A Bioethical Defense of Bayesian Methods in Drug Development

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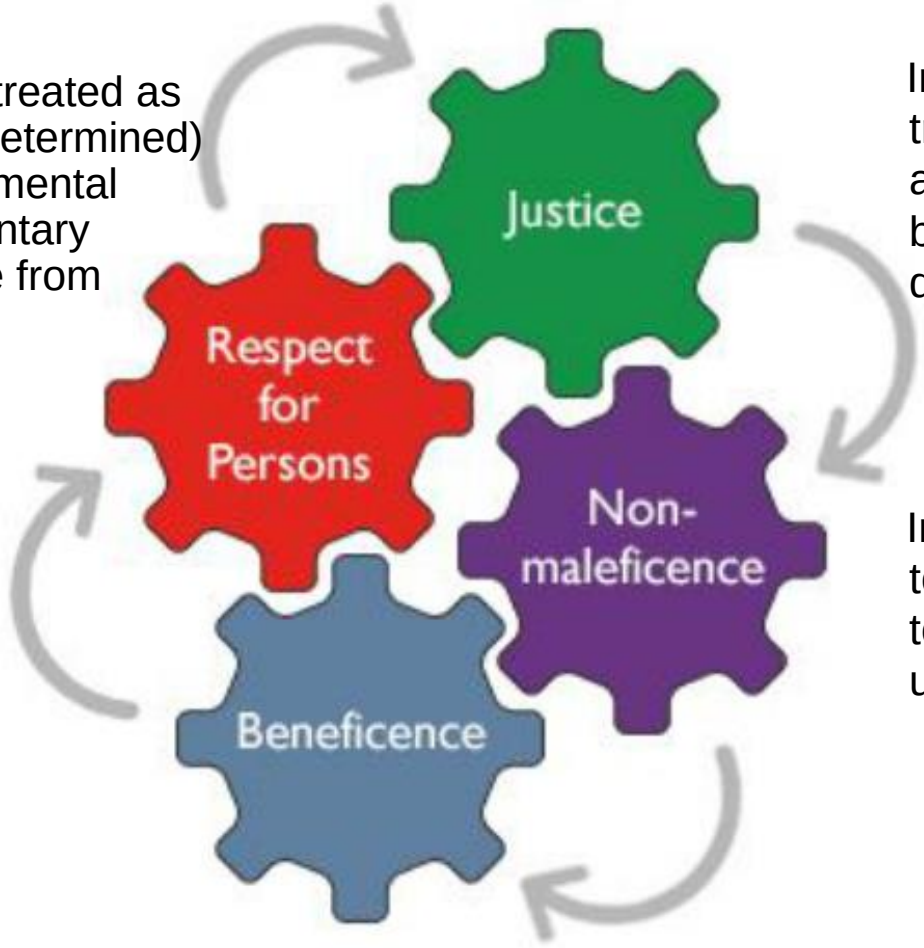
Lilly

4 Principles of Bioethics

Individuals should be treated as autonomous (or self-determined) agents who have the mental capacity to make voluntary decisions that are free from external constraints.

Individuals are obligated to prevent or remove harm and do or promote good; beneficence is the obligation to act for the benefit of others.

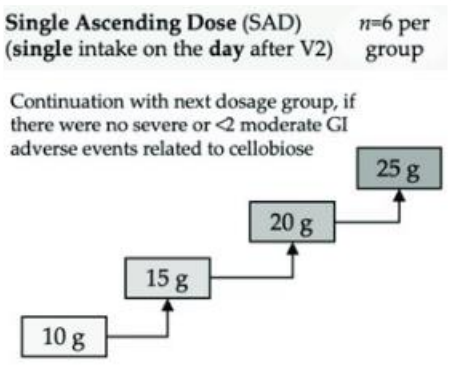


Individuals should be treated fairly, equitably and appropriately based upon what is due or owed to them.

Individuals are obligated to avoid inflicting harm to others or imposing undue risks of harm.

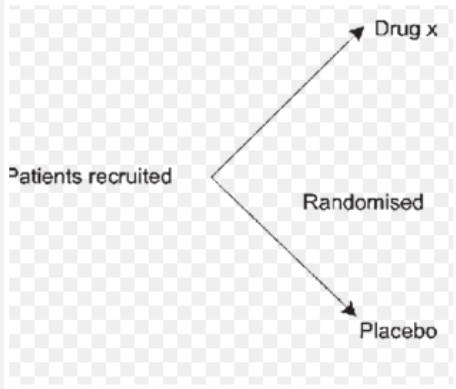
Bioethics & Pediatric Trial Design

PK Study



- Ethical challenge: May pose an unfavorable benefit/risk to pediatric participants if duration is not long enough to have a therapeutic effect.
- Possible solution: Continued access may be necessary to increase potential benefit for children.

Placebo Control



- Ethical challenge: A child randomized to placebo has no prospect of direct benefit from trial participation.
- Possible solution: Placebo arm rollover to treatment (investigational or approved care).

Small “N” Trials

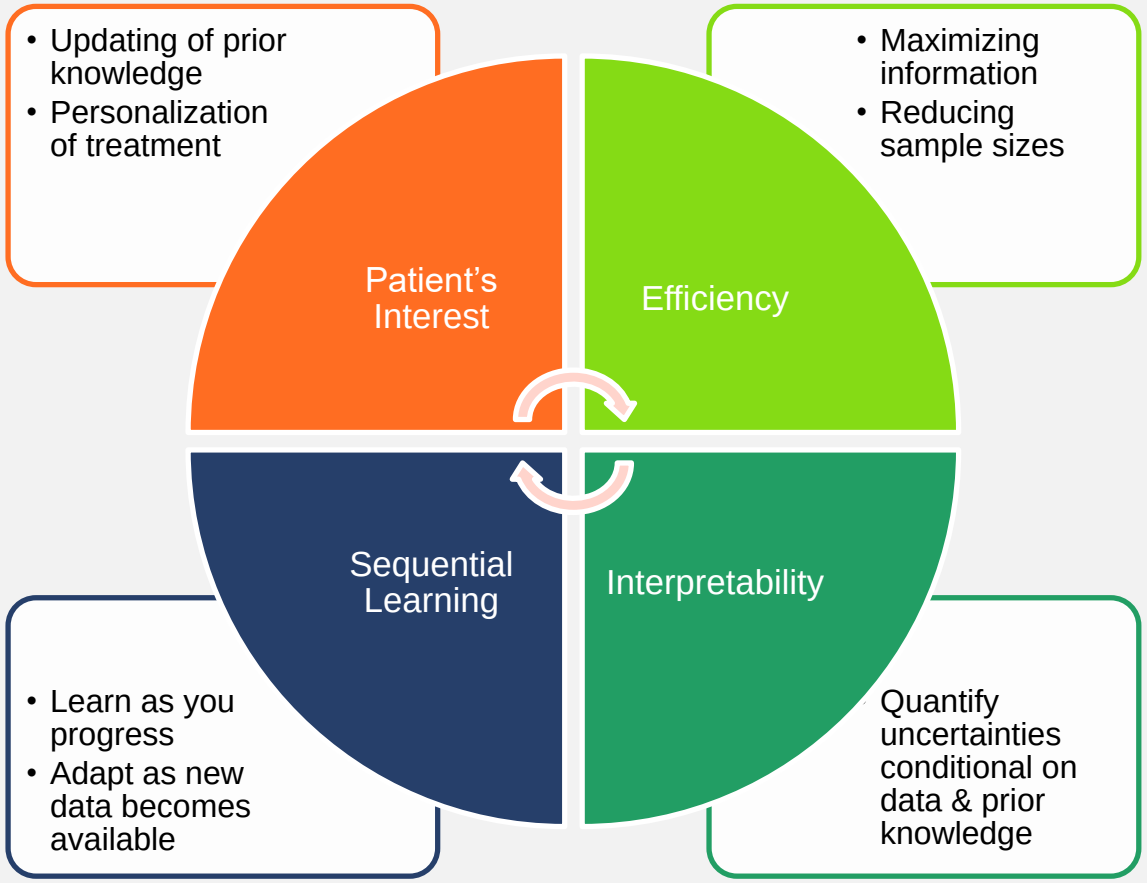
Research should generate sufficient information to provide social value.

Principle of Scientific Necessity implies samples should be kept to the minimum needed to maintain scientific validity.

Timing

- Need sufficient scientific information to justify potential benefit, which may require studies performed in other populations first.
- Waiting too long to initiate trials may encourage off-label use, prolong time kids have fair access to treatments

The Intersection of Bioethics and Bayesian Methods

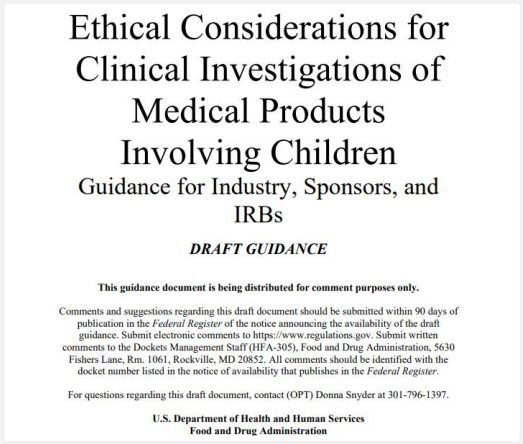


Bayesian approaches may be integral to delivering innovative designs to meet the ethical standards in vulnerable populations.

Proposals for the use of Bayesian methods should include technical, operational and ethical justifications when appropriate (the last of these is largely missing from current examples & guidelines).

Additional References

2019-89-DG- Ethical Considerations for Clinical Investigations of Medical Products Involving Children (9-19-22).docx (fda.gov)



Ethical Considerations for Clinical Investigations of Medical Products Involving Children

Guidance for Industry, Sponsors, and IRBs

DRAFT GUIDANCE

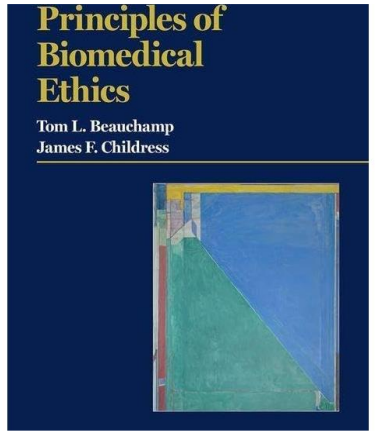
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (OPT) Donna Snyder at 301-796-1397.

U.S. Department of Health and Human Services
Food and Drug Administration

Principles of Biomedical Ethics: 9780190640873: Medicine & Health Science Books @ Amazon.com



Bayesian Methods in Pharmaceutical Research (Chapman & Hall/CRC Biostatistics Series): 9781032241524: Medicine & Health Science Books @ Amazon.com