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Informed Consent

Its Significance within the Continuum of Research Ethics

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Outline

- I. Informed Consent: Meaning & Historical Backdrop
- II. Informed Consent: Processes and Procedures
- III. Informed Consent: Cultural Challenge
- IV. Open Discussion

*Defending Those
Who Cannot Defend Themselves*



Meaning and Historical Backdrop

What is informed consent?

- The making of a decision regarding participation in research on the basis of adequate information received from the investigator, good understanding of the information, and voluntary assent or dissent.
- Informed consent occurs when a participant's assent satisfies all criteria

Informed Consent: Central Process in Human Subjects Protections

The Legacies of Nuremberg, Belmont and Beyond.....

Human subjects protection:

- ...Reaction to various historical situations
- ...Development of scholarly literature and regulatory requirements
- ...Far reaching sanctions, public notoriety for institutions and professional researchers in cross-disciplines.

Informed Consent: Central Process in Human Subjects Protections

Informed consent:

...Is informed consent central only because it is a “reaction?” Is it only a legalistic minimum?

...Is it needed to protect researchers/institutions first, and only secondarily protecting subjects?

...*Or is it something far deeper altogether?*

Moral Development

The centrality of informed consent is grounded in culture's intense interest in what it means to be human and how human nature must be protected.

...Nuremberg: "Moral Outrage;" violations of the fundamental dignity of "the human being."

...Directly tied to human freedom, human dignity, and the fundamental nature of the human species.

Moral Development

“Collision of Values:”

Ethics vs Discovery, Advancement and Genius.

Necessary “frustration” between genius and concerns for preserving and protecting:

- Human nature

- Humane behavior

- Responsibility for the common good

Requires prudence, honesty, dialogue

Moral Development

This “collision” is not new. It is part of the dynamic history of societies and cultures. However, one of the very important debates this collision addresses for scientific research regards:

What is it we *CAN* be doing?
What is it we *SHOULD* be doing?

Moral Development

Stages of Moral Development:

Infancy:	Trust vs Mistrust
Early Childhood:	Autonomy vs Shame & Doubt
Childhood:	Industry vs Inferiority
Adolescence:	Identity vs Role Confusion
Young Adulthood:	Intimacy vs Isolation
Adulthood:	Generativity vs Stagnation
Maturity:	Integrity vs Despair

Moral Development

One of the most critical of the stages of moral development that comes into play *viz a viz* human subjects protections and the legacy of historical problems is the very first stage:

Trust versus Mistrust

Trust versus Mistrust

Medical care and medical research are steeped in the moral imperative of medicine to do no harm and to bring health and healing to the sick.

Patients and research volunteers bring their “trust” to the medical and research table.

Vulnerability!!!!

The Agenda of Trust

Human subject protections are not about law or regulations.

Real purpose is to protect the “agenda of trust” that must be the foundation of the interaction between investigator and research participant.

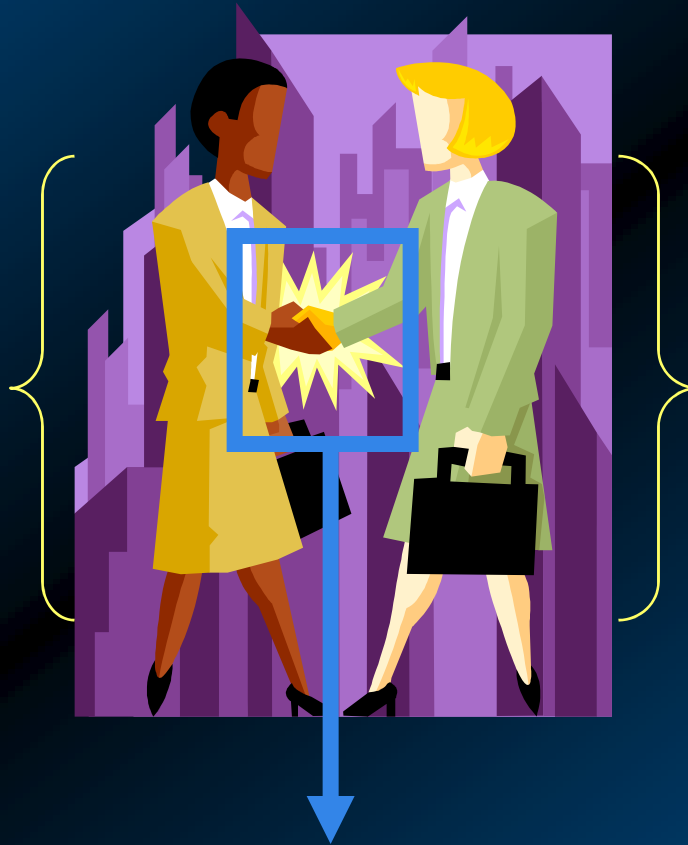
A visual representation may provide the best way of remembering the sensitive importance of the Agenda of Trust as it impacts upon the process of the relationship informed consent represents.

Human Subjects Protections

A Relational Process

Researcher's "Agenda"

Trust vs Mistrust
Autonomy vs Shame & Doubt
Industry vs Inferiority
Identity vs Role Confusion
Intimacy vs Isolation
Generativity vs Stagnation
Integrity vs Despair



Participant's "Agenda"

Trust vs Mistrust
Autonomy vs Shame & Doubt
Industry vs Inferiority
Identity vs Role Confusion
Intimacy vs Isolation
Generativity vs Stagnation
Integrity vs Despair

In the interaction/relationship of human subjects protections, "agenda meets agenda" along a vast number of factors including cultural and personal issues. These issues are most often unarticulated and subconscious. To maintain the delicate balance between ethical protections and scientific enthusiasm, prudence and discerning diligence are required on the part of all.

Or in other words.....



....it's all about relationship.

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Strategies for Successful Relationship

The informed consent process has greatest chance of success if it promotes:

- Honoring of the local community's history
- Trustbuilding and establishing trustworthiness
- The research endeavor as an experience of mutuality
- The recognition of heterogeneity
- Investigator humility:
i.e. Investigator self-reflection/introspection

Informed Consent as Relational Process

What is needed is a matrix in which the moral development relationship between investigator and participant is ordered:

The role of informed consent is about my making informed decisions for my self.

Now for some historical notes....

The Historical Context

The Holocaust, Unit 731 and The Nuremberg Trials

Background:

Nazi/Imperialist Victims: Jewish people, Gypsies, gay persons, Polish Catholic priests, Russian nationals, POW's, the mentally ill, political dissidents and others.

Atrocious medical experiments to secure the position of a "master race" or to provide greater efficiency for Nazi war machinery.

Revelations at 1946 The Doctors' Trial at Nuremberg.

The Human Nadir: Regardless of place or time.

The Historical Context

The Holocaust, Unit 731 and The Nuremberg Trials

Summary and Issues:

As the Nuremberg transcript cites, the Nazi medical atrocities were “crimes committed in the guise of scientific research.”

- High altitude/low pressure experiments
- Freezing experiments
- Malaria experiments
- Sea water experiments
- Mustard gas experiments
- Twin sibling experiments
- Sterilization experiments

The Historical Context

The Holocaust, Unit 731 and The Nuremberg Trials

Afterward:

The Nazi/Japanese experiments: human exploitation, bigotry, and violations of the sacredness of the human person, Hippocratic Oath, bases of civilization's sense of human preservation.

Resulted in the beginnings of human subjects protections

Nuremberg Code:

- ...mandate of voluntary informed consent
- ...medical credentialing, the beneficence of research
- ...just sharing of benefits and risks
- ...freedom to participate and withdraw, freedom from harm etc.

The Historical Context

The Syphilis Experiments at Tuskegee

Background:

From 1932 to 1972, the US Public Health Service conducted an experiment in Macon County, Alabama, to determine the natural course of untreated latent syphilis in black males.

During the forty year history of this experiment, treatment was withheld even after the onset of penicillin therapies.

Only minor compensations were ever afforded to the men and their families. The experiment continued long after original project period estimated time frames had expired.

The Historical Context

The PHS Syphilis Experiments at Tuskegee

Summary and Issues:

The experiments had inherent and vast difficulties:

- Medical research staff lied. Patients not ethically consented.
- Treatment was withheld leading to suffering and death. Withholding of treatment continued even after it was known that penicillin could have cured volunteers of the disease.
- Studies were shaped along assumptions that exploited the men racially, socially and economically.

The Historical Context

The PHS Syphilis Experiments at Tuskegee

Afterward:

Clear evidence that forces that could lead to unethical medical experimentation were not left at the Nazi doorstep.

Clear evidence to the ongoing problems of racial, sexual, social and economic bigotry that can erode medical ethics and humane social progress.

Clear evidence to the problem of substandard scientific review of research and flawed or absent informed consent.

Paved the way: The Belmont Report and the Common Rule.

The Historical Context

Examples of More Contemporary Cases

Background:

The Milgram Experiments: In 1961-1962, Dr. Stanley Milgram of Yale University conducted socio-behavioral studies on authority and obedience using ordinary citizens of New Haven. His deception studies involved his using actors who were supposed to learn word pairs as monitored and overseen research enrollees. Failure to learn was to result in the actors supposedly receiving up to 450 watts of electric shock. He found that 65% of the real subjects were willing to inflict pain on actors who seemed to fail to learn.

The Jesse Gelsinger Case: In September 1999, an 18 year old volunteer died while enrolled in a university gene therapy clinical trial. It was determined that the death was research-related.

The Ellen Roche Case: In June 2001, a 24 year old healthy volunteer died while enrolled in a university asthma challenge study. Determinations on relationship to research remained ongoing throughout the following summer

The Historical Context

Contemporary Cases

Summary and Issues:

The following factors seem to emerge from these cases.

- ...Inadequate protocol design development
- ...Inadequate or inappropriate IRB review/approvals/oversight
- ...Inadequate certification of objectivity in the formation of informed consent and related protections documents.
- ...Inadequate information in original informed consent documents
- ...Inadequate and inaccurate revelation of actual risks
- ...Inadequate or nonexistent understanding that risks in research are not confined to the medical or biological.
- ...Inadequate understanding of the problem of deception in research.
- ...Inadequate adverse event reporting with changes to informed consent as would be expected

The Historical Context

Contemporary Cases

Afterward:

Public more sensitized/educated regarding human; demands more concrete accountability.

Greater sensitivity/awareness of human protections needs in all forms of research.

Need for greater balance between scientific advances, the common good, and the needs of the individual.

Federal authorities/courts taking greater oversight; imposing sanctions.

Quest for greater objectivity for ethical oversight for human protections.

Informed consent no longer an automatic guarantee that a study is ethical or that participants are truly “informed.”

Greater awareness concerning institutional problems that can erode ethical oversight (*e.g. the “produce or perish” climate of modern research*).

Ethical Milestones

- ⑩ 1947 - Nuremberg Code
- ⑩ 1964 – Declaration of Helsinki, World Medical Association
- ⑩ 1979 – The Belmont report
- ⑩ 1982 – International guidelines for biomedical research involving human subjects, Council for International Organisations of Medical Sciences (CIOMS)
- ⑩ 1991 – International guidelines for ethical review of epidemiological studies, CIOMS
- ⑩ 1991 – The Common Rule, Code of Federal Regulations, Part 46 (Protection of Human Subjects)
- ⑩ 1996 – International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH-GCP)
- ⑩ 2000 - World Health Organization (WHO): *Operational Guidelines for Ethics Committees that Review Biomedical Research*
- ⑩ 2001 - European Commission: *Directive on Implementing Good Clinical Practice in the Conduct of Clinical Trials*

Emerging Issues

The Human Stretching of the Informed Consent Reality

...Fluidity between: healthcare context and research context

...Individualism vs “communitas:”

...Internationalization & Multiculturalism

...Issues of trust/trustworthiness *viz a viz* communities of color, ethnic groups, women, sexual minorities, socio-economic minorities etc

...Industry and Power:

...Informed consent as PROCESS vs procedure

...The *fundamentum in re*: RELATIONSHIP

Protecting the Process of Protections

Human subjects protections and the process of informed consent = FRAGILE!!!!!!

Need for principles, guidance, and regulatory requirements!

A need for healthy matrices or frameworks:

Not just about regulatory compliance

Not just about legal adherence

Need for systems that are about Ethos!

*Defending Those
Who Cannot Defend Themselves*



Informed Consent: Processes and Procedures

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Informed consent is central to the protection of human subjects. It is both a **process** and a **procedure**.

The **process** of informed consent takes place in the professional interaction between research or clinical staff and individual enrollees.

The **procedure** of informed consent includes the shaping and **signing** of an informed consent document. It is not appropriate that such documents be “templates.” By their very nature they have to be shaped individually each time for each unique situation and population.

Who are the key players in the informed consent process?

- Investigators
 - Research participants
- Ethics review committees

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Both the process and procedures of informed consent always must include the following key characteristics:

Information

Comprehension

Voluntariness

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(cont'd)

Information: Informed consent must provide clear information regarding the research study, location, procedures to be followed, potential risks, possible benefits, duration of the study, alternatives, confidentiality provisions, contact information, and assurance of freedom to withdraw without penalty.

Informed vs Educated

Standards of disclosure

- Professional standard:
 - the customary information that researchers usually provide
- The reasonable person standard:
 - the information that a reasonable person would want to have to make a decision
- The individual standard:
 - the information the particular individual participant wants

INFORMED CONSENT

(cont'd)

Comprehension: Informed consent must be obtained in a way that is intelligent, rational and with sensitivity to the maturity of participants.

Consent documents must be written in the natural language of enrollees, and in a way that is non-technical/non-scientific.

The informed consent process and informed consent forms are not for the benefit of the scientist.

They are for the subject!!!

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(cont'd)

Voluntariness: Informed consent must preclude any element - or even the appearance of coercion or undue influence.

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Critical Elements

CFR

The Code of Federal Regulations specifies eight (8) elements required in all informed consent forms and six (6) additional requirements where deemed appropriate.

In some instances, the additional six (6) elements must be used for all greater than minimal risks studies. In other cases, required use of the additional six (6) elements is dependent upon a wide variety of factors. Their use may always be directed by the IRB.

A delineation and understanding of all fourteen (14) elements is extremely important to shape each informed consent document.

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Critical Elements

Basic Elements of Informed Consent

1. A statement that the study involves research, an explanation of the research, and the expected duration of the subject's participation, a description of the procedures to be followed, an identification of any procedures that are experimental

2. A description of any reasonably foreseeable risks or discomforts to the subject

3. A description of any benefits to the subject or to others, which may reasonably be expected from the research

INFORMED CONSENT

Critical Elements

Required Basic Elements of Informed Consent

4. A disclosure of appropriate *alternative procedures* or courses of treatment, if any, that might be advantageous to the subject

5. A statement describing the extent, if any, to which *confidentiality of records* identifying the subject will be maintained

6. For research involving *more than minimal risk*, an explanation as to whether any *compensation and/or medical treatment are available if injury occurs* and, if so, what they consist of, or where further information may be obtained

INFORMED CONSENT

Critical Elements

Required Basic Elements of Informed Consent

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject
8. A statement that participation is voluntary, refusal participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled

INFORMED CONSENT

Critical Elements

Additional Elements of Informed Consent

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are presently unforeseeable
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
3. Additional costs to the subject that may result from participation in the research

INFORMED CONSENT

Critical Elements

Additional Elements of Informed Consent

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject without prejudice to the subject. In all instances where abrupt withdrawal would be hazardous to the subject (e.g, medication regimens which require gradual reduction) appropriate safe discontinuation procedures will be followed and the subject advised
5. A statement that major new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject
6. The approximate number of subjects involved in the study; and the number of subjects planned to be involved at the local research site.

Practical Challenges for Researchers and Ethics Committees

Specific Issues for Implementation.....

Beyond the actual critical elements as found in the regulations

Specific Points for Implementation

- Know and understand the Context
 - Training of research teams
 - Sensitivity to the needs of research participants
 - Sensitivity to cultural/traditional issues
- Researchers should not over emphasize on potential benefits.
- Need for innovative ways of describing research to participants i.e. use of pictographs, video presentations etc

Specific Points for Implementation

...The informed consent process and informed consent forms must be reviewed carefully to ensure that no element of coercion can be found. This has special meaning when subjects would come from vulnerable populations or special populations such as the military.

...Multicenter studies requiring multiple full IRB reviews are challenging. Some centers require informed consent forms that still contain language and ideation too technical. To avoid “IRB Gridlock,” supplement such informed consent documents with very detailed informed consent process narratives that “bridge the gap” between what is written and how it will be communicated.

Specific Points for Implementation

(cont'd)

...To ensure that subjects comprehend materials shaped into consent forms, the use of follow-up tests or other measures may be advisable. Researchers need to assess the suitability of enrolling volunteers who exhibit difficulties comprehending procedures, risks and all other aspects of study participation.

...Informed consent forms and processes must be approved. Revisions to consent forms, especially when substantive, require approvals. Only approved forms can be used. Stamps or other formats can be used on documents to indicate approval information and authorizations.

Specific Points for Implementation

(cont'd)

...Informed consent forms for use in international settings have to be translated into the native language of that region. IRB's may require back-translations. Translations and back-translations require signed certification.

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Informed Consent: Socio-Cultural Challenges

Informed Consent Challenges for Developing Countries

- Doctor-patient relationship
- Poverty
 - inducements, how much compensation is too much
- Literacy/Ignorance
- Culture/tradition
 - **Community Consent vs Individual Consent**
 - **Power dynamics (Gender)**
 - Sociocultural influences on comprehension of information, perceptions of risk, and beliefs regarding decisional authority

Informed Consent Challenges for Developing Countries

- Therapeutic misconception
- Religious beliefs- signing/ thumb printing consent forms
- Breach of trust
- Complex concepts which are difficult to explain.

Informed Consent: Cultural Symbol & Totemic Challenge

Cultural anthropology:

- ...Symbols and totems: deep relationship to the identity of a culture & its members
- ...Endemic to communication and the formation of culture.
- ...Most powerful communicators of cultural self-expression.
- ...Symbols: Express and Form
- ...Totem: Welcome and warning

Informed consent:

- ...symbol and totem for the culture of research itself.
- ...expresses and shapes the cultural process
- ...“totemic challenge.”

The Contemporary Research Culture: Absorbing Wider Processes

Culture and Paradigms: An absorbent process

Some of these “absorbed” processes are appropriate,

Some are less than appropriate because they are part of the occupational hazard of life in an information market and a global village.

Some processes, when accepted uncritically, become forms of tyranny that may, if left balanced, erode the integrity of the act of research.

Ethical Imperialism?

The Contemporary Culture: Three Forms of Cultural Tyranny

The Tyranny of Utilitarian Individualism:
“I” VERSUS “Thou!”

The Tyranny of Marketplace Competition:
From Patients to Faceless Metrics

The Tyranny of Anti-Intellectual Industrialism
The Breathing Assembly-Line

Informed Consent as Symbol & Totem: Three Challenges to Cultural Tyranny

Benefiting the Common Good

Retrieving the Human Face of Research

Creating Communities of Inquiry

The

Experience

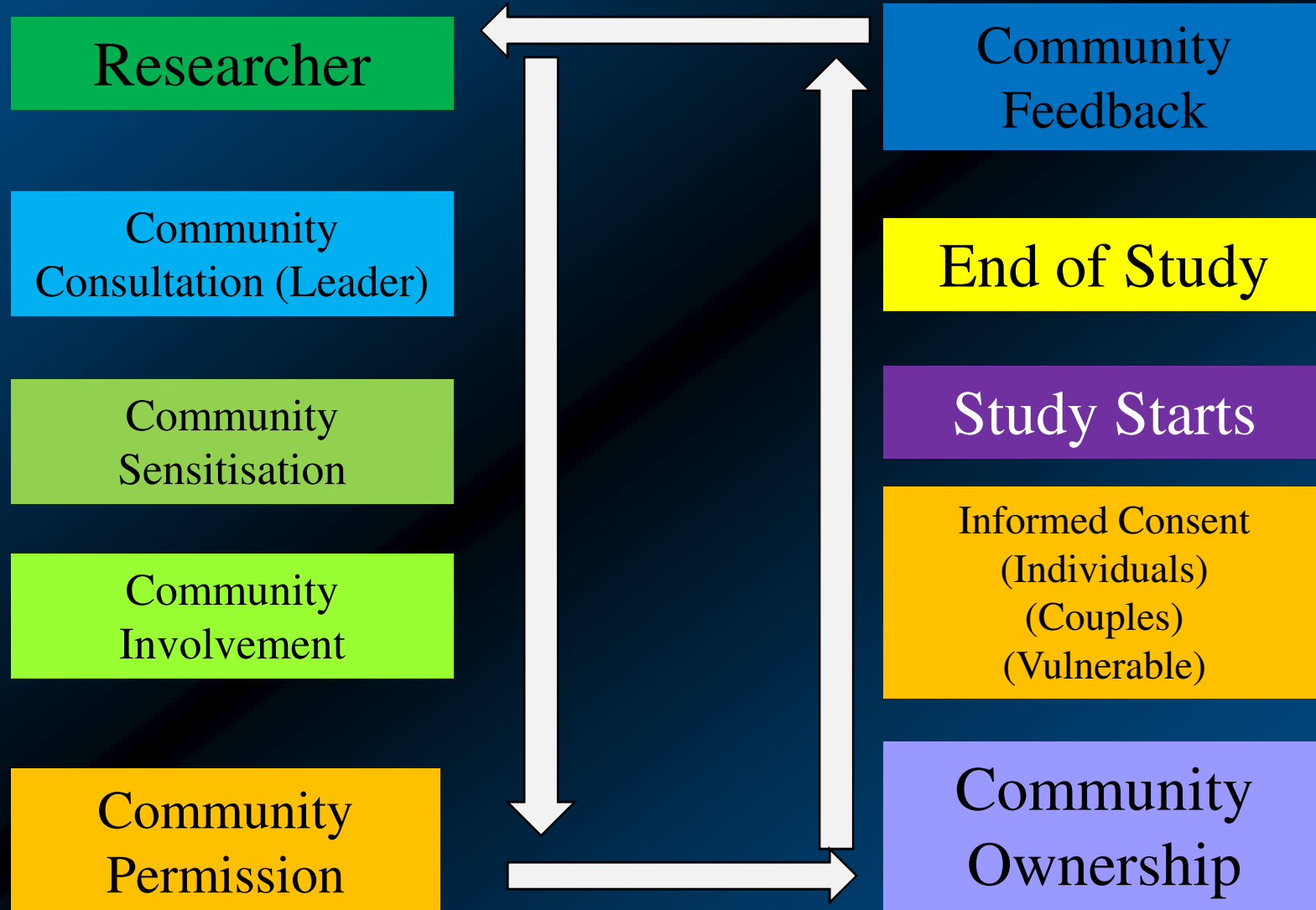
Of

Cultural

Discomfort

Conclusion

Informed Consent & Community Engagement



Conclusion

Remembering the Core

Important to remember why the job needs to be done in the first place: human benefit!!!!

In the end, if research groups have no institutional structures, they lose their skeletons. But if they lose their purpose and charisma, they lose their soul.

What are we choosing now?
What will we choose into the future?

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*Open
Discussion*

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