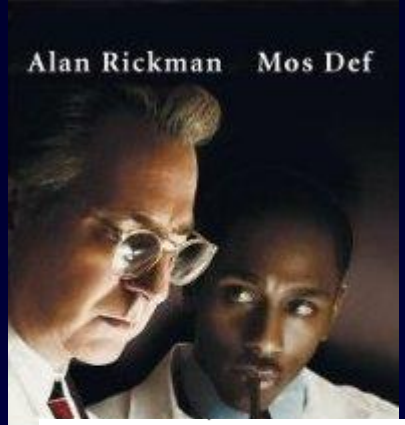


Vivien Thomas Young

Green (winner), Stanfor

Permyos Ruengsakulrach

Medical Center, Melbourr

nalist), Beth Israel Deacon

Henry L. Zhu (finalist), Ur

phia, Pa; Motohisa Tofuku

Medical Center, Boston, Mass (Figure 8).

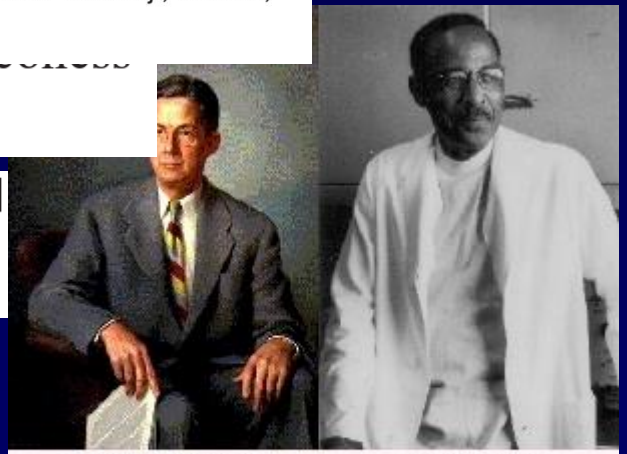
Figure 8. Vivien Thomas Young Investigator Award, Council on Cardio-Thoracic and Vascular Surgery. From left: Permyos Ruengsakulrach, finalist; G. Randall Green, winner; Caroline Metais, finalist; Henry L. Zhu, finalist; Motohisa Tofukuji, finalist; and Hartzell Schaff, program vice chair.

Cardiovascular News

Awards and Named Lecturers at the American Heart Association 71st Scientific Sessions

(*Circulation*. 1999;2492–2495.)

Circulation **is available at http://www.circulationaha.org**



Dr. Alfred Blalock **Vivien Thomas**

PHOTOS BY BY THE ALAN MASON CHESNEY MEDICAL ARCHIVES OF THE JOHNS HOPKINS MEDICAL INSTITUTIONS

Registry and Research Integrity

Permyos Ruengsakulrach, MD, PhD, FRCST, FCCP

ดร. นพ.เพิ่มยศ เรืองสกุลราช

คณะกรรมการจริยธรรมฯ ศูนย์การแพทย์โรงพยาบาลกรุงเทพ

Division of Cardiovascular and Thoracic Surgery
Bangkok Heart Hospital

SIDCER
Globalizing Ethics for Health Research

Middleton Foundation for Ethical Studies

Outline

- Research Integrity
- Registry

SIDCER
Globalizing Ethics for Health Research

Middleton Foundation for Ethical Studies

Disclosure

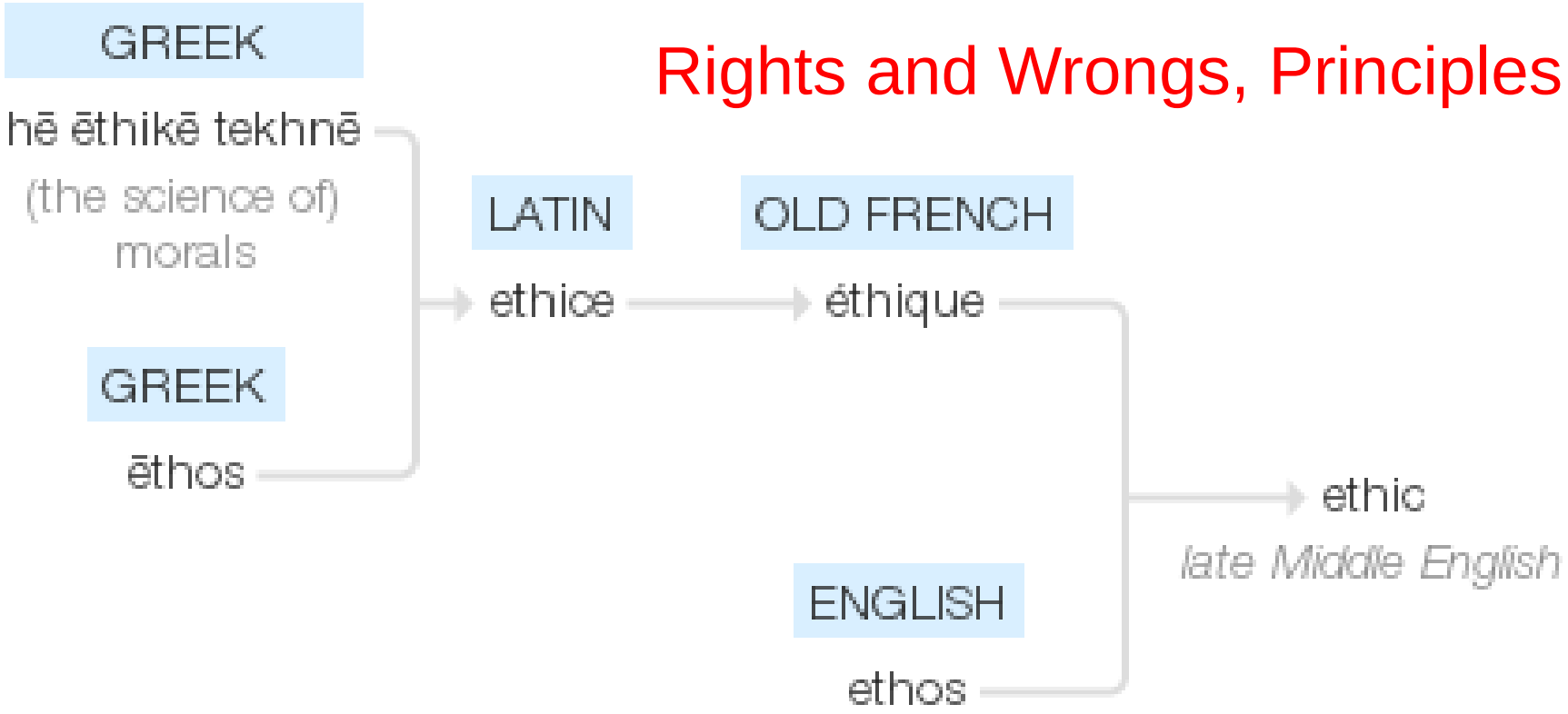
I have no financial relationships with any commercial interest related to the content of this activity.

Integrity

- the quality of being honest and having strong moral principles; moral uprightness.
- the state of being whole and undivided.

Ethics

Rights and Wrongs, Principles



1. **moral principles that govern a person's behavior or the conducting of an activity.**
2. **the branch of knowledge that deals with moral principles.**

Research

Noun: a detailed study of a subject, especially in order to discover (new) information or reach a (new) understanding

Verb: to study a subject in detail, especially in order to discover new information or reach a new understanding

synonyms: investigation · experimentation · testing · exploration · analysis · fact-finding · studies · analyses · work

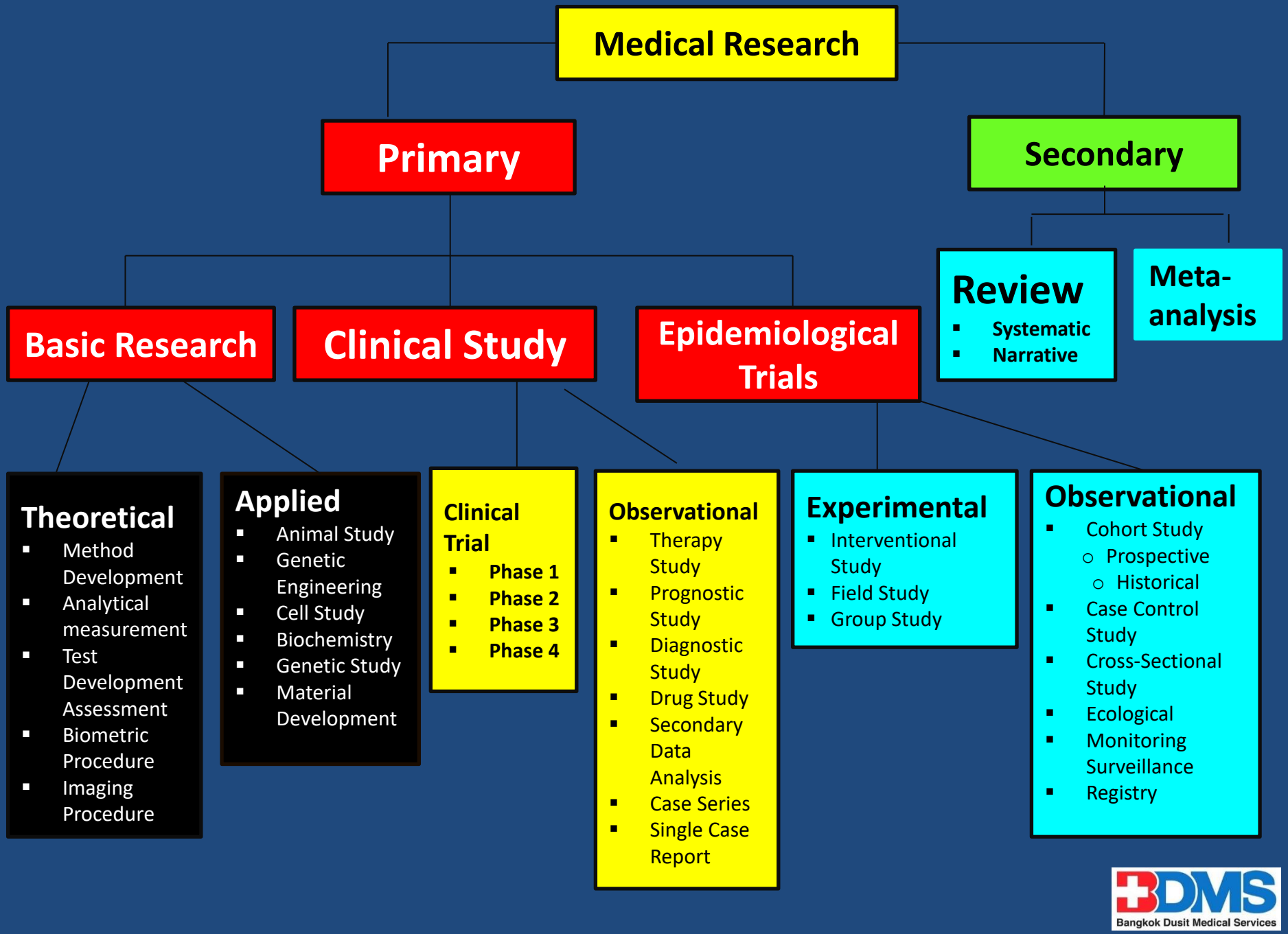
**ORIGIN: late 16th century: from obsolete French recerche (noun), recercher (verb),
from Old French re- (expressing intensive force) + cerchier 'to search'.**

The term "research" refers to a class of activities designed to develop or contribute to generalizable knowledge.

Research involving human subjects includes:

- studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or patients;

- controlled trials of diagnostic, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation;
- studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures; and
- studies concerning human health-related behavior in a variety of circumstances and environments.



Among the first documented human subject research experiments were vaccination trials in the 1700s. In

We're all about this man
Edward Jenner: the pioneer of vaccination. His work set the ball rolling for the eradication of smallpox and the development of vaccines which now save millions of lives every year.

We want to show how science can change the world for the better
And we do this by telling Jenner's story in his former home in Berkeley, Gloucestershire.

We welcome 5,000 visitors every year
People come here from around the world because they believe that it matters.

Dr Jenner's House
Museum and Garden

We love our community
The people of Berkeley had an important role to play in Jenner's work. Today we want to inspire young people to become the Jenners of tomorrow, to support community events and celebrations, and to provide a supportive environment for volunteering.

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20th Century Research Ethics Milestones

Common Rule **1991**

Consolidated HHS/FDA Regulations **1981**

Belmont Report **1979**

1972 Syphilis Study Exposed

1966 The Beecher Article (NEJM)

Declaration of Helsinki **1964**

Kefauver-Harris Amendments
Food, Drug and Cosmetic Act **1962**

Milgram Study

Nuremberg Code 1947

The Thalomide Tragedy

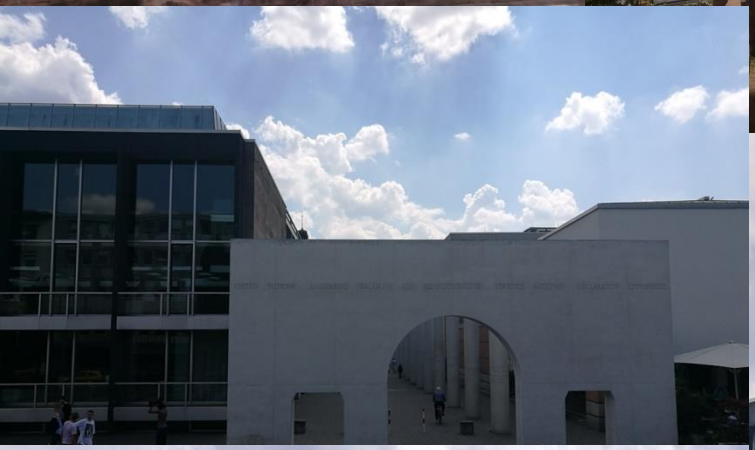
US Human Radiation Experiments

1940 The Nazi Experiments, Unit 731 (1934-1941)
Surgeon General Shirō Ishii

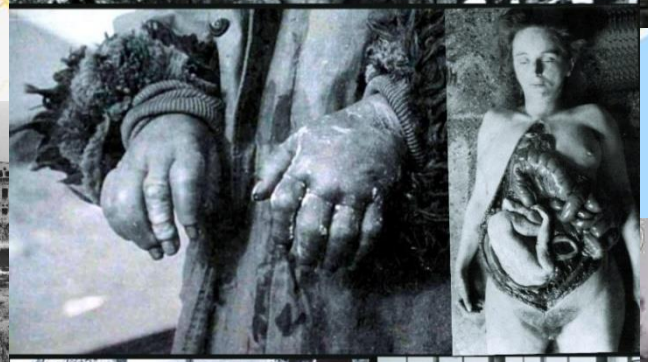
1932 The Syphilis Study Begins

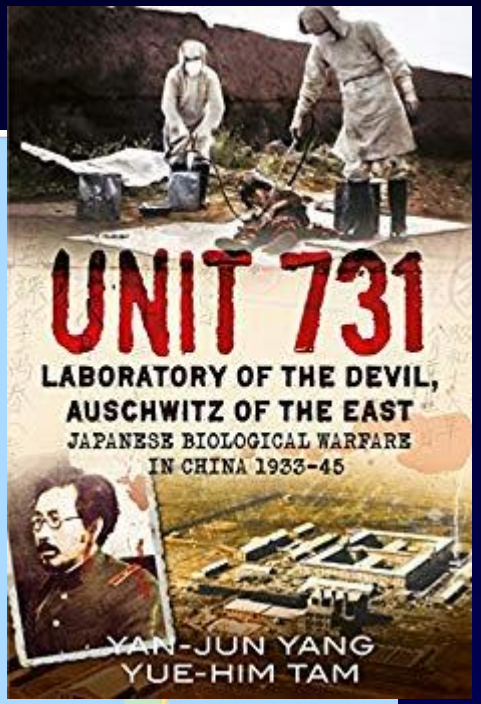
Trigger Events



Unit 731 Nightmare in Manchuria
History Channel





The Nuremberg Code

1. The volu

absolutel

The Belmont Report

Office of the Secretary

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Guidance for Industry

E6 Good Clinical Practice: Consolidated Guidance

Additional copies are available from:
the Drug Information Branch (HFD-210),
Center for Drug Evaluation and Research (CDER),
5600 Fishers Lane, Rockville, MD 20857 (Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm
or
Office of Communication,
Training, and Manufacturers Assistance (HFM-40)
Center for Biologics Evaluation and Research (CBER)
1401 Rockville Pike, Rockville, MD 20852-1448,
http://www.fda.gov/cber/guidelines.htm
(Fax) 888-CBERFAX or 301-827-3844
(Voice Information) 800-835-4709 or 301-827-1800

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
April 1996
ICH

International Ethical Guidelines for Health-related Research Involving Humans

Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO)

CIOMS

Geneva 2016

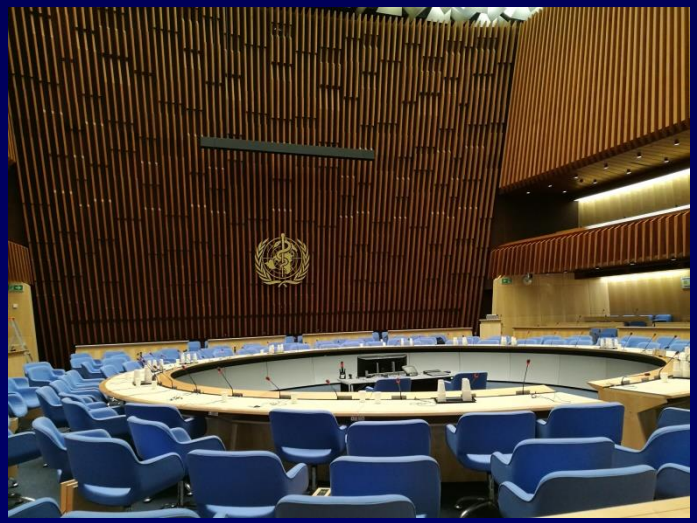
TDR/PRD/ETHICS/2000.1

Operational Guidelines
for
Ethics Committees That
Review Biomedical Research

WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects

World Health Organization
Geneva
2000

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013



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NATURE | NEWS

South Africa's San people issue ethics code to scientists

The indigenous people — known for their click languages — are the first in Africa to draft guidelines for researchers.

Ewen Callaway

20 March 2017

SAN CODE OF RESEARCH ETHICS

South African San Institute 2017

TRUST
Equitable Research Partnerships

Researchers have eagerly studied Africa's San people, some of whom are shown here foraging in a grassland. Now, the San have drawn up a code of ethics to govern scientists' interactions with them.

The principles of ICH GCP as presented in ICH (2016) E6 are:

- **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).**
- **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.**
- **The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.**
- **The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.**

- Clinical trials should be **scientifically sound**, and described in a clear, detailed protocol.
- A trial should be conducted in **compliance with the protocol** that has received prior **Institutional Review Board (IRB) / Independent Ethics Committee (IEC)** approval/favorable opinion.
- 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.
- Each individual involved in conducting a trial should be **qualified by education, training, and experience** to perform his or her respective task(s).
- **Freely given informed consent** should be obtained from every subject prior to clinical trial participation.

- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification. This principle applies to all records (paper or electronic) referenced in this guideline.
- 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).
- 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.
- Systems with procedures that assure the quality of every aspect of the trial should be implemented.

Vulnerable Populations

- Subjects in emergency situations
- Subjects who are marginalized in society
- Members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry and members of the armed forces
- Subjects with fatal or incurable diseases
- The elderly
- Persons in nursing homes
- Unemployed or impoverished persons
- Ethnic minority groups
- Homeless persons, nomads, refugees
- Individuals with impaired decision-making capacity

Serious Adverse Event (SAE) or Serious Suspected Adverse Reactions

1. death, life-threatening
2. inpatient hospitalization or an extension of an existing hospitalization
3. a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
4. congenital anomaly/ birth defect

21 CFR 312 [Investigational New Drug Application 2014]

Electronic Code of Federal Regulations

e-CFR data is current as of June 5, 2019

Title	Volume	Chapter	Browse Parts	Regulatory Entity
Title 21 Food and Drugs	1	I	1-99	FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES
	2		100-169	
	3		170-199	
	4		200-299	
	5		300-499	
	6		500-599	
	7		600-799	
	8		800-1299	
	9	II	1300-1399	DRUG ENFORCEMENT ADMINISTRATION, DEPARTMENT OF JUSTICE
		III	1400-1499	OFFICE OF NATIONAL DRUG CONTROL POLICY

https://www.ecfr.gov/cgi-bin/text-idx?SID=3ee286332416f26a91d9e6d786a604ab&mc=true&tpl=/ecfrbrowse/Title21/21tab_02.tpl

Adverse Event (AE)

- (1) Any untoward medical occurrence in a patient or clinical investigation subject given a pharmaceutical product; does not necessarily have a causal relationship with such treatment; and
- (2) Any unfavorable and unintended sign (including abnormal laboratory findings), symptom, or disease temporally associated with the use of a medicinal (investigational) product; not necessarily related to the product (ICH 2016).

Adverse Event (AE)

- A rash noted during a physical examination
- An abnormal laboratory result
- A headache that the subject mentions during a study visit

Common Categories of Causality	
Definitely related	There is a certainty that the event is related to the investigational product.
Probably related	There is high likelihood that the event is related to the investigational product.
Possibly related	There is a likelihood that the investigational product is the cause of the event, but other causes cannot be ruled out.
Unlikely to be related	It is not likely that the event is related to the investigational product, and other more likely causes are present.
Unrelated	Evidence exists that the event is related to something other than the investigational product.

Unexpected adverse event or Unexpected suspected adverse reaction

An AE or suspected adverse reaction is **not listed** in the **Investigator's Brochure** (IB), the protocol or consent form or elsewhere in the **current Investigational New Drug (IND) application**, or is not listed at the specificity or severity that has been observed.

Unexpected adverse event or Unexpected suspected adverse reaction

- **Hepatic necrosis would be unexpected (by virtue of greater severity) if the IB referred only to elevated hepatic enzymes or hepatitis.**
- **Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the IB listed only cerebral vascular accidents.**

Investigator Reporting Requirements

Investigators must report to the sponsor all AEs and/or laboratory abnormalities. Investigators must also report any serious adverse event (SAE). According to ICH (2016) E6 Section 4.11.1 "all serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting."

ICH E6 goes on to note that the immediate reports should then be followed promptly by detailed, written reports. All reports should identify subjects by unique code numbers assigned rather than other identifiers (such as subjects' names, personal identification numbers, and/or addresses).

- **SAEs must be reported immediately. The term "immediately" is not defined in the regulation, but the industry standard is to report the event within 24 hours.**
- **For reported deaths, the investigator should supply the sponsor and IRB/IEC with any additional requested information (for example, autopsy reports and terminal medical reports) (ICH [2016] E6 Section 4.11.3).**
- **If the event does not meet the definition of "serious," but reporting is required by the protocol, the investigator must report the events according to the timetable specified in the protocol.**

Reporting Timeframes (ICH E2)

- **Fatal or Life-Threatening Unexpected ADRs**

Regulatory agencies should be notified (for example, by telephone, facsimile transmission, or in writing) as soon as possible but no later than 7 calendar days after first knowledge by the sponsor that a case qualifies, followed by as complete a report as possible within 8 additional calendar days.

- **All Other Serious, Unexpected ADRs**

must be filed as soon as possible but no later than 15 calendar days after first knowledge by the sponsor

Unanticipated Adverse Device Effects (UADE)

- "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application ... or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."

Unanticipated Adverse Device Effects (UADE)

Investigators are required to report UADEs to the sponsor and the reviewing IRB/IEC within ten (10) working days after becoming aware of the event. According to the regulations, the sponsor evaluates the UADE report, and then is responsible for reporting the event to the FDA.

TGN1412

In March 2006, six healthy
human trial of TGN1412, a n
developed as a therapy to treat
experienced a serious adverse
infusion of the agent in a priva
in London, the six developed a
in multi-organ failure. As is t
United Kingdom, the design of
and authorized by the appro
raised awareness of the risks
and potentially risky candidate
of State for Health for the UK
Phase One Clinical Trials which

The widely reported TGN1412 trials in the UK [2] may provide an instructive test case for Kimmelman and London's proposal. Six healthy volunteers were given the test agent, TGN1412 (an immune modulator), which triggered a cytokine storm and subsequent multiple organ failure, even at a fraction of the dose found to be safe in macaque monkeys [2]. Kimmelman and London's proposal could have been useful, in principle, in the TGN1412 trial in that it would have required reviewers to question whether the animal models truly are sufficiently similar to the relevant human systems to permit the right kind of conclusions about safety and potential benefits in humans. One theory about the TGN1412 trials [3] is that the catastrophic effects were mediated by memory B cells, which may have been absent or under-developed in the laboratory animals. The animal data,

- Jesse Gelsinger
- Born 18th of June 1981
- Pretty normal infancy
- At ~3 years: first signs of metabolic disorder

Final diagnosis: OTC
(Ornithine transcarbamylase deficency syndrome)

- High level of ammo
- Mild (6% enzyme ef
- Could be controlled

James Wilson (1999)

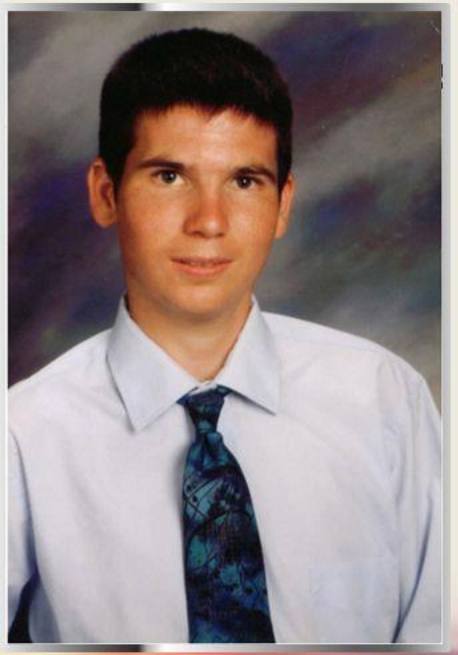
http://tinyurl.com/jwilson11

- Conducted clinical trial using gene therapy to combat OTC deficiency at U of Pennsylvania in which Jesse Gelsinger died
- President and major shareholder (30%) in Genova, company developing product under test
- Failed to report extent of adverse reactions during animal testing

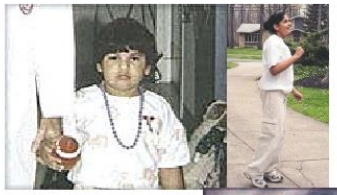
☒ Consent
☒ Conduct of clinical trial
☒ Conflict of Interest (financial)

Adenovirus

- Jesse Gelsinger
  - Patient in clinical trial
  - Ornithine transcarbamylase deficiency
    - Couldn't metabolize ammonia
  - Administered adenovirus
    - Died 4 days later



Gene Therapy: A Brief History



1990 Ashanti de Silva， USA
(ADA 所致联合免疫缺陷)
1999 Jesse Gelsinger， USA
2003 Alain Fischer， France
2003 Adrian Thrasher， UK

Ashanti de Silva， 1990

Jesse Gelsinger， 1999

Alain Fischer， 2003

Lacks' story was made famous in 2010 after publication of Rebecca Skloot's award-winning book, "The Immortal Life of Henrietta Lacks," which stayed on The New York Times best-seller list for two years.

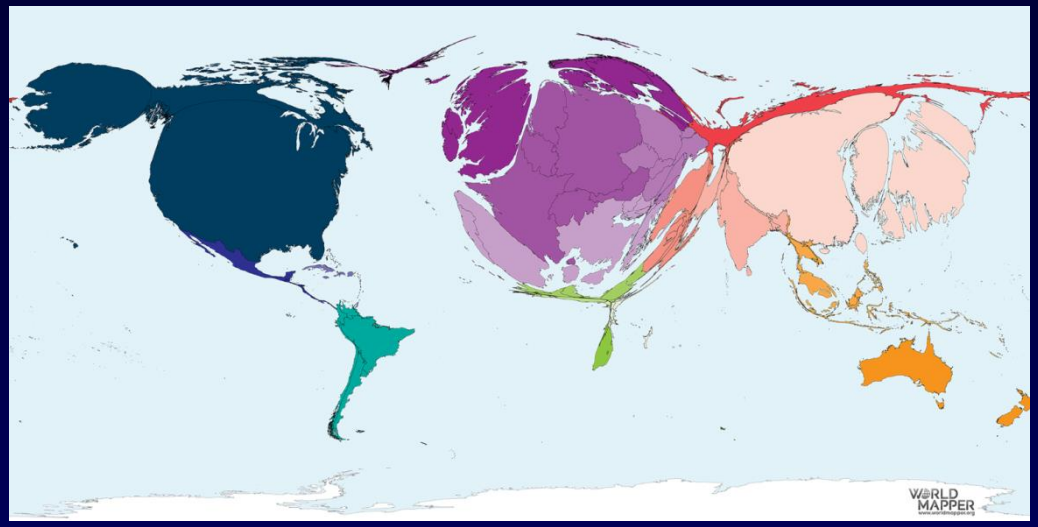
The book chronicled how before Lacks died, a research team at Johns Hopkins University in Baltimore led by George Otto Gey took a sample of tissue from her cervix. He found he was able to grow them in dishes outside the human body. This was a major research breakthrough: having an immortal cell line gave researchers a crucial new tool against disease.
Indeed, the first benefits from HeLa cells came in their use by Jonas Salk in developing the first vaccine against polio.

Subsequently, scientists went on to use the cells in many experiments. More than 60,000 articles have appeared based on HeLa cell research including cancer and AIDS and even in developing vaccines for dogs, cats and other animals.

Complete genome sequence

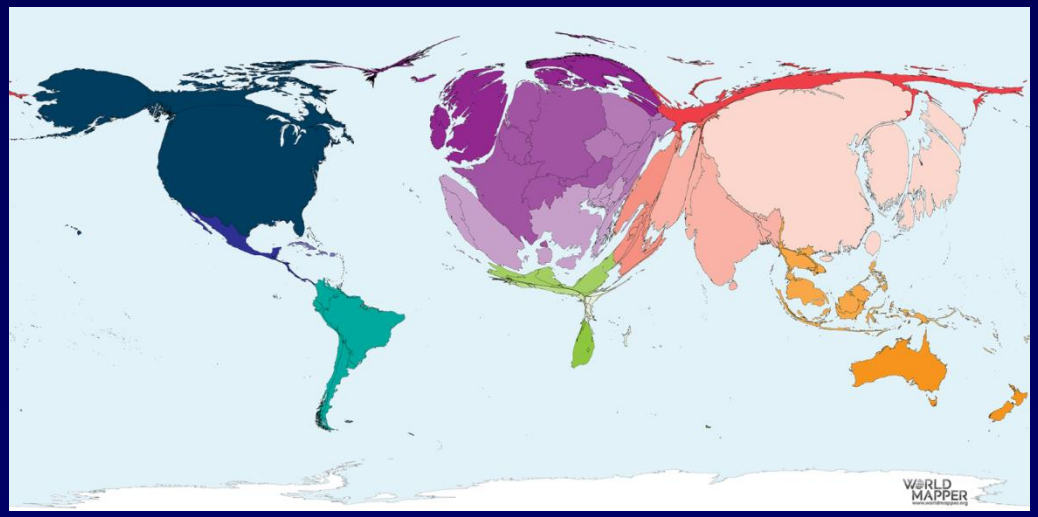
The complete genome of the HeLa cells was sequenced and published on 11 March 2013[39][42] without the Lacks family's knowledge.[43] Concerns were raised by the family, so the authors voluntarily withheld access to the sequence data.[43] Jay Shendure led a HeLa sequencing project at the University of Washington which produced a paper that had been accepted for publication in March 2013 — but that was also put on hold while the Lacks family's privacy concerns were being addressed.[44] On August 7, 2013, NIH director Francis Collins announced a policy of controlled access to the cell line genome based on an agreement reached after three meetings with the Lacks family.[45] A data-access committee will review requests from researchers for access to the genome sequence under the criteria that the study is for medical research and the users will abide by terms in the HeLa Genome Data Use Agreement, which includes that all NIH-funded researchers will deposit the data into a single database for future sharing. The committee consists of six members including representatives from the medical, scientific, and bioethics fields, as well as two members of the Lacks family.[45] In an interview, Collins praised the Lacks family's willingness to participate in this situation that was thrust upon them. He described the whole experience with them as "powerful", saying that it brought together "*science, scientific history and ethical concerns*" in a unique way.[46]

A World Map Based on Science Papers Published 2005 and 2016



2005

USA, China, Japan, UK, Germany



2016

China, USA, Japan, Germany, UK

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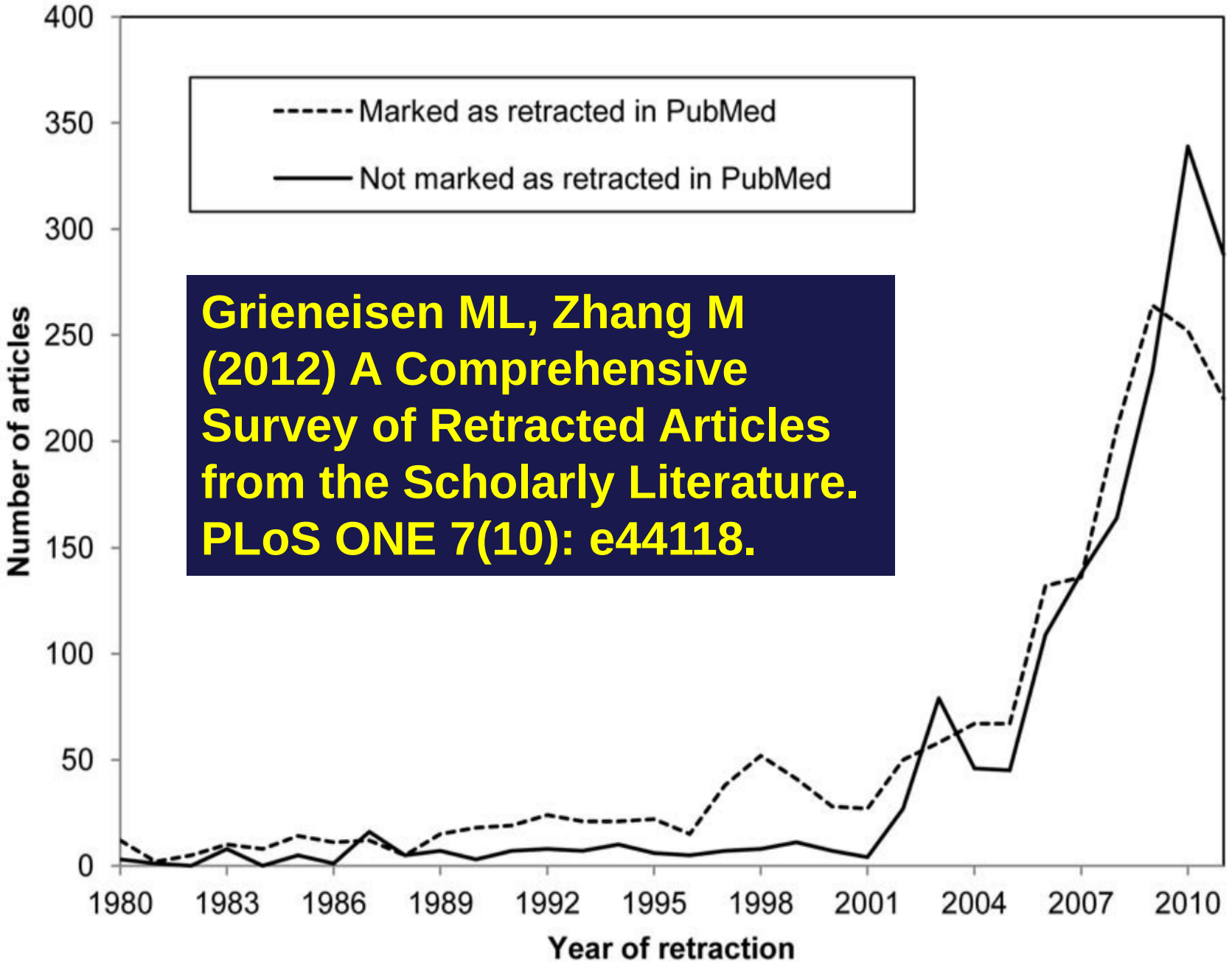
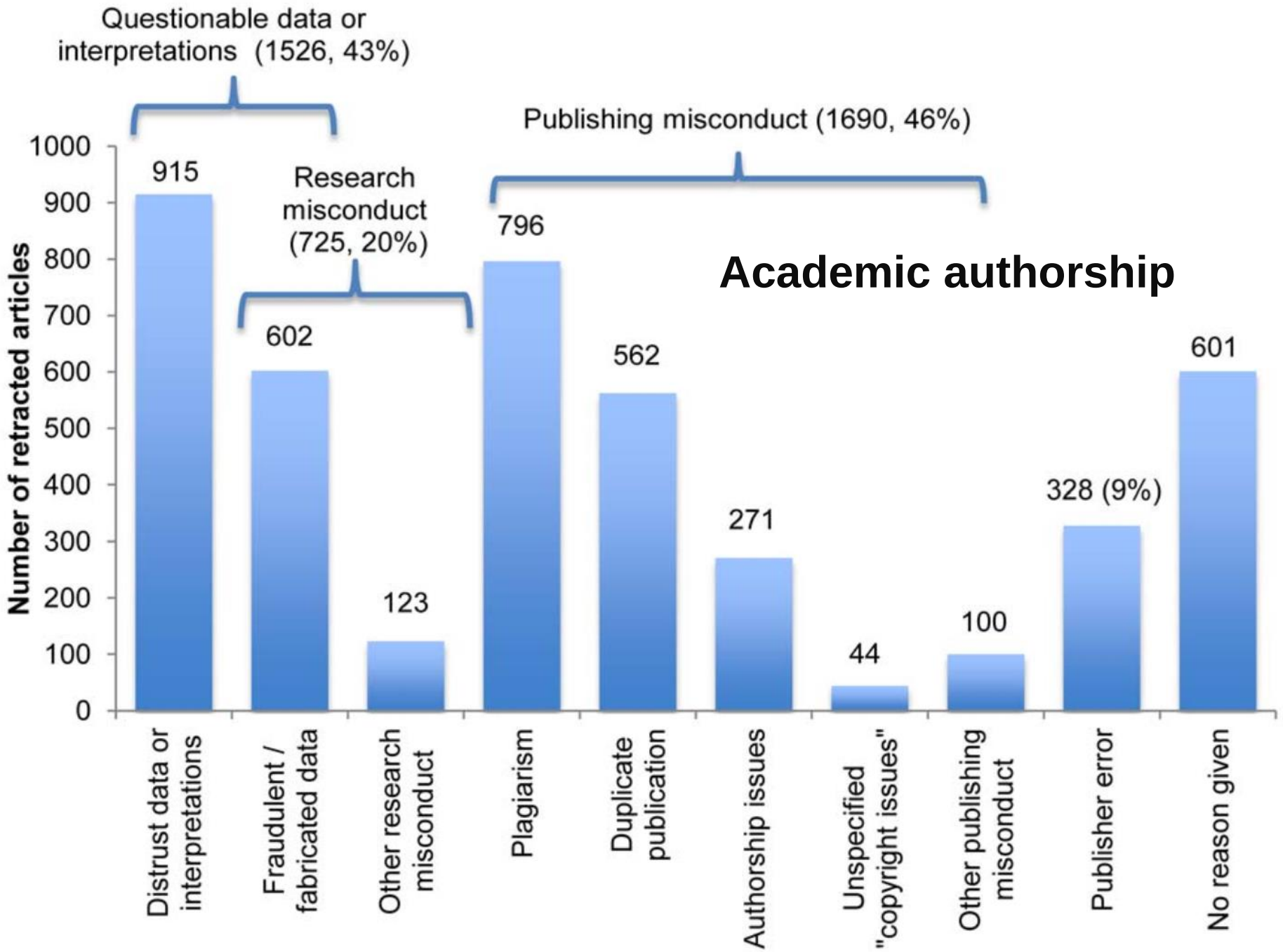

Marked as retracted in PubMed
Not marked as retracted in PubMed
Grieneisen ML, Zhang M (2012) A Comprehensive Survey of Retracted Articles from the Scholarly Literature. PLoS ONE 7(10): e44118.
Number of articles
Year of retraction
0
50
100
150
200
250
300
350
400
1980
1983
1986
1989
1992
1995
1998
2001
2004
2007
2010

Journal title abbreviation	Number of retracted articles	WoS records since 1980	Percent of articles retracted
Acta Crystallogr E	123	31,152	0.39[1]
Science	73	76,801	0.09
PNAS	73	85,064	0.08
J Biol Chem	59	130,667	0.04
Gene Expr Patterns	49	871	5.62[2]
Nature	47		
Anesth Analg			
Biochem Biophys Res Commun			
J Immunol			
Blood			
J Hazard Mater			
J Am Chem Soc			
Cell			
J Clin Invest			
Tissue Eng Regen Med			
N Engl J Med			
Hear Res			
Appl Phys Lett			
EMBO J	15		
FEBS Lett	15		
Infect Immun	15		
Mol Cell Biol	15		

Science
Nature
Anesth Analg
Blood
Cell
J Clin Invest
N Engl J Med

Journal	Number of articles	2011 impact factor
The Journal of Biological Chemistry	37	5.12
Anesthesia & Analgesia	33	3.07
Science	32	32.45
The Journal of Immunology	30	5.86
Proceedings of the National Academy of Sciences	27	10.47
Blood	21	9.79
Nature	19	36.24
The Journal of Clinical Investigation	17	15.43
Cancer Research	16	8.16
Cell	13	34.77


Questionable data or interpretations (1526, 43%)
Research misconduct (725, 20%)
Publishing misconduct (1690, 46%)
Academic authorship
Number of retracted articles
0
100
200
300
400
500
600
700
800
900
1000
915
602
123
796
562
271
44
100
328 (9%)
601
Distrust data or interpretations
Fraudulent / fabricated data
Other research misconduct
Plagiarism
Duplicate publication
Authorship issues
Unspecified "copyright issues"
Other publishing misconduct
Publisher error
No reason given

Research Misconduct

- Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.
- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results. The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records, both physical and electronic, progress reports, abstracts, theses, oral presentations, internal reports, and journal articles.

OPEN ACCESS Freely available online

PLOS ONE

A Comprehensive Survey of Retracted Articles from the Scholarly Literature

Michael L. Grieneisen[1,2], Minghua Zhang[1,2]*

1 Wenzhou Medical College, Wenzhou, Zhejiang, China, **2** Department of Land, Air and Water Resources, University of California Davis, Davis, California, United States of America

Author Error

1. Allegations of data fraud, including data falsification, fabrication or manipulation, or intentionally biasing design to favor a particular outcome
2. No IRB approval
3. Plagiarism
4. Authorship issues
5. Distrust data or interpretations

Plagiarism

Plagiarism is the appropriation of another person's ideas, processes, results or words without giving appropriate credit.

US Department of Health and Human Services. Office of Research Integrity. ORI Policy on Plagiarism. http://ori.dhhs.gov/policies/plagiarism.html

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Self-plagiarism

Self-Plagiarism is defined as a type of plagiarism in which the writer republishes a work in its entirety or reuses portions of a previously written text while authoring a new work.

…copyright infringement is possible if an author reuses portions of a previously published work.

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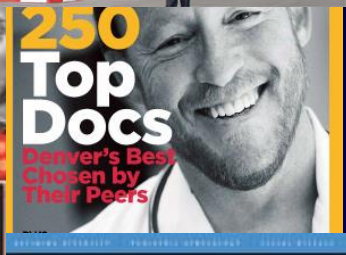
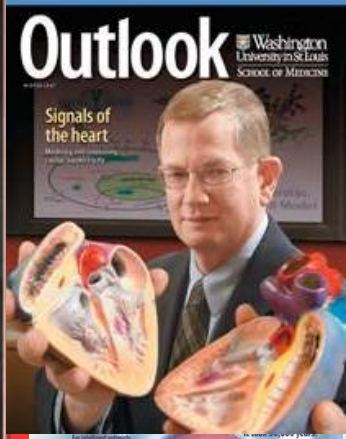
BANGKOK HOSPITAL

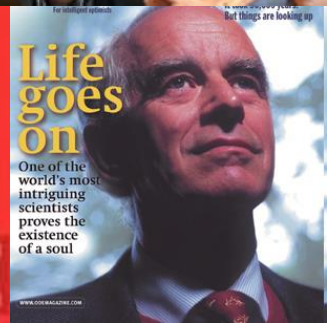

Et gennembrud,
der ændrede den
lægelige
fagkundskab.
Et makkerskab,
der brød alle regler.
SOMETHING THE LORD MADE
11

THE COOKING CARDIOLOGIST
RICHARD COLLINS, M.D.


TIME
The Clintons: Their Future
THE COMMITTEE TO SAVE THE WORLD
The inside story of how the Three Marketeers have prevented a global economic meltdown—so far


250 Top Docs
Denver's Best Chosen by Their Peers


Outlook
Washington University in St. Louis
School of Medicine
Signals of the heart


Life goes on
One of the world's most intriguing scientists proves the existence of a soul

IRB Responsibilities

- to determine that the proposed research is scientifically sound or to verify that another competent expert body has done so;
- to ensure that all other ethical concerns arising from a protocol are satisfactorily resolved both in principle and in practice;
- to consider the qualifications of the investigators, including education in the principles of research practice, and the conditions of the research site with a view to ensuring the safe conduct of the trial; and
- to keep records of decisions and to take measures to follow up on the conduct of ongoing research projects.

Registry

- A "registry is a collection—for one or more purposes—of standardized information about a group of patients who share a condition or experience".
- The definition is similar to the general definition of a database. A database can be defined as a "collection of data or information, typically organized for ease and speed of search and retrieval".

- **The results of randomized controlled trials cannot be confirmed under real world conditions.**

- **Registry data can provide externally valid long-term comparative effectiveness data for little expense. Therefore, registry-based studies could be a valuable information source for evidence based medicine.**

- **The classifications of epidemiologic study designs (e.g. case-control study, cohort study) are usually based on inherent design features.**

- **Registries have no inherent design features and consequently these cannot be used to classify the study design.**

World Medical Association Declaration of Helsinki

Ethical Principles for Medical Research Involving Human Subjects

World Medical Association

https://www.wma.net/wp-content/uploads/2016/11/DoH-Oct2013-JAMA.pdf

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington, DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

DECLARATION OF GENEVA

The "Modern Hippocratic Oath"

The Declaration of Geneva is one of the World Medical Association's (WMA) oldest policies adopted by the 2nd General Assembly in Geneva in 1947. It builds on the principles of the Hippocratic Oath, and is now known as its modern version.

WMA Policy Resources

Related Readings

Declaration of Geneva

The "Modern Hippocratic Oath"

Learn More

Declaration of Helsinki

Medical Research Involving Human Subjects

Learn More

Declaration of Tokyo

Guidelines for Physicians to Prevent Torture

Learn More

Declaration of Taipei

Research on Health Databases, Big Data and Biobanks

Learn More

https://www.wma.net/what-we-do/medical-ethics/declaration-of-geneva/

WORLD MEDICAL ASSOCIATION

WMA DECLARATION OF TAIPEI ON ETHICAL CONSIDERATIONS REGARDING HEALTH DATABASES AND BIOBANKS

Adopted by the 53rd WMA General Assembly, Washington, DC, USA, October 2002
and revised by the 67th WMA General Assembly, Taipei, Taiwan, October 2016

PREAMBLE

1. The Declaration of Helsinki lays down ethical principles for medical research involving human subjects, including the importance of protecting the dignity, autonomy, privacy and confidentiality of research subjects, and obtaining informed consent for using identifiable human biological material and data.

2. In health care provision, health information is gathered by physicians or other members of the medical team to record health care events and to aid physicians in the on-going care of their patient.

https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/

Informed Consent Process

- **Recruiting subjects, including advertising for research subjects and discussions that occur during the screening process**
- **Providing specific information about the study in a way that is understandable to potential subjects while giving them adequate time to consider participation**
- **Answering the potential subjects' questions**
- **Obtaining the voluntary agreement of subjects to take part in the study**
- **Verifying the subjects' continued consent to participate as the study progresses**

Information must be given

- Information that the study involves research …
- Foreseeable risks, inconveniences, or discomforts
- Potential benefits including a statement that there is no intended benefit to the subject, when appropriate.
- Any alternative procedures or treatments
- Confidentiality of records
- For research involving more than minimal risk, an explanation should describe:

  Any compensation and medical treatment offered if injury occurs; and if so, how and to what extent; or If subjects will be paid for participation, information about payment

HHS regulation at 45 CFR 46 (Protection of Human Subjects 2017)

The consent form must also include (if appropriate):

- **The subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;**
- **Whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and**
- **Whether the research will (if known) or might include whole genome sequencing**

https://www.hhs.gov/ **U.S. Department of Health & Human Services**

FDA Regulations for Exceptions from Informed Consent Requirements

- Emergency research (21 CFR 50.24);
- An individual has a life-threatening condition and the following requirements are met and documented (21 CFR 50.23):
- The investigator, with the concurrence of another physician not directly involved in the care of the patient, believes the situation necessitates the use of a test article (in other words, an investigational drug, device, or biologic).
- The subject and/or LAR is unable to communicate consent.
- There is insufficient time to obtain consent.
- No alternative exists that will provide an equal or better chance of saving the subject's life.
- The IRB/IEC is informed of the use of the investigational product without informed consent within five (5) working days of the event.

FDA Guidance for Waiving and Altering Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects

- The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3[k] or 56.102[i]) to subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Electronic Informed Consent (eIC)

- Electronic informed consent (eIC) can be used in a variety of ways during the consent process – from use of a video to demonstrate a study procedure, use of a tablet instead of a paper-based consent form, and use of electronic signatures.
- Investigators and IRB members should be aware of both the benefits and challenges associated with the use of eIC to ensure the study's eIC consent process complies with regulations and ICH E6 guideline.
- The FDA and HHS issued joint guidance for IRBs, investigators, and sponsors on the use of electronic systems to obtain informed consent.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-informed-consent-clinical-investigations-questions-and-answers

Use of Electronic Informed Consent

Questions and Answers

Guidance for Institutional Review Boards, Investigators, and Sponsors

U.S. Department of Health and Human Services
Office for Human Research Protections (OHRP)
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Good Clinical Practice (OGCP)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2016
Procedural

https://www.hhs.gov/ohrp/regulations-and-policy/guidance/use-electronic-informed-consent-questions-and-answers/index.html#tocq10

Conclusions

Not Scientific ---- Not Ethical

Risk and Benefit

Vulnerable populations

Confidentiality and protection of privacy

Informed consent

BDMS
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Thank you

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