Integrity, ALLEA-All European Academies, Berlin 2017

Thank you