MAHIDOL UNIVERSITY
Wisdom of the Land

Informed consent process

From

Declaration of Helsinki 2013

CIOMS Guideline 2016

MU-CERT
Center of Ethical Reinforcement for Human Research

Nuremberg Code

1. The voluntary consent of the human subject is absolutely essential.

- ….the person involved should have legal capacity to give consent;
- …be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion;
- and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision.

Nuremberg Code

- The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

Informed consent process

The Belmont Report
- Respect for person
- Beneficence & nonmaleficence
- Justice

- Declaration of Helsinki item 25 -32
- CIOMS guideline
  - 9: individual capable of giving informed consent
  - 10: modification & Waivers of informed consent
  - 15: research involving vulnerable person and groups
  - 16: research involving adults incapable for giving informed consent
  - 17: research involving children and adolescents
  - 18: women as research participants
  - 19: pregnant and breastfeeding women as research participants

Vulnerable subjects

Informed consent process

Researchers

- Relationship with human subjects: dependent or independent
- Provide informed consent document or non-written consent

Human Subjects

- Capacity for self-determination: autonomy or diminished autonomy (vulnerable subjects)
- Legal capacity to give consent

Media to convey message: recruitment materials, consent documents

Declaration of Helsinki item 25 -32

25. No individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

26. Information for competent human subject should include

Content of the informed consent

the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researchers, the anticipated benefits and potential risks and the discomfort, post-trial access and general outcome/ the result of the study

The potential subject must be informed of the right to refuse to participate or to withdraw consent at any time without reprisal.

the potential subject's freely-given informed consent, preferably in writing

the non-written consent must be formally documented and witnessed.

CIOMS informed consent (guideline 9)

- It is the *principal investigator's responsibility* to ensure that all personnel obtaining informed consent for a study comply with this Guideline
  - seek and obtain consent only after providing relevant information about the research and ascertaining that the potential participant has adequate understanding of the material facts
  - refrain from unjustified deception or withholding of relevant information, undue influence, or coercion
  - ensure that the potential participant has been given sufficient opportunity and time to consider whether to participate; and
  - as a general rule, obtain from each potential participant a signed form as evidence of informed consent.
- any exceptions to this general rule - seek the approval of the research ethics committee.

CIOMS informed consent (guideline 9)

- Access to research populations: - *obtaining permission from an institution*
- Process: a *two-way communicative process* that begins when initial contact is made with a potential participant and ends when consent is provided and documented, but can be revisited later during the conduct of the study.
- Language
- Contents of the information leaflet: *short and preferably not exceed 2 or 3 pages*, not made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the institution from liability for negligence.
- Comprehension: The participant's understanding also depends on the researcher's ability and willingness to communicate with patience and sensitivity, as well as the atmosphere, situation and location where the informed consent process takes place.
- Documentation
- Voluntariness and undue influence, Who? dependent relationship

Declaration of Helsinki

27. if the potential subject is in a dependent relationship with the physician or may consent under duress, the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.

28. For a potential research subject who is incompetent, the physician must seek informed consent from the legally authorized representative.

These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the population represented by the potential subject, the research *cannot instead be performed with competent* persons, and the research entails only minimal risk and minimal burden.

CIOMS informed consent (guideline 9)

- Researchers must renew the informed consent of each participant if
  - there is a substantive change in the conditions or procedures of the research,
  - new information becomes available that could affect the willingness of participants to continue.
  - In long-term studies, researchers should ensure at pre-determined intervals that each participant is willing to stay in the study, even if there are no changes in the design or objectives of the research.

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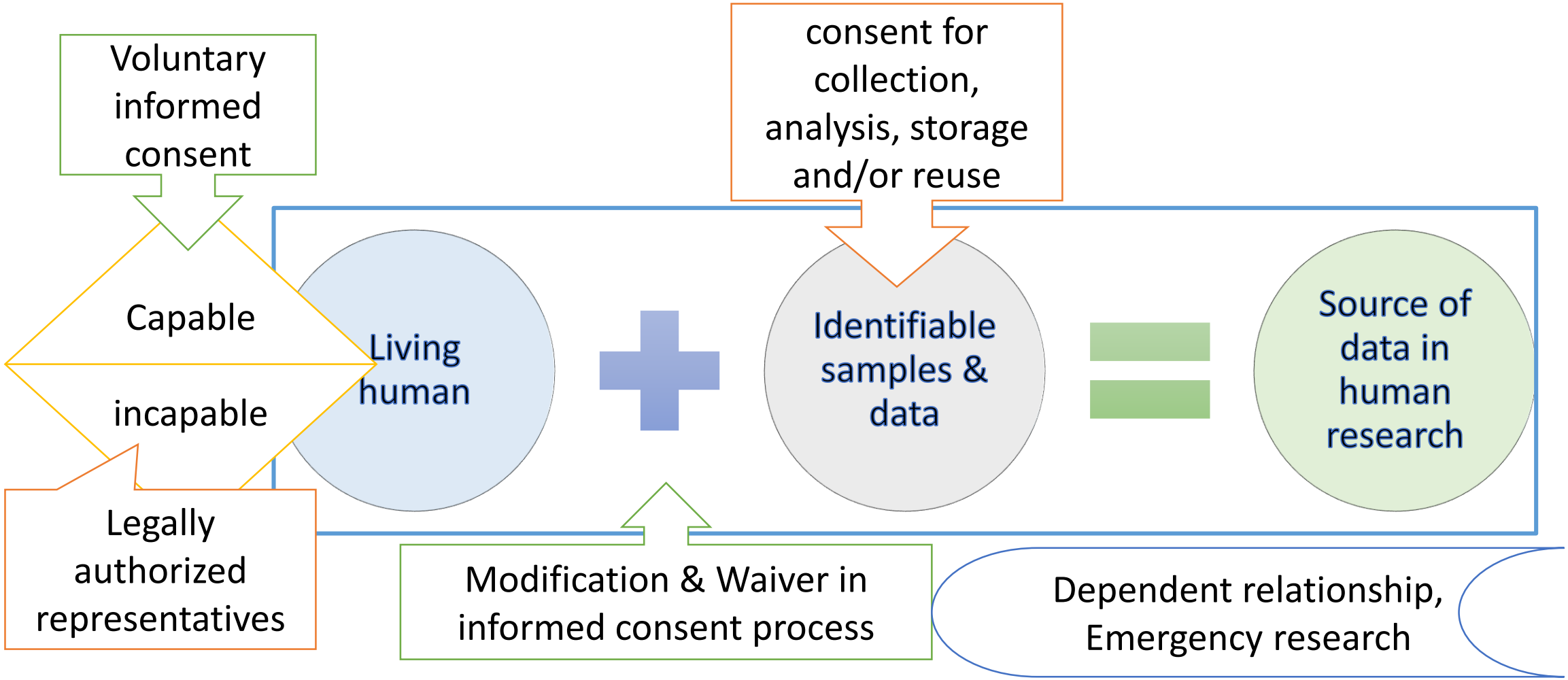
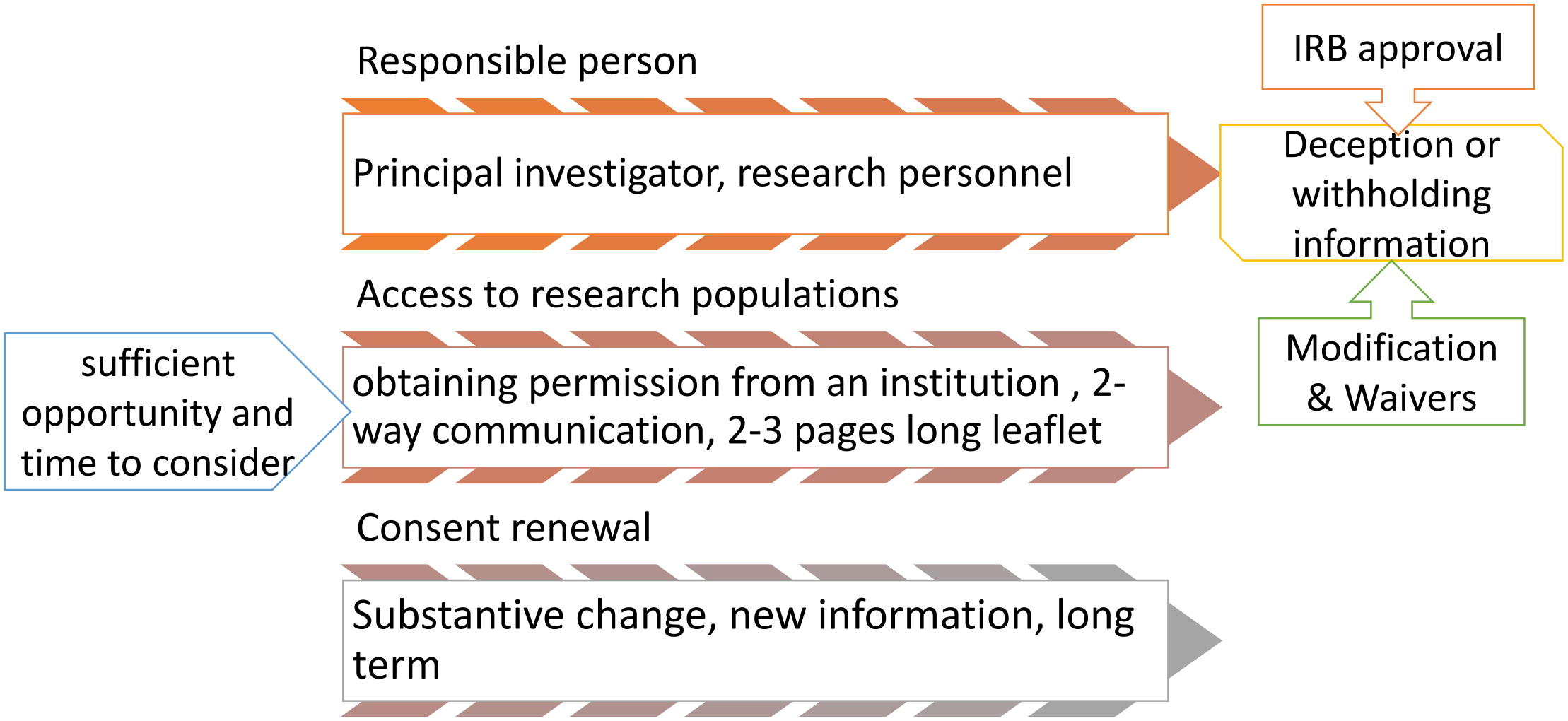
31. The physician must fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never interfere with the patient-physician relationship.

32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must normally seek consent for collection, analysis, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.

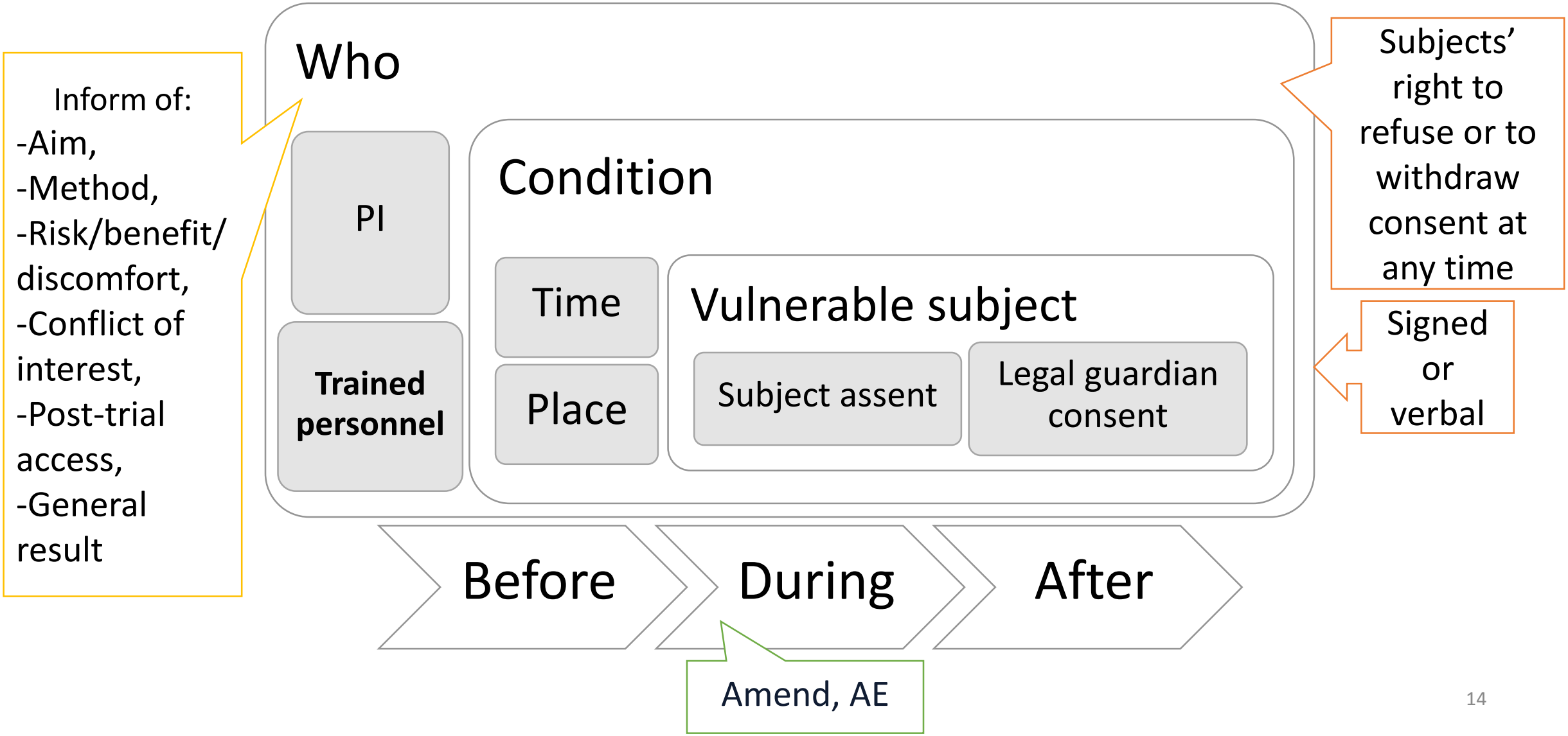
Human research & informed consent process Declaration of Helsinki



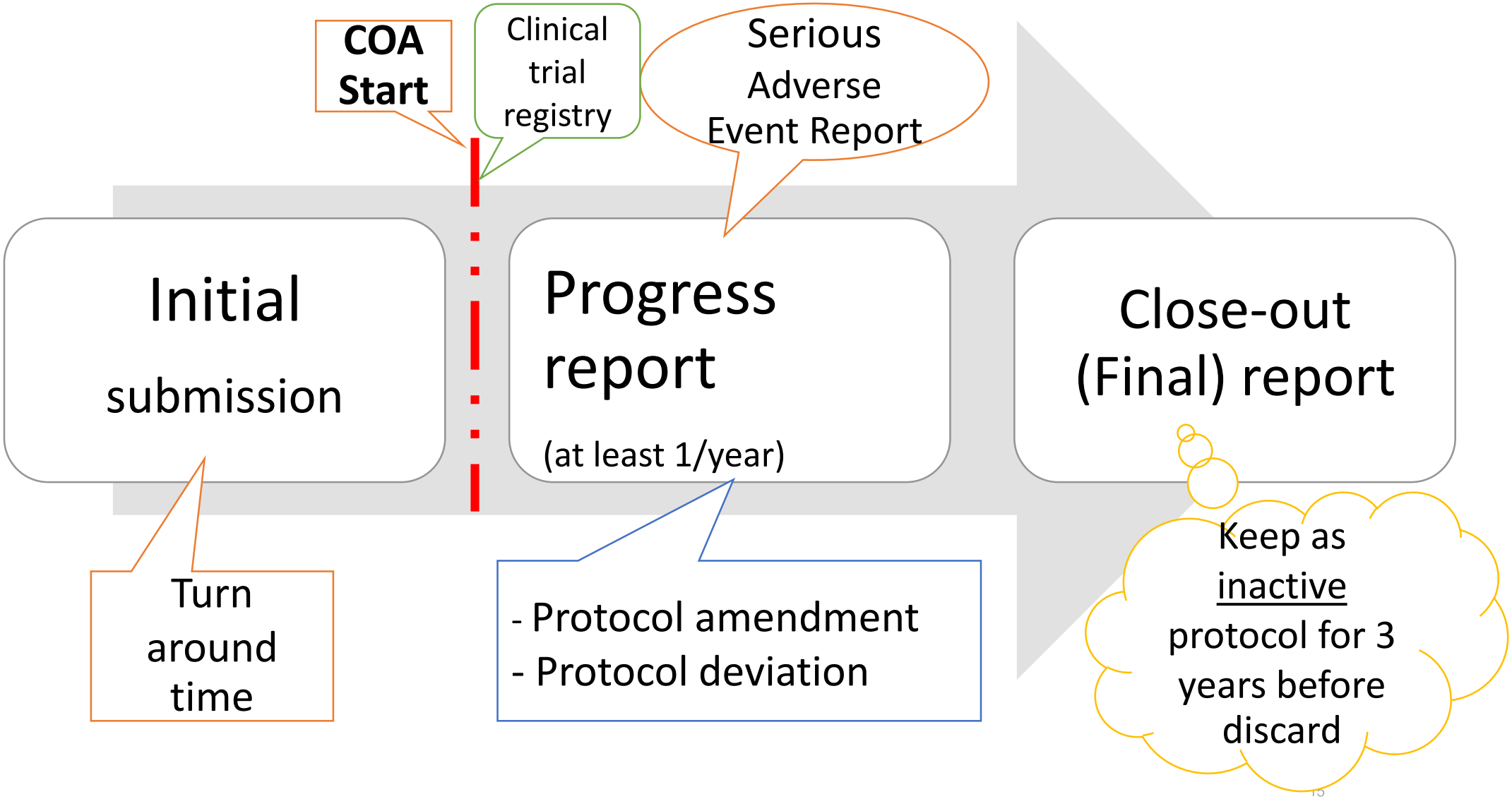
Informed consent process – CIOMS guideline



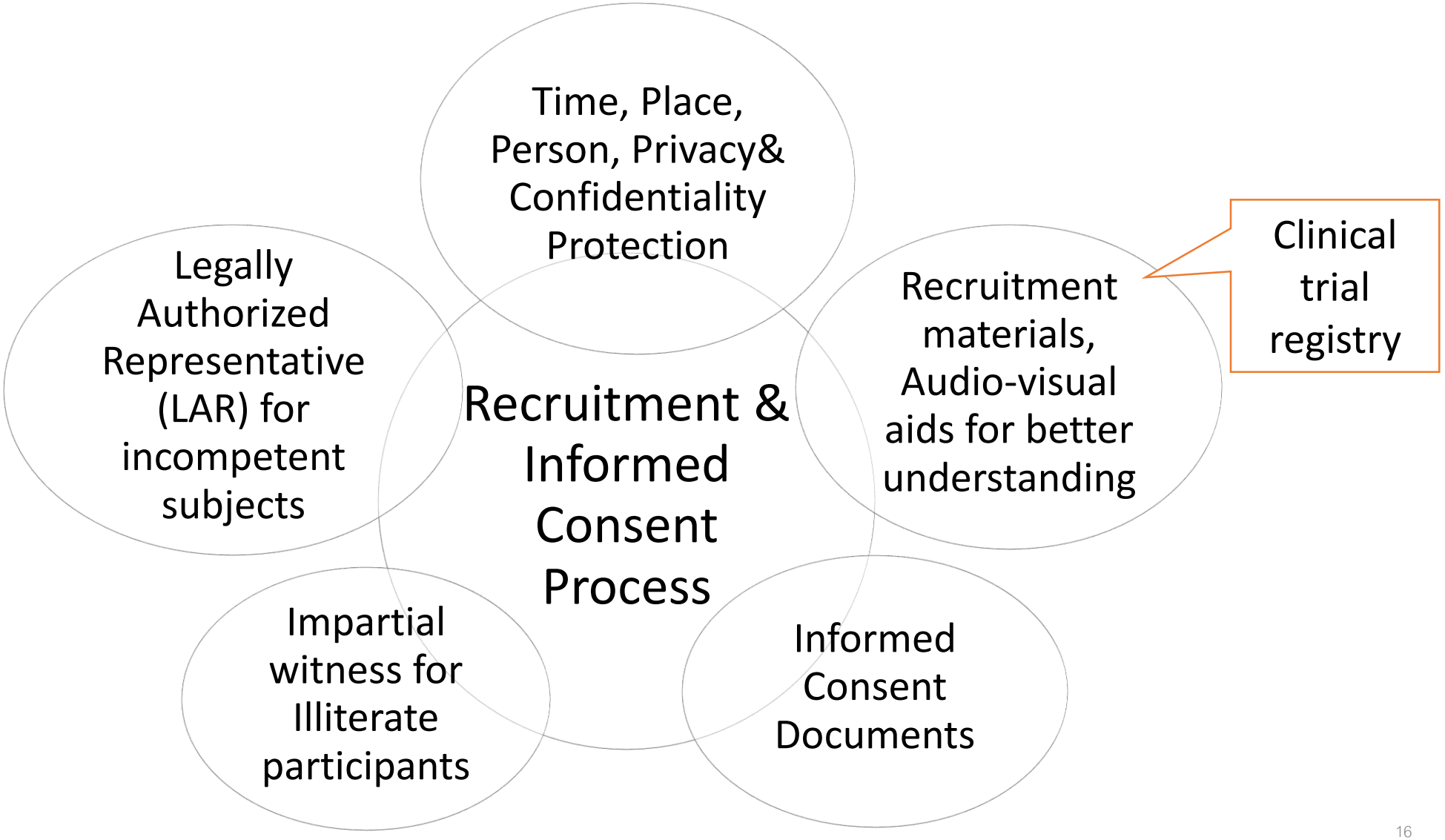
Informed consent process



IRB Oversight of Human Research

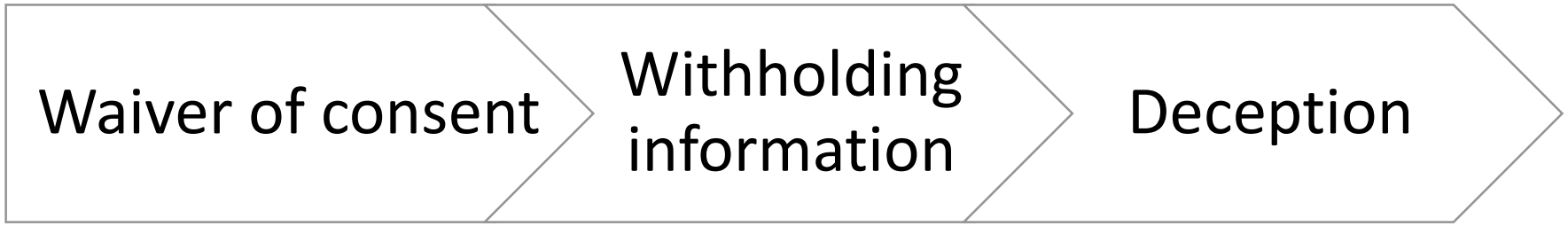


Respect for Research Participants



MODIFICATIONS AND WAIVERS OF INFORMED CONSENT (CIOMS guideline 10)

- Before a waiver of informed consent is granted, researchers and research ethics committees should first seek to establish whether informed consent could be modified in a way that would preserve the participant's ability to understand the general nature of the investigation and to decide whether to participate.
- Additional provisions may apply when waivers or modifications of informed consent are approved in specific research contexts.



Waiving informed consent

These 3 conditions must be met

1. the research would not be feasible or practicable to carry out without the waiver,
2. the research has important social value, and
3. the research poses no more than minimal risks to participants.

Beneficence

Non maleficence

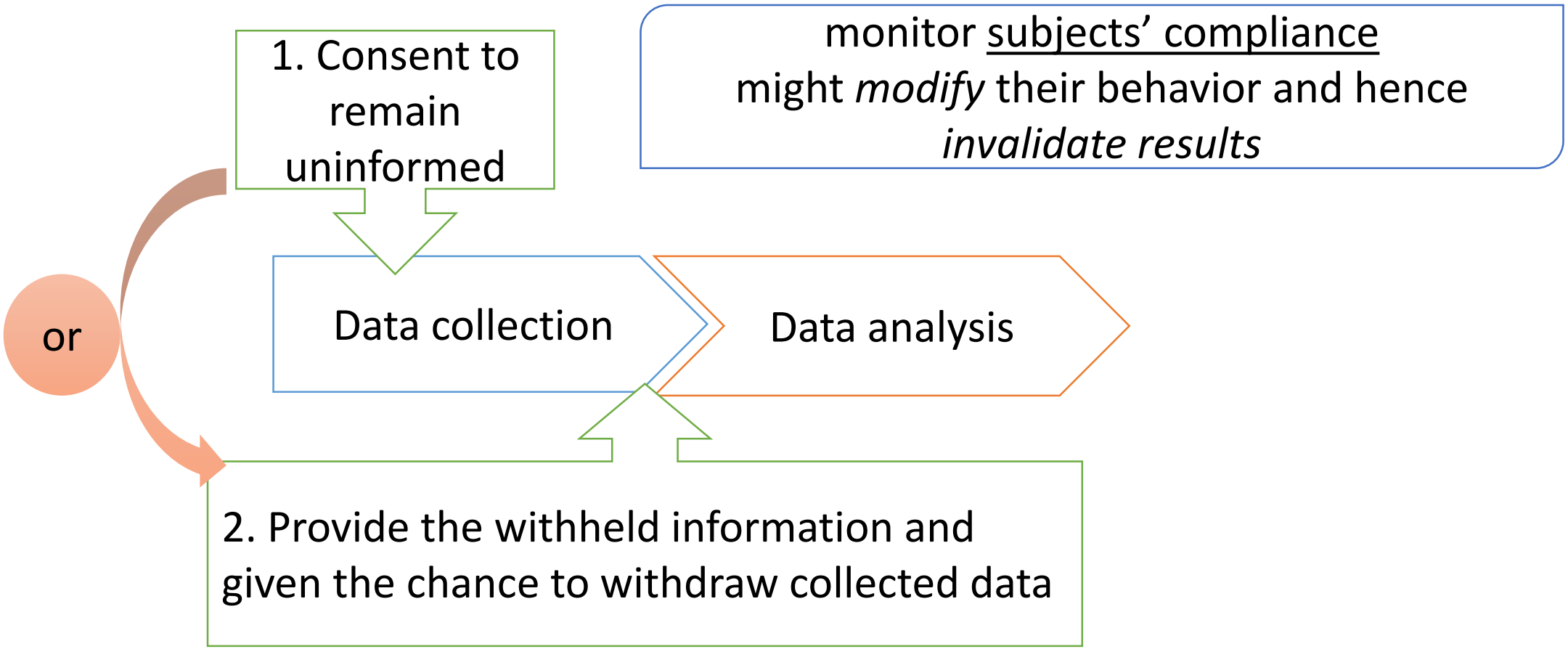
a study involves *identifiable* data or biological specimens, existing data from health-related registries

data or biological specimens are ***not*** *personally identifiable*, the participants are unknown to the researcher and hence cannot be contacted to obtain informed consent

Modifying the informed consent process by withholding information in order to maintain the scientific validity of the research

- the purpose of tests performed to monitor their compliance
- if they knew their compliance was being monitored they might modify their behavior and hence invalidate results.
- potential participants may be asked
  - to consent to remain uninformed of the purpose of some procedures until the research is completed. After their participation in the study ends, they must be given the omitted information, or
  - withheld until the data have been collected.
- *Before* study results are *analysed*, participants must be *provided with the information withheld* and given the *possibility to withdraw their data* collected under the study.
- The potential impact on the validity of the study when participants withdraw their data must be considered before a study starts.

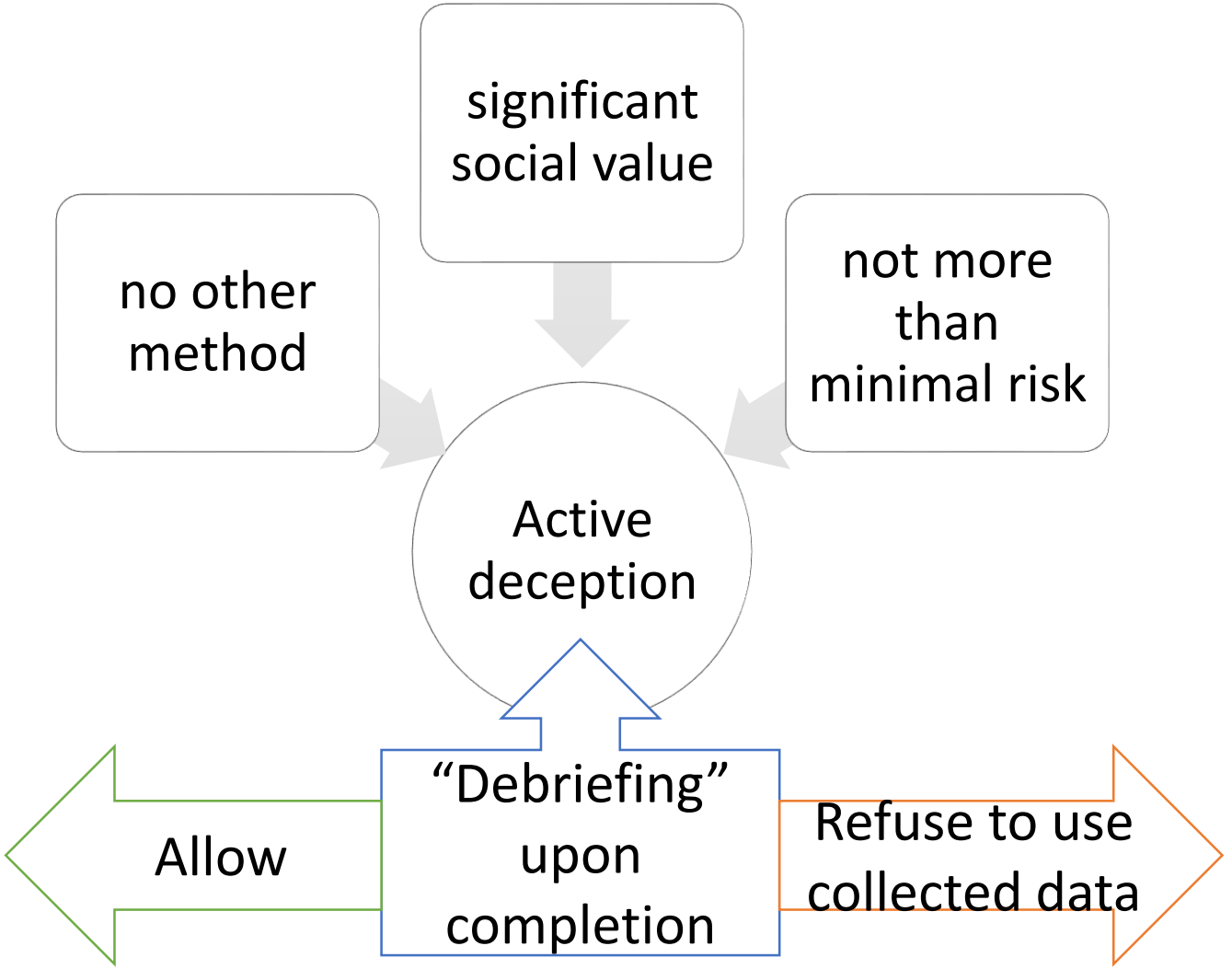
Modifying the informed consent process by withholding information



Modifying the informed consent process by actively deceiving participants

- to study their attitudes and behavior
- no other method could obtain valid and reliable data;
- the research has significant social value; and
- no information has been withheld that, if divulged, would cause a reasonable person to refuse to participate.
- exposes participants **not** more than minimal risk
- The research ethics committee must determine how participants must be informed of the deception upon completion of the research = "debriefing", ordinarily entails explaining the reasons for the deception.
- Participants who disapprove of having been deceived for research purposes must be offered an opportunity to refuse to allow the researcher to use their data obtained through deception.
- In exceptional cases, a research ethics committee may approve the retention of non-identifiable information.

Actively deceiving participants to study attitudes and behavior



Research in emergency care situation

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- Physically or mentally incapable of giving consent is a necessary characteristic of the research population
- If no such representative is available and if the research cannot be delayed, the study may *proceed without informed consent*
- Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative

CIOMS guidelines 16

- For examples: sepsis, head trauma, cardiopulmonary arrest and stroke
- Researchers should ideally contact potential participants while capable of informed consent, and obtain their agreement to be involved during future periods of incapacitation
- If there is no opportunity to solicit informed consent of participants while fully capable, plans to conduct emergency care research must be publicized within the community
- Maximum time of involvement of an individual without consent → withdrawn
- Opportunity to object to the use of data

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29. For incompetent subject, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

30. Research involving subjects who are physically or mentally incapable of giving consent, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population.

If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee.

Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.

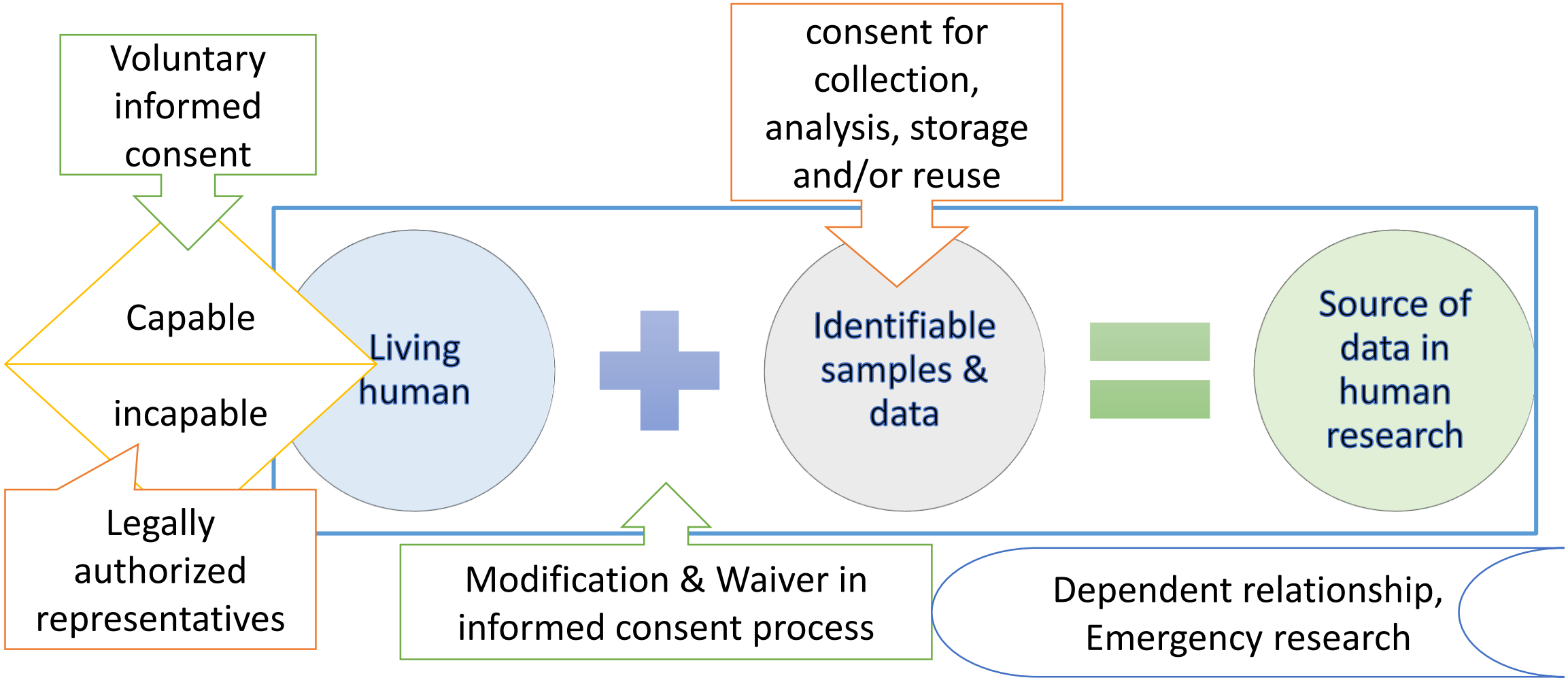
Emergency care situations that many participants will be unable to consent.

- For examples: sepsis, head trauma, cardiopulmonary arrest and stroke
- necessary to proceed with the research interventions very soon after the onset of the condition
- If possible, an attempt must be made to identify a population that is likely to develop the condition to be studied - researchers should ideally contact potential participants while fully capable of informed consent, and obtain their agreement to be involved in the research during future periods of incapacitation
- If there is no opportunity to solicit informed consent of participants while fully capable of informed consent, plans to conduct emergency care research with incapacitated persons must be publicized within the community in which it will be carried out, where feasible.

Emergency care situations that many participants will be unable to consent.

- The researcher and the research ethics committee should agree to a maximum time of involvement of an individual without obtaining either the individual's own informed consent or surrogate consent
- If, by that time, there is no individual or surrogate consent, the participant should be withdrawn from the study provided that withdrawal will not make the participant worse off.
- The participant or the surrogate should be offered an opportunity to object to the use of data derived from participation of the patient without consent or permission.

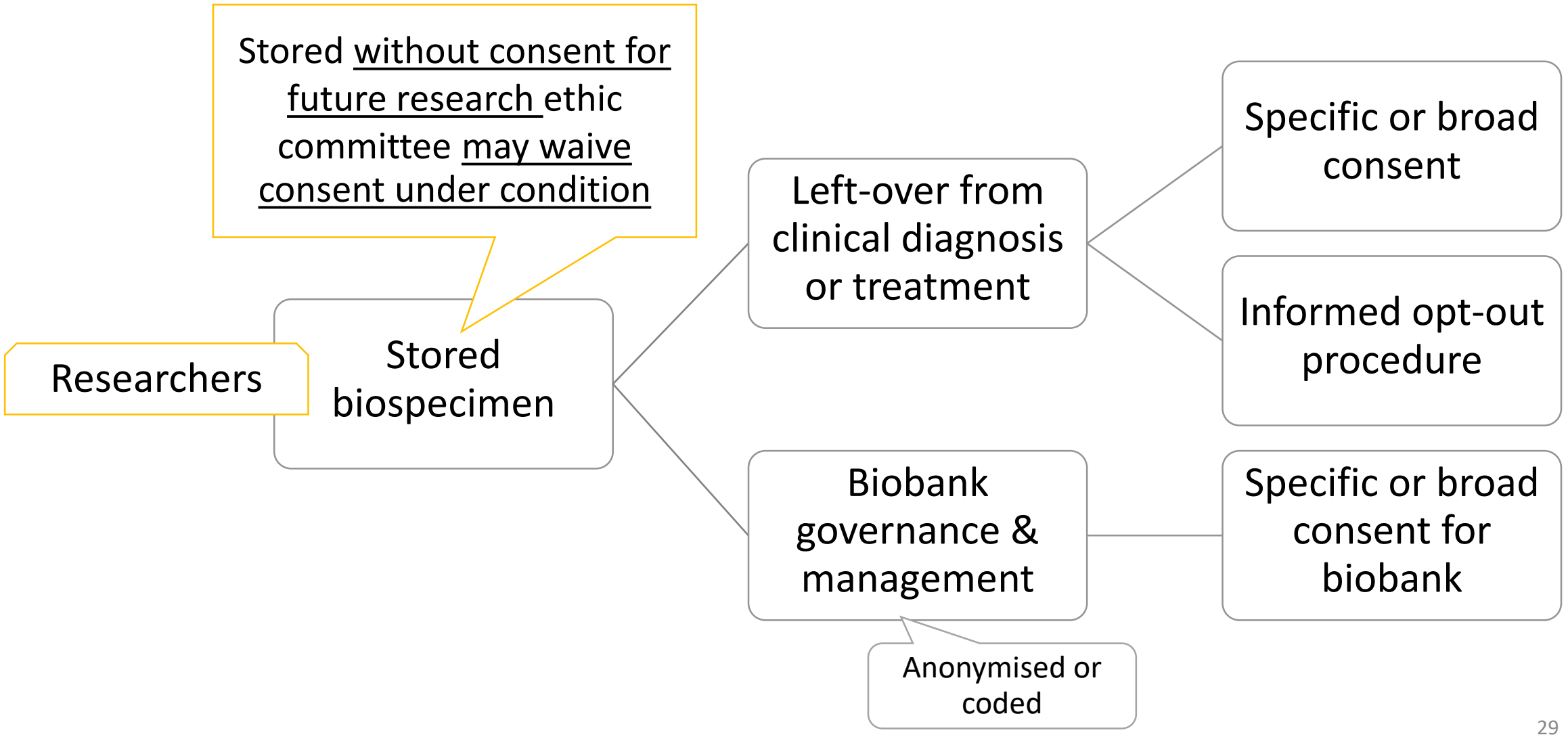
Human research & informed consent process Declaration of Helsinki



CIOMS Guideline 11: Use of stored biological materials 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.
- Such broad informed consent relies on proper governance and management of the biobank.
- 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.

Use of Stored specimen in research



Stored left over biospecimen after clinical diagnosis or treatment (so-called residual tissue) for future research

Consent

Broad consent

-the range of future uses

-the conditions and duration of storage;

-who will manage access to the materials;

-the foreseeable uses of the materials,

-the intended goal of such use, whether only for research, basic or applied, or also for commercial purposes,

-the possibility of unsolicited findings and how they will be dealt with.

An informed opt-out procedure

- **An informed opt-out procedure** = the material is stored and used for research unless the person from whom it originates explicitly objects
- The informed opt-out procedure has to fulfill 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; and

4) a genuine possibility to object has to be offered.

Research ethics committees and biobanks

The protocol must be submitted to a research ethics committee,

- Appropriateness of specific or broad informed consent for future research.
- Necessity for re-consent
- Waiver of consent

  1) the research would not be feasible or practicable to carry out without the waiver; and

  2) the research has important social value; and

  3) the research poses no more than minimal risks to participants when research interventions or procedures offer participants no potential benefits.

CIOMS Vulnerability

- GUIDELINE 15: RESEARCH INVOLVING VULNERABLE PERSONS AND GROUPS
- GUIDELINE 16: RESEARCH INVOLVING ADULTS INCAPABLE OF GIVING INFORMED CONSENT
- GUIDELINE 17: RESEARCH INVOLVING CHILDREN AND ADOLESCENTS
- GUIDELINE 18: WOMEN AS RESEARCH PARTICIPANTS
- GUIDELINE 19: PREGNANT AND BREASTFEEDING WOMEN AS RESEARCH PARTICIPANTS

Consent VS. Assent

Consent

- Competent person (Autonomy)
- Method
  - Written consent
  - Verbal consent
  - Modification & Waivers

Assent

- Incompetent person
  - **Children**
  - Incompetent Adult (physical or mental condition that prevents giving informed consent)
- Assent form - content

Research involving incompetent adults

Benefit

- For research interventions or procedures that have the potential to benefit incompetent adults the risks must be minimized and outweighed by the prospect of potential individual benefit.
- For research interventions or procedures that have **no** potential individual benefits for participants, 2 conditions apply:
    1. the interventions and procedures should be studied first in persons who can give consent when these interventions and procedures target conditions that affect persons who are not capable as well as those who are capable, unless the necessary data cannot be obtained without participation of persons who are incapable
    2. the risks must be minimized and no more than minimal.

Research involving children & adolescent

Benefit

- For research interventions or procedures that have **no potential individual benefits** for participants, 2 conditions apply:
- the interventions and procedures should be studied in adults first, when these interventions and procedures target conditions that affect adults as well as children and adolescents, unless the necessary data cannot be obtained without participation of children or adolescents; and
- the risks must be minimized and no more than minimal.

Research involving incompetent adults

consent

- a legally authorized representative of the person who is incapable of giving informed consent has given permission and this permission takes account of the participant's previously formed preferences and values (if any); and
- the assent of the subject has been obtained to the extent of that person's capacity, after having been provided with adequate information about the research at the level of the subject's capacity for understanding this information.

Research involving children & adolescent

consent

- a parent or a legally authorized representative of the child or adolescent has given permission; and
- the agreement (assent) of the child or adolescent has been obtained in keeping with the child's or adolescent's capacity, after having been provided with adequate information about the research tailored to the child's or adolescent's level of maturity.
- If children reach the legal age of maturity during the research, their consent to continued participation should be obtained.

Assent and parental permission requirements

Age of minor	Assent form	Parental permission form
Infant-6 years old	No	Yes
7-12 years old	Yes	Yes
13-17 years old (Option A)	Yes	Yes (same form)
13-17 years old (Option B)	Yes	Yes (separate form)

Permission of a parent or legally authorized representative

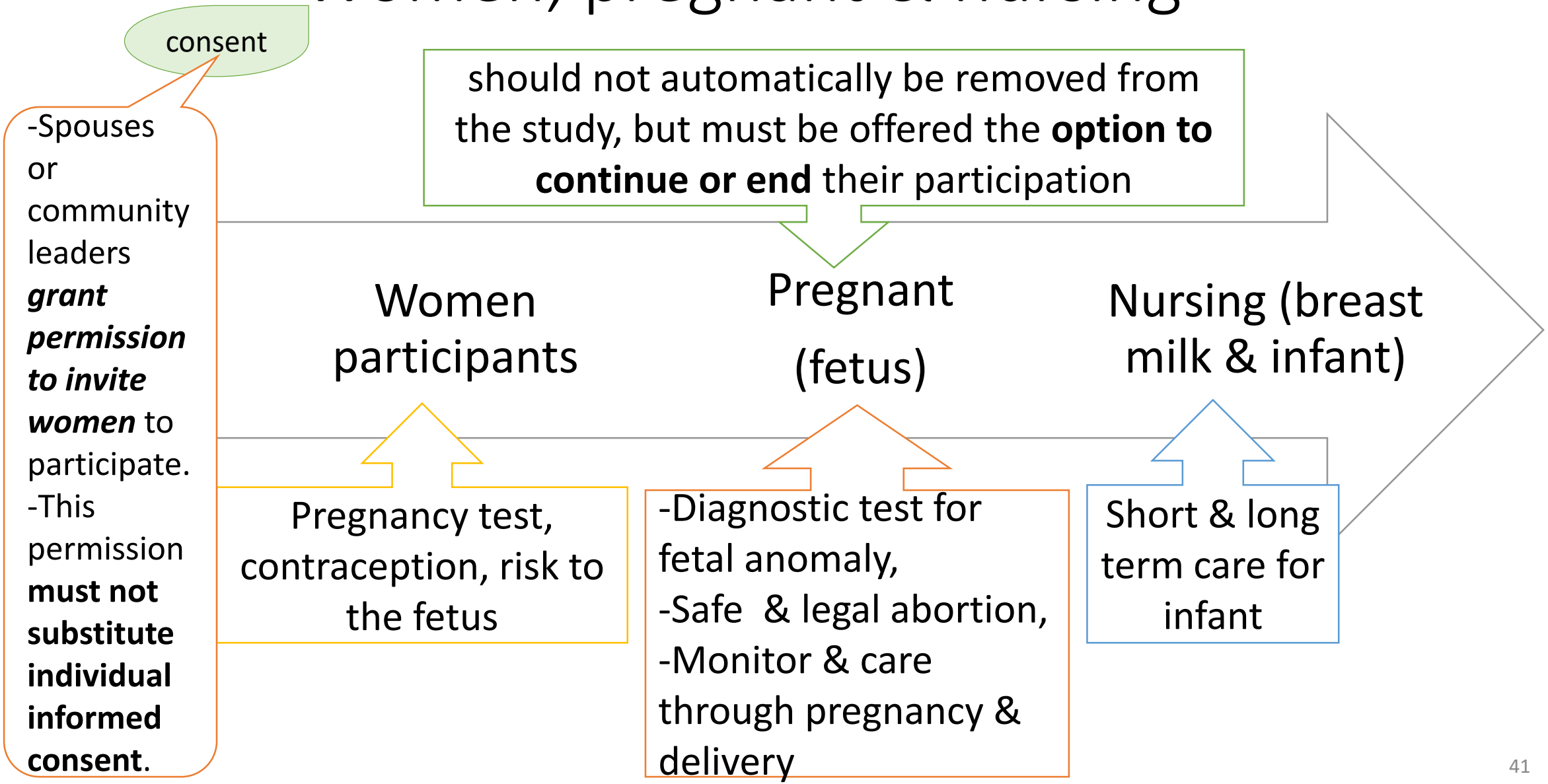
consent

- at least one parent or guardian in writing, consistent with applicable laws and regulations.
- **Waiver of parental permission**
  - "emancipated" or "mature" minors
  - be married,
  - pregnant or be parents themselves, or
  - live independently.
  - studies involve investigation of adolescents' beliefs and behaviour regarding sexuality, sexually transmitted diseases, pregnancy, abortion
  - Studies the use of recreational drugs.
  - Research address domestic violence, or child abuse.
- In these cases, parental knowledge of the topic of the research may place the children or adolescents at risk of questioning, intimidation, or even physical harm by their parents.

Additional safeguard for children & adolescents

- the involvement of independent child advocates: a relative, trusted friend, or family physician who is not involved in the research project
- Independent psychological and medical support for the participating children and adolescents
- Observation of the study by a parent or guardian - enable the child to be withdrawn if the parent or guardian decides it is in the child's best interests to do so

Women, pregnant & nursing



Women as research participants

Inclusion of women of child-bearing potential

- must be informed that the research could include risks to the fetus if they become pregnant during the research
- Access to a pregnancy test, to effective contraceptive methods and to safe, legal abortion must be guaranteed before exposure to a potential teratogenic or mutagenic intervention.

Women as research participants

Women who become pregnant during research

- pregnant women must be removed from the study, and followed up and provided care through the duration of their pregnancy and delivery.
- Access to diagnostic tests must be provided to reveal any fetal anomalies.
- If anomalies are detected, women who wish may be referred for an abortion.
- When there is no evidence on the basis of which a potential harm to the fetus can be assumed, women who become pregnant should not automatically be removed from the study, but must be offered the option to continue or end their participation.
- If the woman opts for continued participation, researchers and sponsors must offer adequate monitoring and support.

Pregnant & breastfeeding women in a research

Research designed to obtain knowledge relevant to the health needs of pregnant and breastfeeding women should be promoted in the following areas:

- interventions for conditions resulting from pregnancy;
- interventions for conditions that affect the general population and are reasonably expected to be used without adequate evidence during pregnancy (for example off-label use of medications); and
- interventions for conditions that affect the developing fetus.

Informed consent, risks and potential individual benefits.

- Research in pregnant and breastfeeding women must be initiated only after careful consideration of the best available data from preclinical research in pregnant animal models, research in non-pregnant women, retrospective observational studies, and pregnancy registries.
- 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.

วิธีการติดต่อกับ MU CERif

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Thank you for your attention

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