THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

111 Criteria for Approval #2

Risks to subjects are reasonable….

Belmont Report & 45 CFR 46.111 & 21 CFR 56.111

1)	Risks minimized	Belmont: Respect for Persons & Beneficence
2)	Favorable risk : benefit ratio	Belmont: Respect for Persons & Beneficence
3)	Equitable selection of subjects	Belmont: Justice
4)	Informed consent sought	Belmont: Respect for Persons
5)	Informed consent documented	Belmont: Respect for Persons
6)	Monitoring plan for safety	Belmont: Beneficence
7)	Privacy & confidentiality protected	Belmont: Respect for Persons
8)	Additional safeguards for vulnerable populations	Belmont: Respect for Persons, Beneficence & Justice

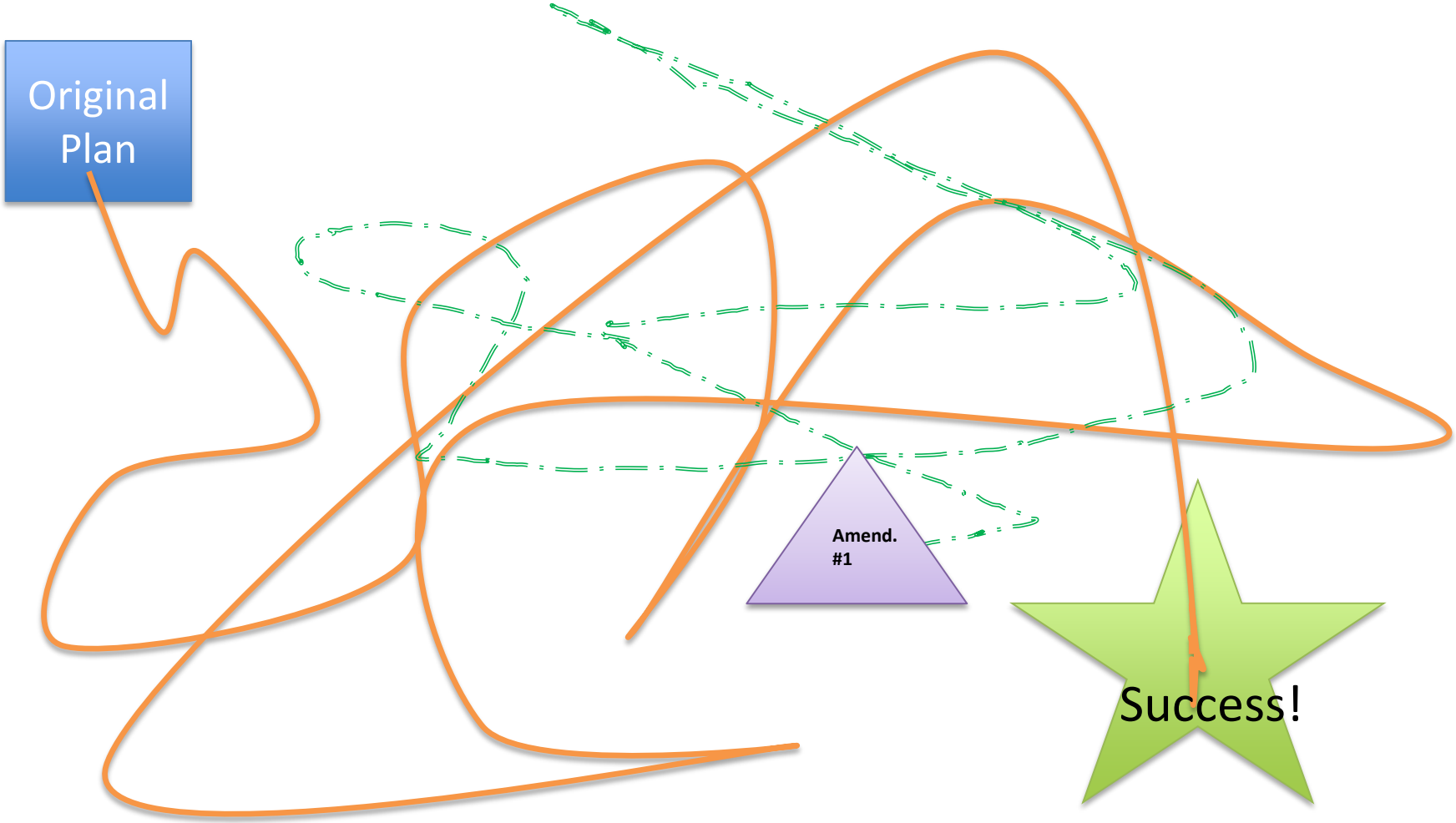
§46.111 & §56.111 (2)

Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

In evaluating risks and benefits, the IRB should consider **only those risks and benefits that may result from the research** (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).

The ***IRB should not consider*** possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

Research path, kinda like raising children!



Criteria 2: Most challenging of the list!

Risk for sick & healthy children? Well Child standard.

Cat 9?

SAE?

Benefits? What? To Whom?

How many parental signatures?

CAPA: Y/N?

Which Vulnerable Group?

Why?

Really??

IRB Makes a Risk Determination or Assessment When You Vote to …..

- Approve a study (& it's design); protocol amendment; waiver of consent element(s) or documentation & every Cat 9
- Decide the child research risk level -- 404, 405 which requires 1 parent signature or 406 which requires both parents' signature*
- Decide if an event is a serious, a serious adverse event, a UPIRTSO, non-compliance, serious non-compliance, continuing serious non-compliance
- If the Corrective Action Plan (CAPA) is appropriate to prevent renewed risk to subjects

**Unless 1 parent is deceased, unknown, incompetent, not reasonably available, or only 1 parent has legal custody.*

So, how?

- Can the end justify the means?
  - Nuremburg Declaration & Belmont say NO!
- If not, where are the boundaries?
- What do the regulations say?
- What clues & guidance does OHRP give us?

What the Regulations say about:
Minimal Risk (see expedited review standard)

- *45 CFR 46.102(i)* defines minimal risk as: "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.*"
- Well-child exam or healthy adult exam
- ***The IRB makes the determination of risk level.***
- **45 CFR 46.101.b.2.I & ii:** any disclosure of the human subjects' responses outside the research could ***reasonably*** place the subjects at risk of **criminal** or **civil liability** or be damaging to the subjects' **financial standing**, **employability**, or **reputation**."

Kinds of Risks

- **Physical** (e.g. pain, drug side effects, or injury)
- **Psychological** (e.g. emotional distress)
- **Social** (e.g. stigmatization)
- **Economic** (e.g. loss of job—breach of confidentiality that relates to stigma, or workplace competency issues or employability)
- **Legal** (requirements to report some illegal activities, whether the focus of the study, or which emerge without prompting)

Belmont Guidance

- Nature & Scope of Risks & Benefits
- The Systemic Assessment of Risks & Benefits
- Assessment of the justifiability of research:
  1. Brutal or inhumane treatment of subject never morally justified
  2. Risks should be reduced to those necessary to achieve the research objective. What alternatives are available?
  3. If there is significant risk, IRB should insist on justification from PI
  4. If there are vulnerable populations in the research, must have justification for their inclusion
  5. Risks & benefits must be thoroughly included in communications & consent.

§46.111 & §56.111 (2)

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The ***IRB should not consider*** possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

Key Words

- Reasonable → Benefits
- Reasonability → Results, data, knowledge
- Limit risks to those of the research ONLY, not treatment
- Can not consider any potential long-range possible policy applications.
- Benefit is not any renumerations offered,
- Can research be done without inclusion of vulnerable populations?