
# 111 Criteria for Approval #1

## Risks to subjects are minimized


APRIL 22, 2002
Powell's Mission Impossible
TIME
HOW MEDICAL TESTING HAS TURNED MILLIONS OF US INTO...
HUMAN GUINEA PIGS
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# *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

***(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:***

(i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and

(ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

# Sound research design

"Research design is the general plan for testing a specific hypothesis and obtaining results. A primary ethical consideration of research design is its scientific merit. Ethical research design also must be scientifically sound. ***It would be unethical to subject participants to risk, inconvenience, or discomfort if the research design is flawed and cannot yield valid results."***

**Presidential Commission for the Study of Bioethical Issues**

**Last Update: September 30, 2016**

# Moral Science: Protecting Participants in Human Subjects Research

**Recommendation 12:** Ensure Ethical Study Design for Control Trials

When assessing how to reconcile the requirements of rigorous study design with the interests of research subjects, a nuanced approach is recommended that permits subjects to receive a placebo or an active agent that otherwise might not represent the "best-proven" approach when the site selected is ethically justifiable and the following conditions are met:

a) the "best proven" intervention is not known to be the best for a particular population due to local infrastructural, behavioral, genetic, or other relevant circumstances; and

b**) the scientific rationale *and* the ethical justification for the study design have undergone careful review to ensure all of the following:**

***i) use of placebo or other comparators is of limited duration;***

***ii) subjects are carefully monitored;***

***iii) rescue measures are in place should serious symptoms develop; and***

***iv) there are established withdrawal criteria in place for subjects who experience adverse events.***

# Design Issues

1. Is there evidence of through preparation?
2. Is this the best design for this study & population?
3. Does the design allow for the most diverse cohort?
4. Does the consent ***really*** inform?
    1. Any cohersion, renumeriation appropriate, too much jargon, too long, ….

# For Example…

- Relabeling of Ambient to include dosage for women.
- Dangerous heart issues & Vioxx resulting in withdrawal of the drug.
- John Hopkins Asthma trial:  wrong administration of study drug resulted in healthy subject death.

# 111 (a)(2) Requirements
# Risk-Benefit Assessment

Slide from C. Myers

Commonly referred to the "Risk-Benefit Ratio", however a risk-benefit assessment is preferred as risks and benefits are not measured using comparable scales.

- Risk= Measurement in terms of probability or harm
- Benefit=Valued outcome where probability generally can't be measured.

**Risk-Benefit Ratio**


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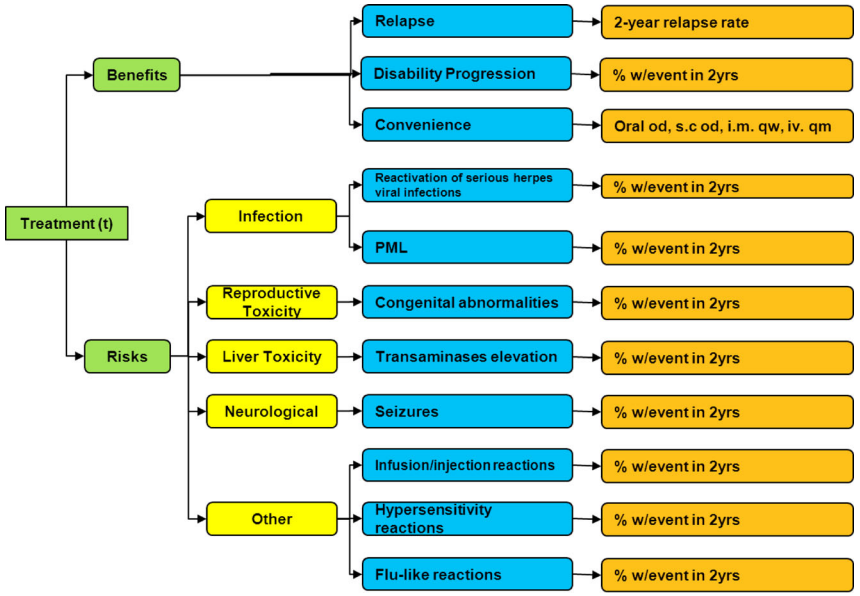
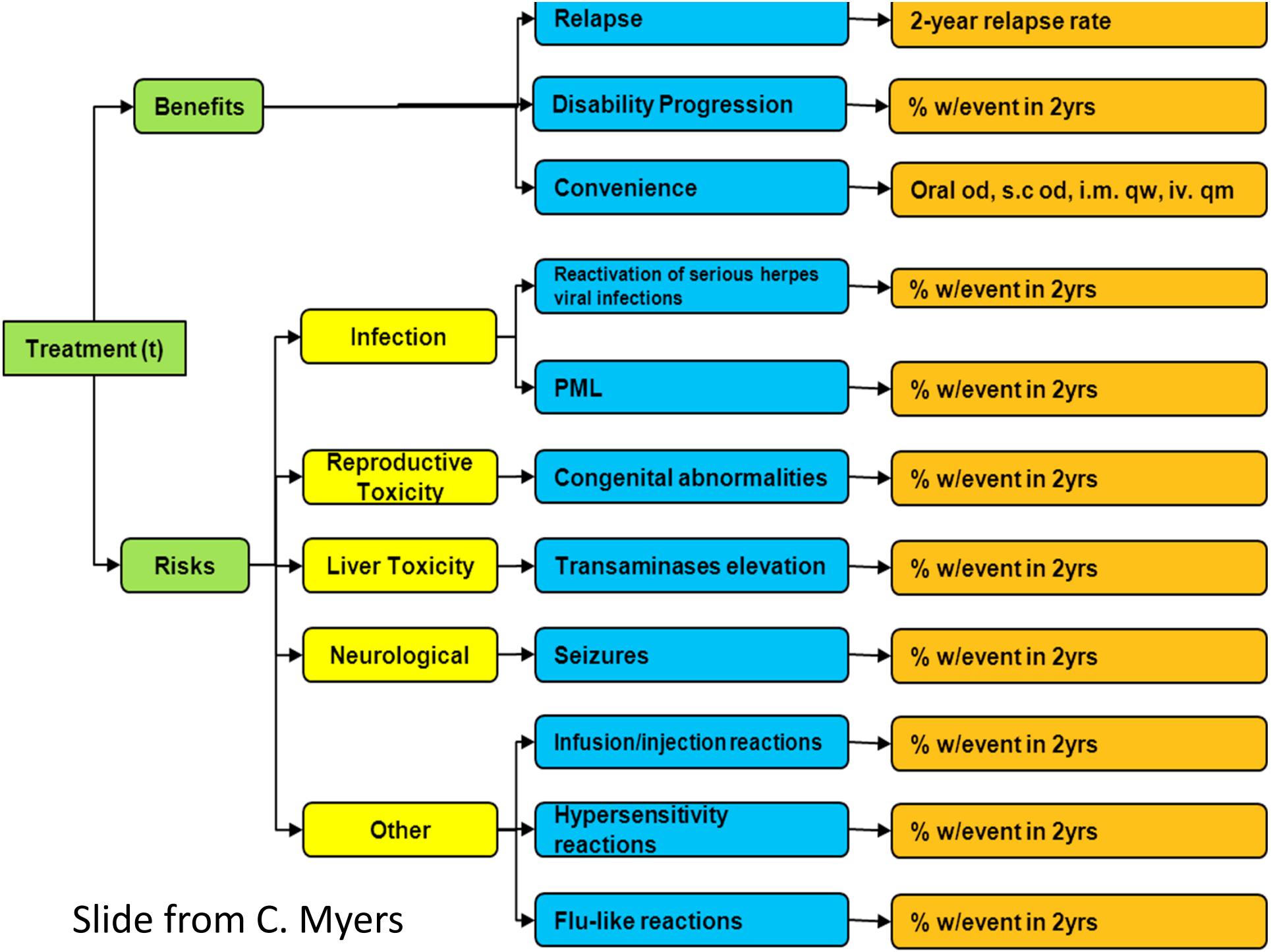
**Risk-Benefit Assessment**






Slide from C. Myers

Presidential Commission for the Study of Biomedical Issues: Research Design: Background September 30, 2016

## A closing note…

"…studies designed to achieve valid & meaningful results justify the risks to which participants are exposed & respect their time & effort."

- protected from avoidable harm & unethical treatment.
- maximize advancement of scientific knowledge & public benefit
- minimize risks to society & the environment."
- undue burden not on any specific group without compensating benefits."