

Protecting Human Research Subjects

- What Is An Acceptable Literature Search For A Medical Research Proposal?

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Outline

- Research ethics in biomedicine
- The Johns Hopkins case
- Agenda for action

Research ethics in biomedicine (1)

- research involving human subjects requires approval on ethical and scientific grounds
- most countries have legal requirement for official bodies to evaluate research applications (Research Ethics Committees, Institutional Review Boards, &c)

Research ethics in biomedicine (2)

- applicant must show evidence that previous literature justifies further research on scientific grounds
- applicant must provide risk assessment for research participants, based on previous literature

Research ethics in biomedicine (3)

- ethics committee members assess application using their own expertise
- no official criteria for assessing validity of literature search

Johns Hopkins (1)

- research into asthma attacks
- healthy volunteer (Ellen Roche) died in June 2001 after inhaling hexamethonium administered during research project
- all JH research on human subjects halted pending investigation
- internal and external inquiries

Johns Hopkins (2)

- Principal Investigator's research proposal cited 4 articles
- internal inquiry reported that the JH Institutional Review Board "did not conduct an independent search of the literature, as it relied on the information supplied by the investigator, who was known to them as an experienced researcher"

Johns Hopkins (3)

- internal inquiry found 12 articles published between 1953 and 1960 that linked hexamethonium with pulmonary toxicity
- ... and a 1972 review article that listed 6 of these 12
- ...AND learned of *unpublished* evidence of possible pulmonary complications found in a 1978 research project in San Francisco

Johns Hopkins (4)

- the Principal Investigator stated that "he had performed a standard PubMed search...and consulted standard, current edition textbooks"
- the inquiry accepted that the PI had "made a good-faith effort to uncover previous reports of hexamethonium-related pulmonary toxicity"

Johns Hopkins (5)

- JH response: "committed to the development of a standard ... to determine that a literature search ... is both adequate and comprehensive"
- investigators required to "collaborate with a librarian and a pharmacist to strengthen literature searches..."

Johns Hopkins (6)

- new JH literature searching standards:
see "JHU SOM IRB guidelines for literature searches (revised 4/2002)"
- <http://www.hopkinsmedicine.org/irb/jcci>
- (follow link to "Literature Search of Drug Safety...")

Agenda for action (1)

- involve the library in the research review process
 - researcher to supply literature search strategy with project application
 - librarian to approve (or remedy) the strategy
 - librarian to run repeat searches during the project

Agenda for action (2)

- improve researchers' search skills
 - provide literature search guidelines
 - provide literature search training
 - "certification" of search skills (compulsory?)

Agenda for action (3)

- encourage researchers to publish negative results (remember the unpublished 1978 San Francisco project)
- make the case for more resources
 - bibliographic databases
 - retention of, or access to, older material
 - training facilities and opportunities
 - your organisation runs risk of litigation

Keep a sense of proportion

- one adverse event at JH is not a strong evidence base
- knowledge of the earlier literature would have changed the risk assessment but probably not the IRB's approval decision
- other factors contributed to the volunteer's death

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