Ethical and regulatory issues in conducting research involving pediatric bioemergencies

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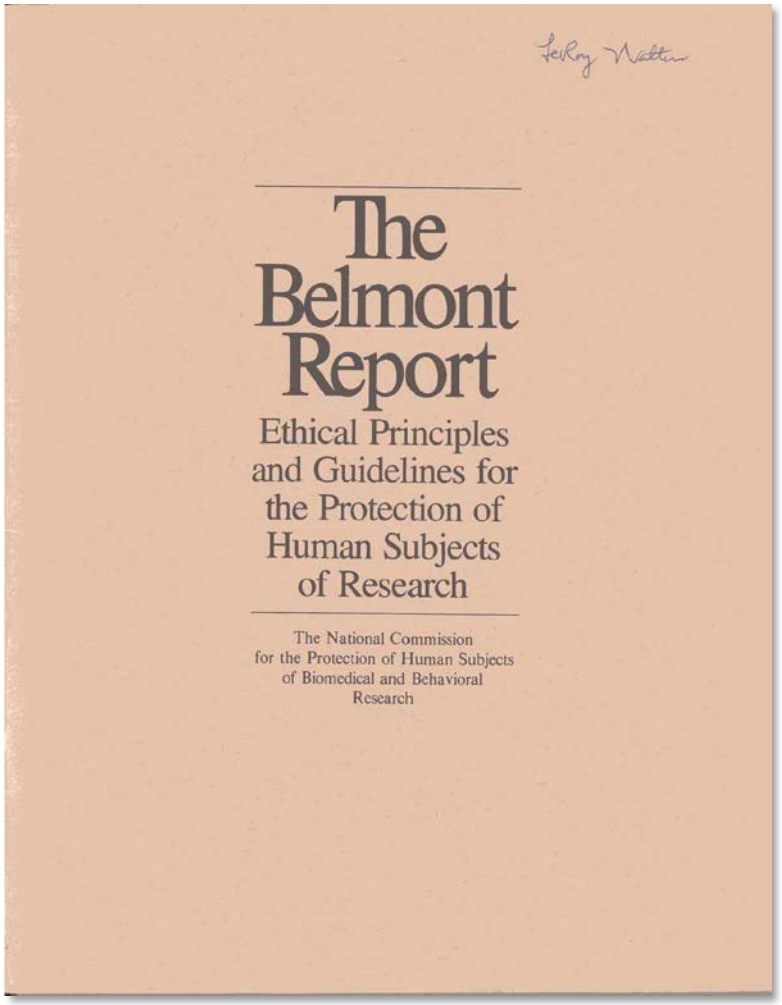
Disclosures

- I have no relevant personal, professional or financial relationships with respect to this educational activity

"The patient in the next bed is highly infectious. Thank God for these curtains."

Belmont Report (1979)



- three basic ethical principles that should govern human subject research:
  - respect for persons
  - beneficence
  - justice

Criteria for approval of research
(45 CFR 46.111 and 21 CFR 56.111)

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent is sought from each subject
- Informed consent is documented
- Adequate provisions for monitoring data to ensure safety
- Adequate provisions to protect the privacy of subjects and the confidentiality of data
- Additional safeguards for vulnerable subjects

What are the ethical challenges arising when conducting human subject research during a bioemergency?

- Informed consent
- Confidentiality/privacy
- Fair subject selection
- Risk/benefit of use of untested interventions
- Scientific validity and study design
- Independent review
- …

Independent Review

- Multiple jurisdictions (or multiple countries)
- Inadequate review infrastructure
- Review infrastructure affected by bioemergency
- Pressure for approval may compromise independence of review
- Time constraints

Independent Review

- Ethics / regulatory review options
  - Pre-review
    - research ethics committee of MSF pre-approves some generic research protocols
  - Local Rapid Response IRBs
    - UNMC RR-IRB
  - Central (single) IRB
    - Public Health Emergency Research Review Board (PHERRB)
    - Consortium IRBs (NETEC SPRN sIRB)

Local Rapid Response IRBs

- UNMC RR-IRB approach
  - Small IRB, many alternate members
  - Extensive collaboration with the investigator
    - thorough pre-review
    - investigator present at meeting to answer questions, respond to IRB conditions
  - Non-linear workflow
    - concurrent ancillary committee reviews
    - review of draft documents by RR-IRB members

Local Rapid Response IRBs

- UNMC RR-IRB approach
  - IRB uses a familiar, standard review paradigm
    - not different from other early phase studies in ill subjects

Independent Review

- Ethics / regulatory review options
  - Pre-review
    - research ethics committee of Médecins Sans Frontières pre-approves some generic research protocols
  - Local Rapid Response IRBs
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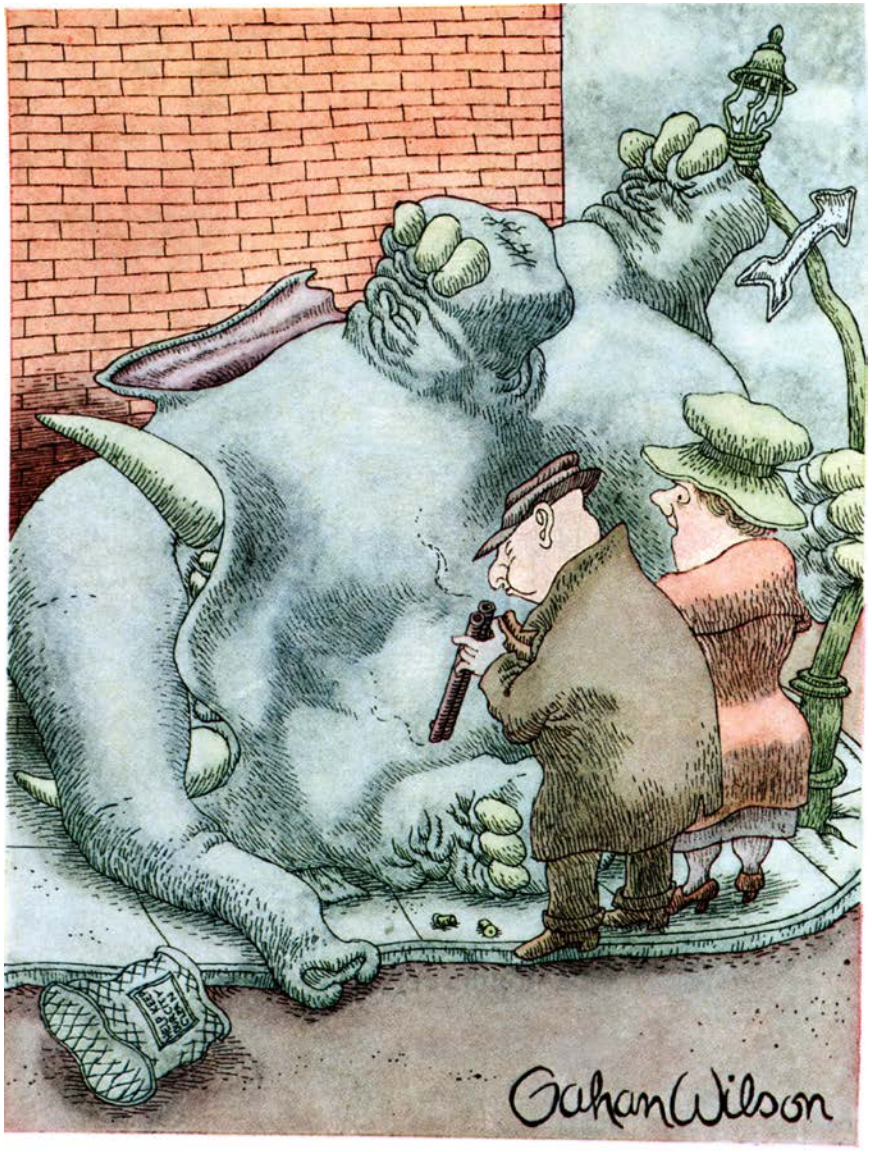
NETEC SPRN RR-sIRB

- Follows the model of the RR-IRB
  - small IRB, many alternate members
  - extensive collaboration with investigator
- Development required close collaboration with other components of the HRPP and with external partners (NETEC SPRN)

- Advanced preparation and practice are crucial



"Honestly, Harry, I'll never tease you again for carrying around that elephant gun!"

Conclusions

- Research must satisfy regulatory criteria for approval by IRB
- Research during a bio-emergency faces additional ethical challenges (related to informed consent, confidentiality/privacy, fair subject selection, risk/benefit, scientific validity, independent review, and others)
- Various models exist for rapid review in the face of a bio-emergency, but preparation is critical