Introduction to Research Ethics

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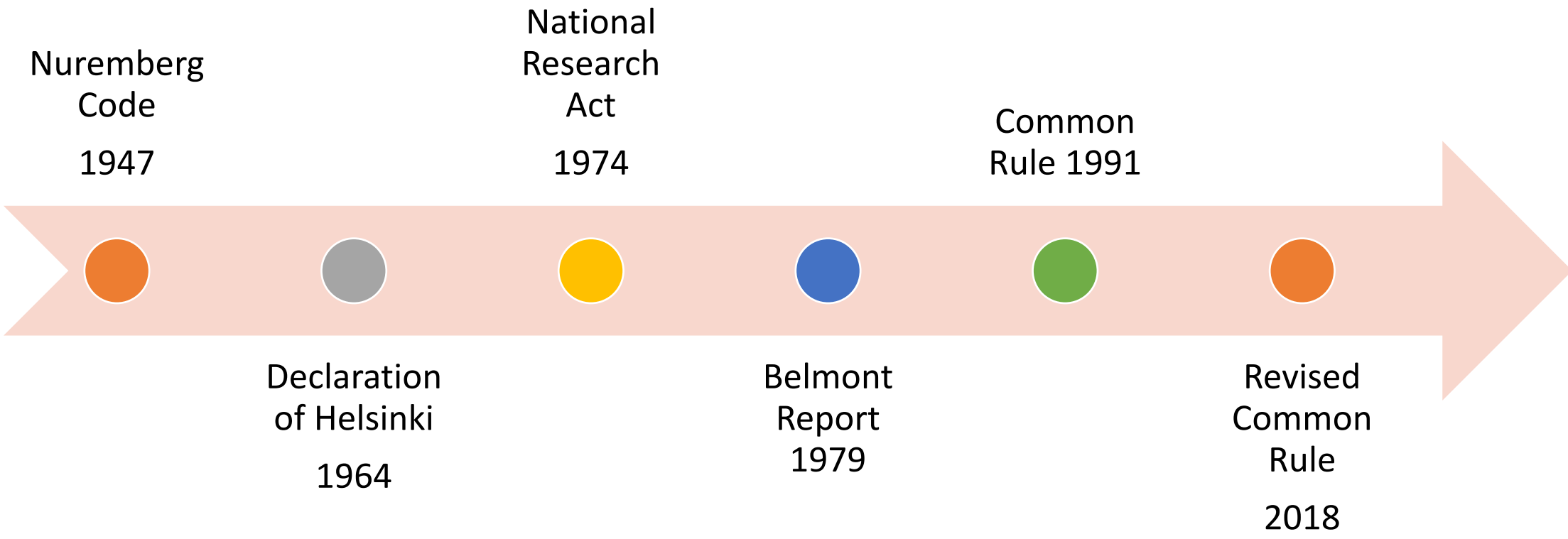
May 19, 2022

ALASKA NATIVE
TRIBAL HEALTH
CONSORTIUM


Nuremberg Code
1947
Declaration of Helsinki
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National Research Act
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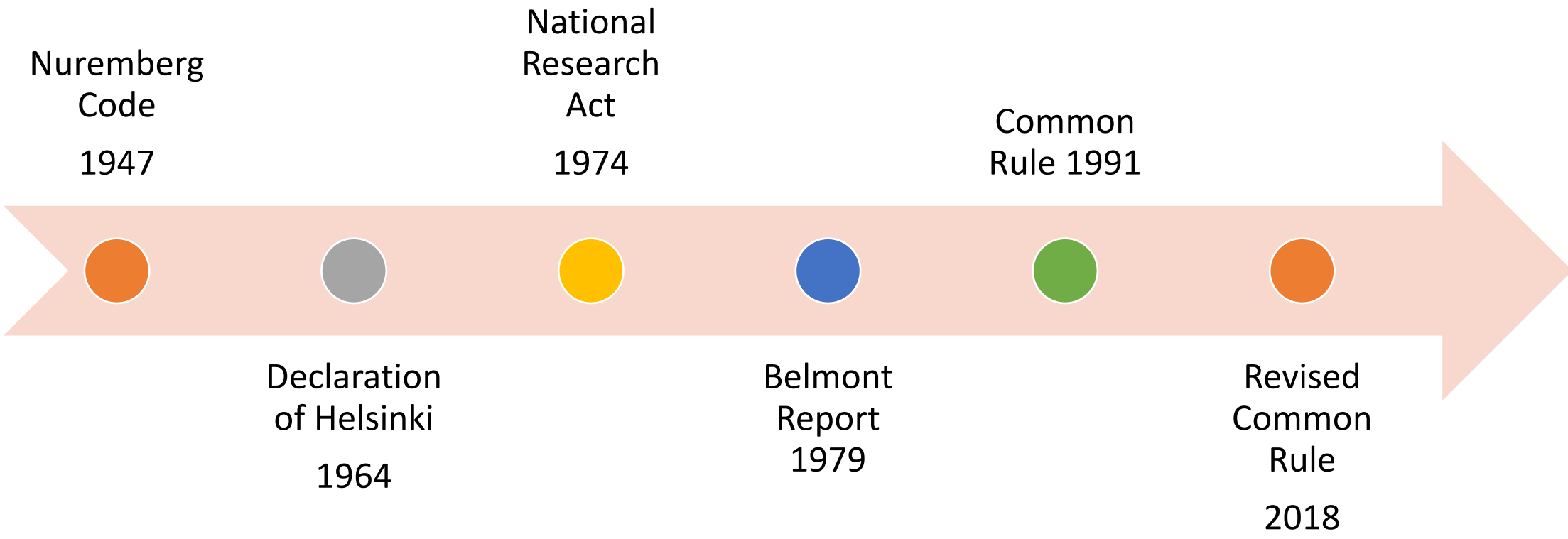
Belmont Report
1979
Common Rule 1991
Revised Common Rule
2018

USPHS Syphilis Study at Tuskegee

- Study of natural history of syphilis by US Public Health Service
- Enrolled black men without informed consent beginning in 1932
- Projected to last 6 months but continued for 40 years
- Penicillin became widely accepted as a treatment in 1945
- News articles first published in 1972 led to several responses

https://www.cdc.gov/tuskegee/timeline.htm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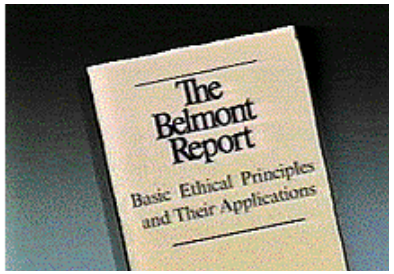
The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects (Participants) of Research



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

April 18, 1979

Principles of the Belmont Report

Justice

Respect for Persons

Beneficence

Principles of the Belmont Report

Justice

Respect for Persons

Beneficence

- Recruit participants fairly without discrimination, bias, or undue influence.
- Distribute the benefits of research equitably.
- Distribute the burdens of research fairly.

Principles of the Belmont Report

Justice

<u>Respect for Persons</u>

Beneficence

- Identify potential participants without violating their right to privacy.
- If information is individually identifiable “de-link” the information.
- When using consent emphasis the process of informed consent, in addition to a signed informed consent form.

Principles of the Belmont Report

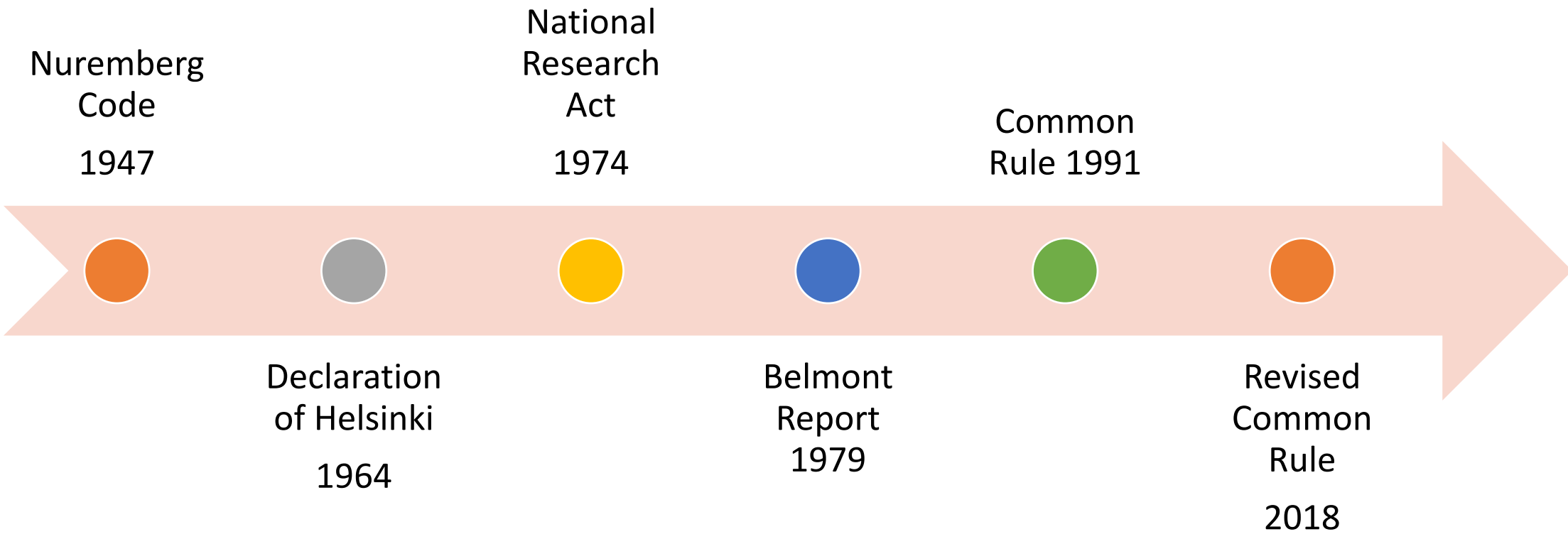
Justice

Respect for Persons

<u>Beneficence</u>

First Do No Harm:

Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well being and maximize possible benefits.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Common Rule

- Issued in 1991 following the principles of the Belmont Report
- “Common”: accepted by 19 federal departments and agencies
- Uniform policy to protection of human “subjects” in human “subjects” research that is federally funded
  - 45 CRP 46 Subpart A: The Common Rule
  - Includes requirements for IRBs and IRB review of research
  - Requirements for informed consent
  - Subpart B, C, D: additional protections for pregnant women, prisoners, and children in research
- FDA did not adopt the common rule but has similar regulations

Revised Common Rule (2018)

- Changes intended to “modernize, strengthen, and make more effective” the current system of oversight that has been the Common Rule since 1991
- Revisions by HHS intended to:
  - Better protect humans “subjects” in research
  - Facilitate research
  - Remove ambiguity
  - Reduce regulatory burden.
- Allowed public input starting in 2011
- Compliance date January 21, 2019

Institutional Review Boards (IRBs)

- Membership
  - At least 5 members, varied experience and expertise
  - At least one community member (unaffiliated)
  - “Diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes”
- Functions and operations
  - Meeting space, roster, policies/procedures, quorum
- Review of research
  - Authority to review and approve research (or require modifications)
  - Review informed consent form and processes
  - Continuing review if indicated

45 CFR 46 107, 108, 109

Definition of Research

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that m

45 CFR 46.102 (Revised Common Rule)

Generalizable Knowledge

- Knowledge from which conclusions will be drawn that can be applied to populations outside of the specific study population.

- Examples:
  - Contributes to a theoretical framework
  - Dissemination of the results is intended to inform the field of study
  - Results are expected to be generalized to a larger population beyond the site of data collection
- Publication of findings does not necessarily mean it is research

Not Research

- Oral histories, journalism, legal research, historical scholarship.
- Public health surveillance.
- Collection and analysis of information, biospecimens or records by a criminal justice agency.
- Authorized operational activity (homeland security, support of national security).

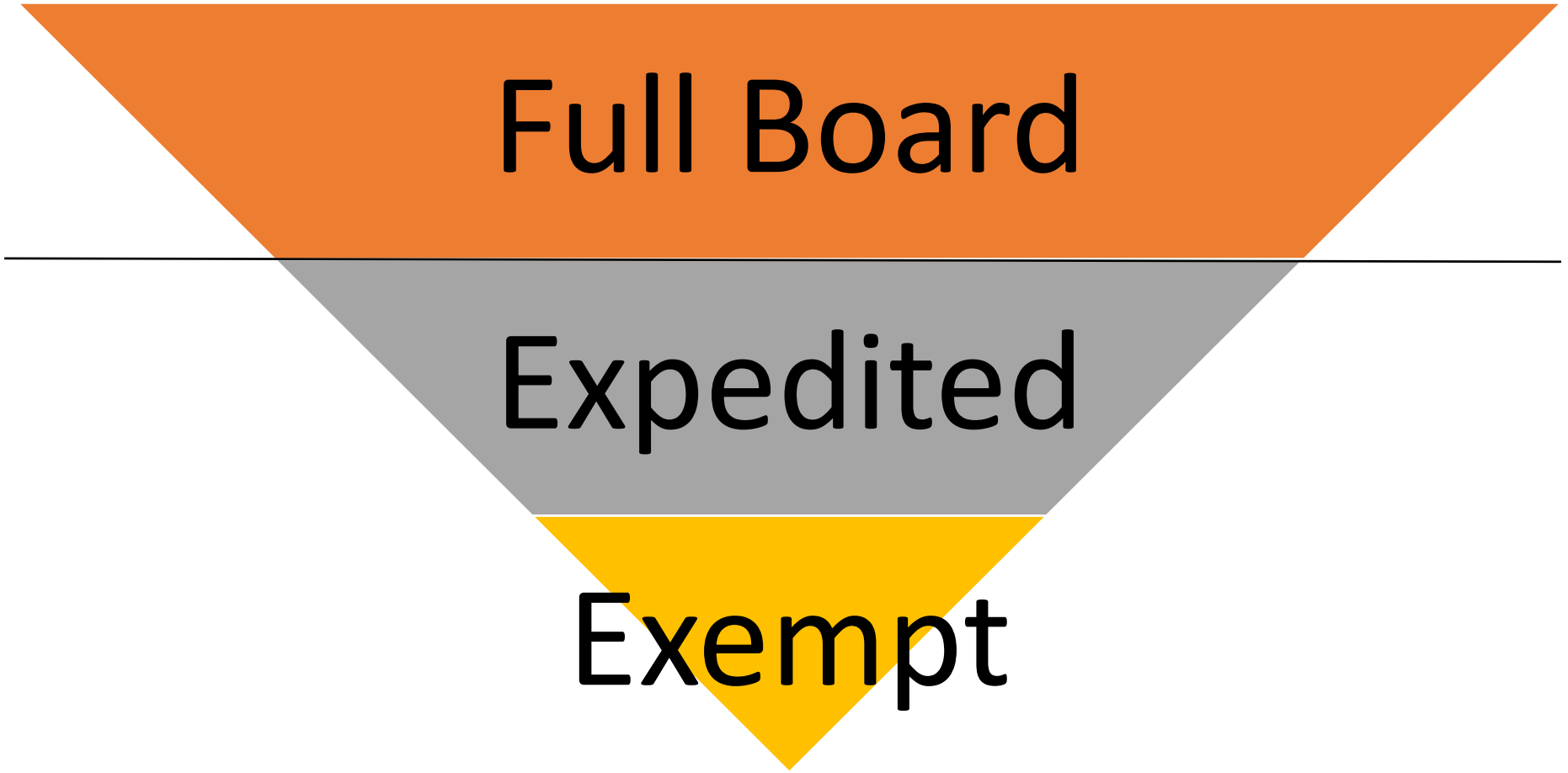
Definition of “Human Subject” (preferred term “Participant” or “Volunteer”)

- Living individual about whom an investigator conducting research:

  i. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

  ii. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Research Review Categories



Caveats – Minimal Risk Definition

- Federal regulations define “minimal risk” as:
  - *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

- Tribes and tribal organizations may consider risk to be higher than that identified by an outside/university IRB
  - Community harm
  - Stigmatization

General Requirements for Informed Consent

- Before involving a human “subject” in research, an investigator shall obtain informed consent.
- An investigator shall seek informed consent only under circumstances that provide sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion.
- The information that is given shall be in language understandable to the subject.
- Informed consent as a whole must present information in sufficient detail to facilitate understanding of the reasons why one might or might not want to participate.
- No informed consent may include any exculpatory language.

Informed Consent New Elements Revised Common Rule

- Consent form and process should provide information a *reasonable person* would want to have in order to make an informed decision.
- Key information about the study at the beginning
- Notice about whether information or biospecimens collected for the research might be de-identified and used for other research or not
- Notice about possible commercial profit
- Notice about whether clinically relevant results will be returned to participants
- Could this involve whole genome sequencing?

Certificate of Confidentiality (CoC)

- CoC can be issued by federal government agency
  - Issued by NIH for all projects now
  - Can be requested from other agencies
- Avoid involuntary disclosures by researcher of sensitive information collected from participants (e.g. subpoena)

Waiver of Consent

- An IRB may waive the requirement for the investigator to obtain a signed informed consent form if it finds any of the following:
  - (i) That the only record linking the subject and the research would be the informed consent form and the principal risk would be a breach of confidentiality.
  - (ii) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
  - (iii) If the subjects are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

- In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

Continuing Review

- Common Rule required IRBs to review and approve continuation of all non-exempt research at intervals no longer than one year
- Revised Common Rule no longer requires continuing review for minimal risk research
  - Unless an IRB determines otherwise
- Full Board Research requires continuing review with exceptions as noted

Single IRB Review

- Implemented January 20, 2020
- Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States

- Exceptions:
  - Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe)
  - Funding agencies have the authority to determine that a single IRB review is inappropriate for certain types of research.

What is missing in the Belmont Report?

Extending Research Protections to Tribal Communities

Bobby Saunkeah, Julie A. Beans, Michael T. Peercy, Vanessa Y. Hiratsuka & Paul Spicer

Pages 5-12 | Published online: 15 Jan 2021

Open Peer Commentaries

Considering "Respect for Sovereignty" Beyond the Belmont Report and the Common Rule: Ethical and Legal Implications for American Indian and Alaska Native Peoples

Krystal S. Tsosie, Katrina G. Claw & Nanibaa' A. Garrison

Pages 27-30 | Published online: 23 Sep 2021

THE AMERICAN JOURNAL OF BIOETHICS
2021, VOL. 21, NO. 10, 1–4
https://doi.org/10.1080/15265161.2021.1972649

GUEST EDITORIAL

Beyond the Belmont Report

Wamia Siddiqui and Richard R. Sharp

Mayo Clinic

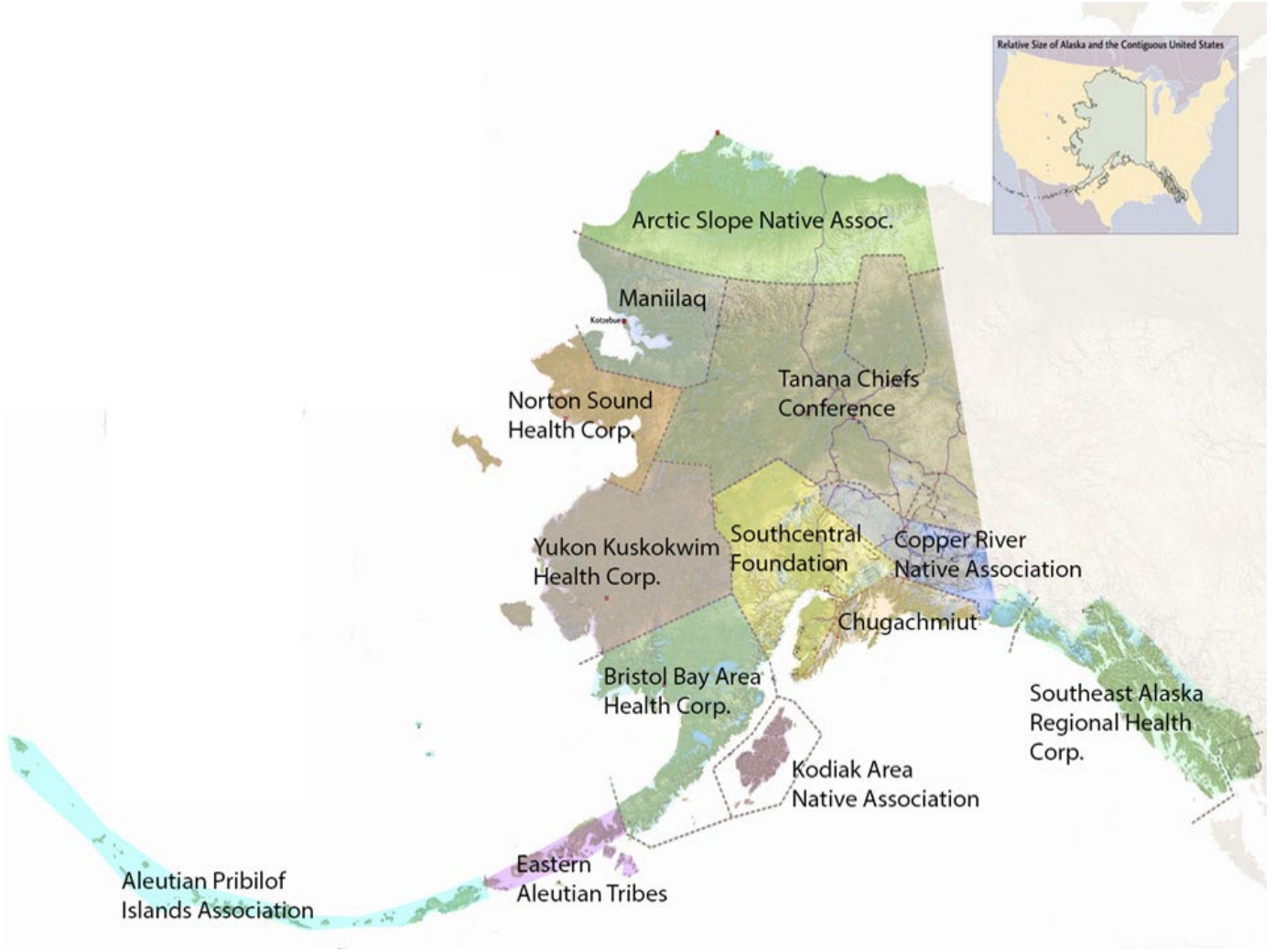
Tribal Research Review

- Federal regulations should be considered to be the minimum level of protection.
- Regulations focus on protecting individuals, not communities.

Alaska Tribal Health System

- Alaska Area IRB (IHS) serves as IRB of record in most cases
- Tribal health organizations have research review processes (in addition to IRB)

- Unique situations for different tribes/regions in other places – tribal IRBs / university IRBs / IHS IRBs / tribal review committees
  - Get to know your communities and processes!



Secondary use of Identifiable Information/ Biospecimens

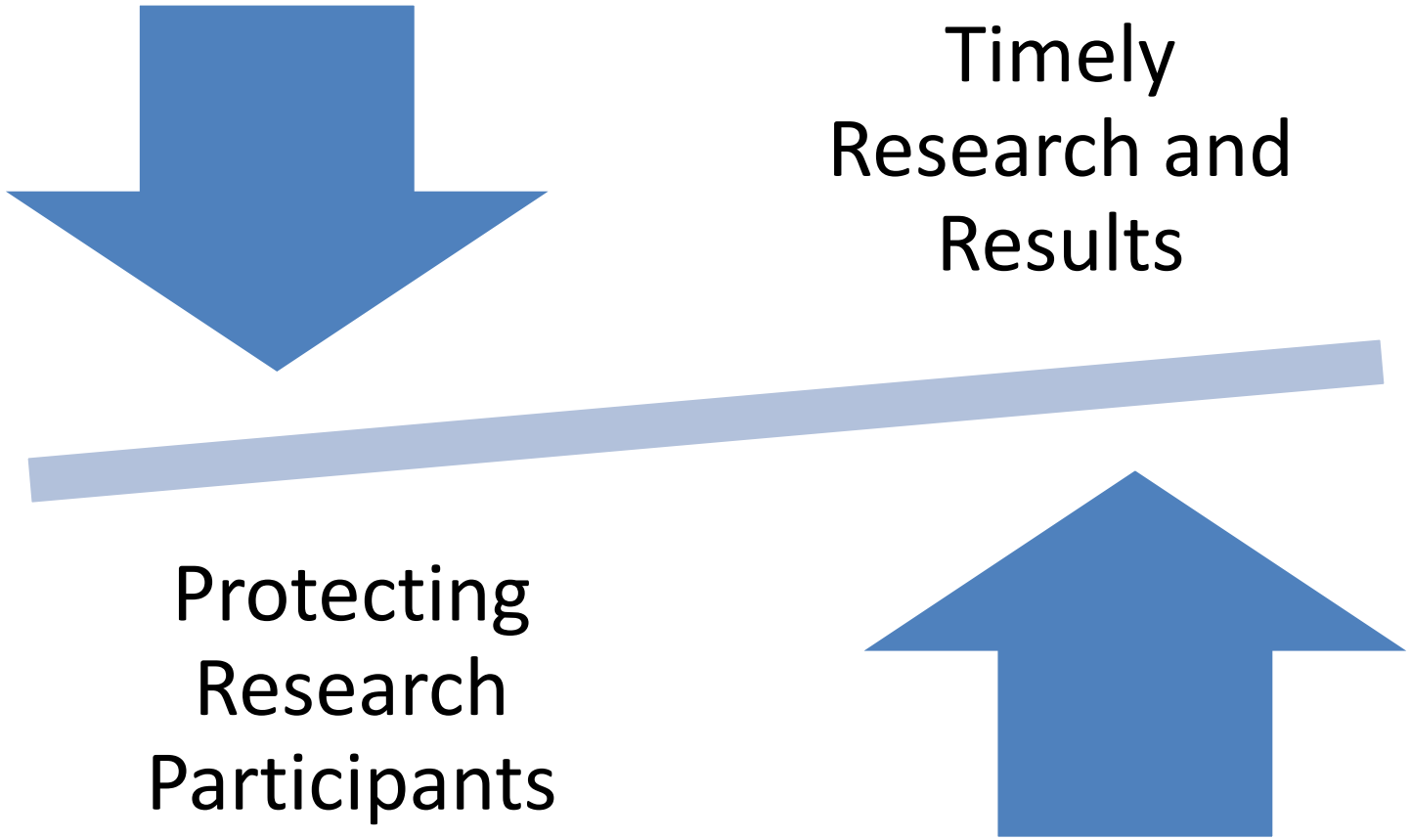
- Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Biospecimens

- Can be de-identified and used for secondary research without additional consent from participant.

- Tribes do not have to agree to secondary use for tribal specimens.
  -Define Process to Access Specimens

Conflicts


Timely
Research and
Results
Protecting
Research
Participants

quyanaa • gunalchéesh • háw'aa • way dankoo • qağaasakung • mahsi' chin'an • 'awa'ahdah •