The History of Human Subjects Regulations and IRBs

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Overview

- A brief history… why do we have rules?
- The Belmont Report
- IRBs

A brief history…

- Ethics & law is highly reactive to seminal events:
  - 1898 Albert Neisser, Breslau – Prussian I/C regulations in 1900
  - 1906 Food & Drug Act – truthful labeling
  - 1930 Lübeck BCG TB Vaccine tragedy – ‘31 German regulations
  - 1938 Elixer of sulfanilamide and FFDCA
  - 1948 Nuremberg Dr’s trial and Code
  - 1954 Wichita Jury Study and state bans
  - 1962 Thalidomide and FFDCA amendment
  - 1964 – 1st WMA Declaration of Helskinki
    - Milgrim experiments
    - Jewish Chronic Disease Hosp. case

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A brief history… continued

- 1966 – Willowbrook hepatitis experiments
  - PHS requirements for IRBs and Informed Consent
  - Henry Beecher's little study (*NEJM* 274:367)
  - Life Mag: "Concentration Camp for Dogs" and AWA
- 1971 Laud Humphries "Tearoom Trade"
- 1972 Stanford Prison Experiment
- 1973 – Rosenhan's psychiatric hospital case (*Science* 179:250)
  - Tuskeegee Syphilis Study revealed and Nat'l Research Act
    - » Created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- 1974 DHHS requirement for IRBs and Informed Consent (FDA and NIH)
- 1976 Dalkon Shield case and Medical Device Amendment of the FFDCA
- 1979 National Commission's **Belmont Report** issued
- 1981 Federal Regulation of Human Subjects Research (now Common Rule)
- 1985 Penn head trauma & Edward Taub cases - AWA amended, IACUCs
- Late 1990s OPRR shutdowns and Gelsinger - increased attention to IRBs

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The Belmont Report (1979)

- "a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects"

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  - Respect for Persons - "first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection."; Informed Consent

  - Beneficence - "(1) do no harm and (2) maximize possible benefits and minimize possible harms"

  - Justice - treating people fairly (equally); selection of subjects should avoid exploitation: "simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied"; and "research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research"

- Discusses IRB decision-making and Informed Consent

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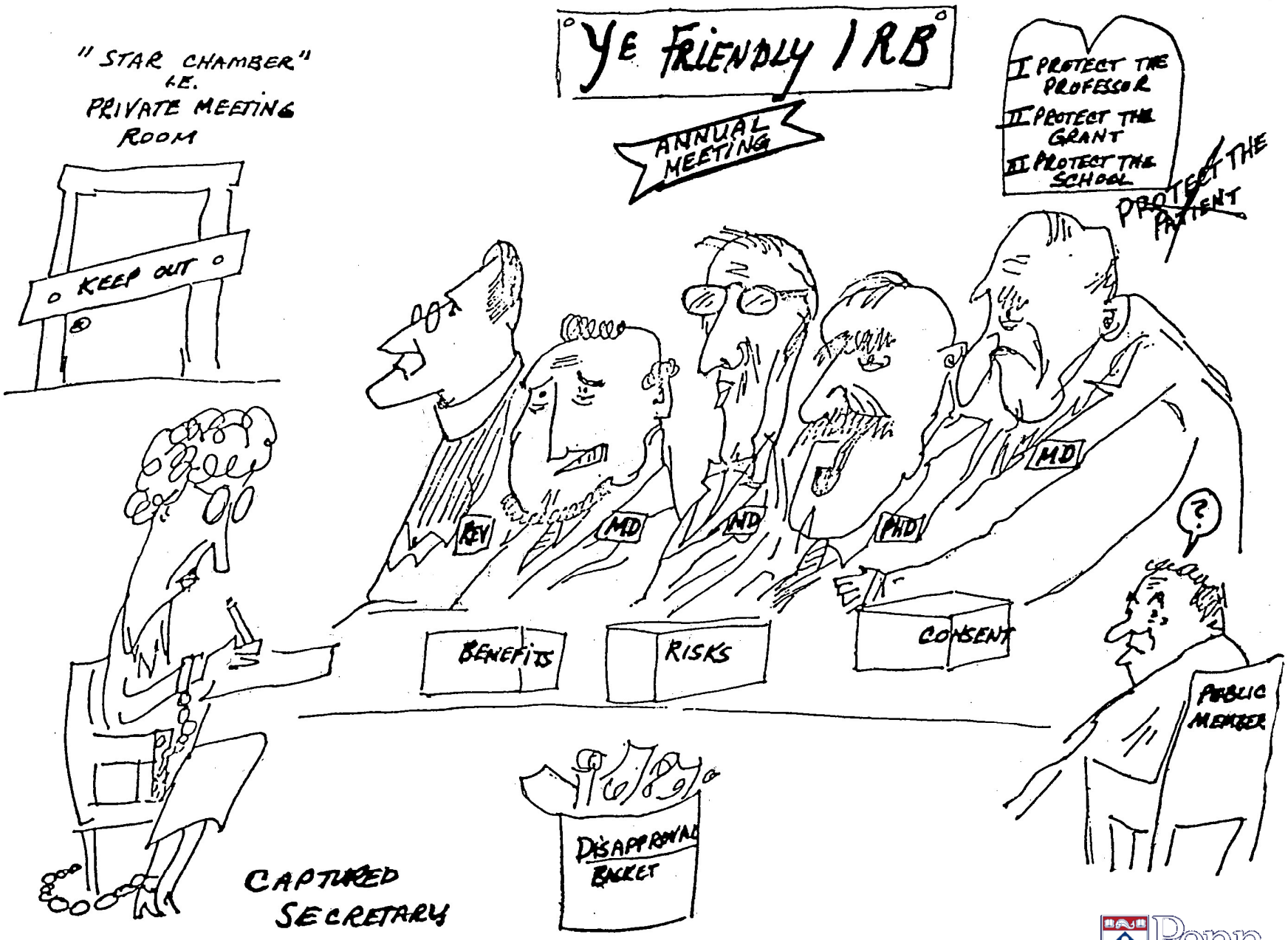

Source: Al Jonsen circa 1977

What are IRBs Supposed to do?

- The Common Rule (45 CFR 46.111) requires the IRB to:
  - *Minimize risks* to subjects
  - Assure that *risks to Ss are outweighed by potential benefits* to Ss and others and the importance of the knowledge to be gained
  - Assure that *potential subjects are adequately informed* and are asked to consent in ways that ensures *their choices are free from coercion or undue influences*
  - Assure that subjects are *selected fairly*
  - Take other measures necessary to *protect vulnerable populations*

- These requirements map directly onto the Belmont "principles"

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What do we know...?

- IRBs tend to be hyper conservative (e.g., HIPAA; over-review)
- Overworked (or under-resourced), causing delays
- Inconsistent/arbitrary – high variation across IRBs
- Members suffer a lack of knowledge (turnover, inconsistent training)
- IRBs suffer from a research and institutional bias / CoI
- IRBs sometimes assume their role is to protect the institution
- IRBs fail their paternal role of protecting subject *welfare*
  - poor risk/potential benefit decision-making
  - more risk averse than investigators
- IRBs focus efforts on upholding *rights*
  - spend most of their effort on consent forms
  - not on the *process* of consent (who, how, when)
  - IRBs often make CFs more complex
    - completeness trumps clarity

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