Beyond the Ice Bucket Challenge: The Ethics of Early Release of Experimental Drugs

Margie Hodges Shaw, J.D., Ph.D.

Division of Medical Humanities & Bioethics

2015

MEDICINE *of* THE HIGHEST ORDER

UNIVERSITY *of* ROCHESTER MEDICAL CENTER

COIs, Disclosures and Disclaimers

- I am conflicted about many things, including some of the content in this presentation.
  - These interesting conflicts exist in my mind and do not involve relationships with industry.
- I work in the Division of Medical Humanities & Bioethics
- Disclaimer: Nothing in this presentation should be considered legal advice. I am originally from Georgia and will not use subtitles, listen carefully.

Acknowledgements

- Faculty in the Division of Medical Humanities & Bioethics
  - Stephanie Brown Clark
  - Rich Demme
  - Bernie Sussman
  - Richard Dees
  - Marianne Chiaffery
  - Patrick Hopkins
  - Carl D'Angio
  - David Kaufman
  - Susie Diass
  - Clayton Baker
- Everyone else, including Kelly Unsworth, Tracy Cherry, and especially Brian Shaw

#ALSIceBucketChallenge

Amazon CEO Jeff Bezos: ©amazon/YouTube

Narrative Structure

- Introduction and the role of perspective
  - Place
  - Person
  - Time
    - Before 1900
    - 1900-2000
    - 2000-2015
    - 2015-

Perspective frames how one approaches the ethical issues in early release for individual use

The US Constitution, 1787

"The powers not delegated to the United States by the Constitution, nor prohibited by it to the states, are reserved to the States respectively, or to the people."

Rights

- American Constitutional History
  - The Bill of Rights, 1791
- Natural Rights/Human Rights
- Legal Rights
  - Negative (limits on what can do)
  - Positive (requirements to do)

Is There an Ethical Imperative to Increase Access to Experimental Therapies?

What are the ethical considerations when considering whether to implement laws, policies, and/or regulatory amendments?

The Characters

Patient

Research subject

Family

Members of treating team

Members of research team

Drug sponsor

Everyone else/society

Governments (legislative, judicial, executive)

The Patient and Family

The Research Subject

http://www.heatherkirkwood.com

The Treating Team and the Nature of Health Care

The Research Team and the Nature of Research

The Drug Sponsor

Mission Statement

"Our aspiration is to make great things happen. With our research-driven specialty businesses, we help patients, customers, partners and our communities around the world to live a better life…."

Everyone Else

The Setting: Before 1900

Observation

Lithography depicting the inoculation of James Phipps

By Gaston Mélingue

(circa 1894)

Experimentation

June 6, 1822

Beaumont tended gunshot wound on Alexis St. Martin

Beaumont and St. Martin

By Dean Cornewell, (circa 1938)

Drug Sponsor

Publication of almanacs to advertise products

Began in 1843 when C.C. Bristol of Buffalo, NY published almanac to advertise Extract of Sarsaparilla

http://www.nlm.nih.gov/hmd/index.html

The Patient and Family

Self-portrait with Dr. Arrieta

Francisco Goya

Painted in 1820

"Goya, in gratitude to his friend Arrieta: for the compassion and care with which he saved his life during the acute and dangerous illness he suffered towards the end of the year 1819 in his seventy-third year."

The Setting: 1900 - 2000

Hazards of the Marketplace

1906: The Pure Food and Drug Act

- Prohibited interstate commerce in adulterated and misbranded food and drugs
- Administered by Bureau of Chemistry

Hazards of the Marketplace

1937: US Food, Drug, and Cosmetic Act

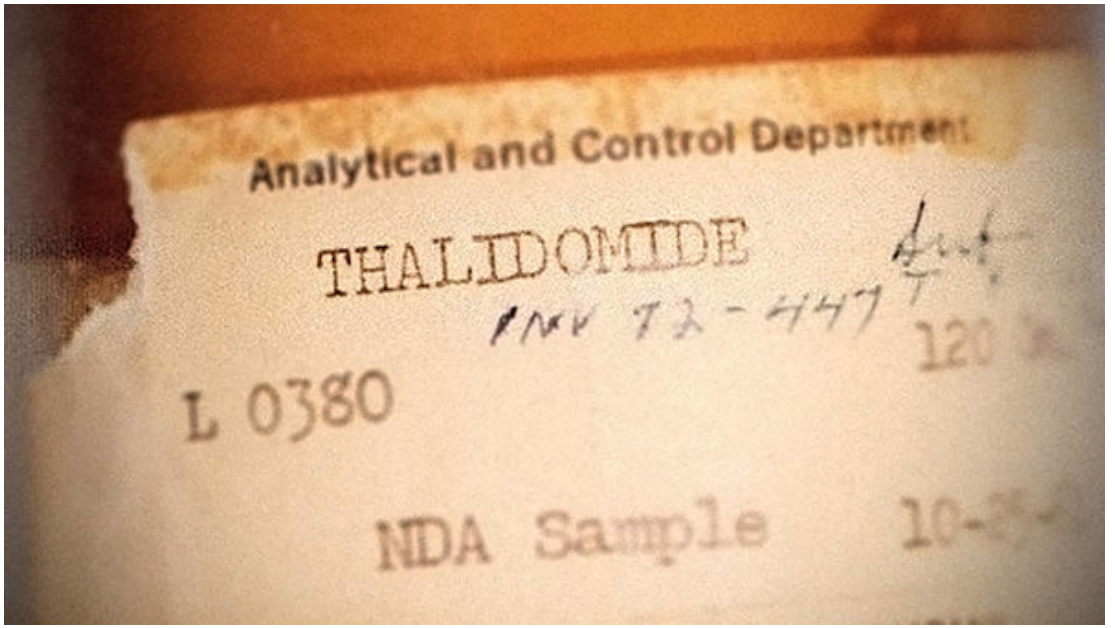
- Required premarket safety evaluations
- Pre-clinical trial review
- Clinical trial review

Elixir Sulfanilamide

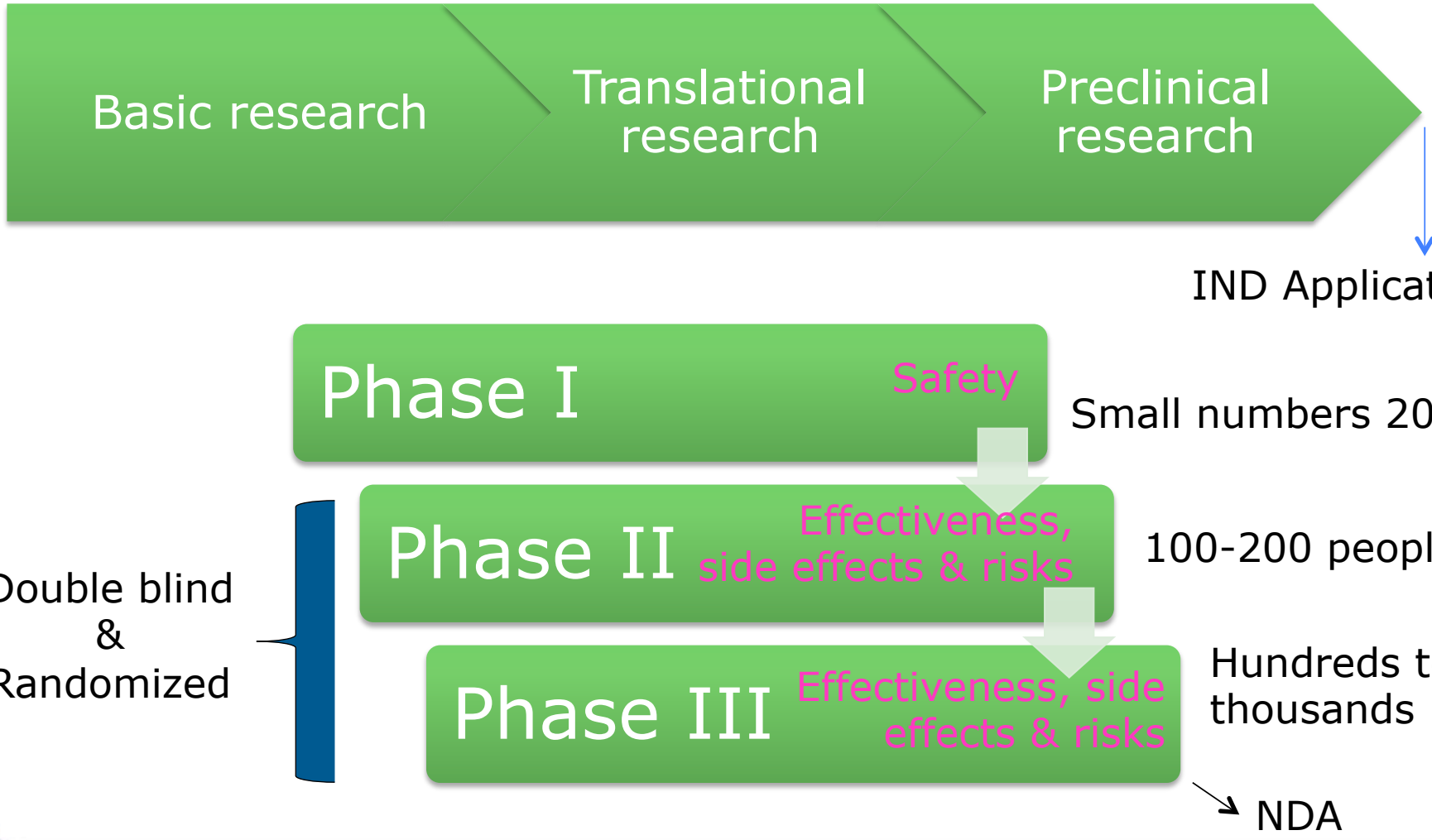
Hazards of the Marketplace

1962: US Food, Drug, and Cosmetic Act

Required proof of safety and effectiveness in intended use



Clinical Research



Compassionate IND

This allowed patients to request FDA permission to use promising, but unapproved drugs.

Some patients did gain access to beta-blockers and calcium blockers, but this process is not, retrospectively, viewed as successful.

United States v. Rutherford

442 U.S. 544 (1979).

The question presented in this case is whether the Federal Food, Drug, and Cosmetic Act precludes terminally ill cancer patients from obtaining Laetrile, a drug not recognized as "safe and effective" within the meaning of § 201 (p) (1) of the Act, 52 Stat. 1041, as amended, 21 U. S. C. § 321 (p) (1).

AIDS Activism Resulted in New FDA Regulations

FDA created Treatment IND in 1987 to "facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible."

1) serious or life threatening

2) "no comparable or satisfactory alternative"

3) drug currently in clinical control trial (or through)

4) sponsor must be "actively pursuing marketing approval"

The Setting: 2000-2015

Abigail Burroughs

March 2001

- No more conventional therapy
- Launched campaign for access
  - Lobbied 2 pharm companies
  - Solicited Congressional help
  - Initiated media campaign

"there is no fundamental right . . . to experimental drugs for the terminally ill."

Abigail Alliance v. von Eschenbach, 495 F.3d 695 (D.C. Cir. 2007).

Activism (Again) Resulted in New FDA Regulations

During the Abigail Alliance litigation, the FDA began drafting new expanded access regulation.

FDA "clarified" existing regulations by creating 3 explicit levels of access

- Individual, intermediate, expanded

The Setting: 2015 -

Social Media: The New Activism

#SaveJosh

#4Nathalie

#kickasps

Keep Up the Fight Justin

Darlene Gant video

Mikaela Knapp

Danielle Grimbilas (for brother Bryan Cadigan)

Darcy Doherty

Change.org

MyTomorrows.com

First, Return to Principles

The Principle of Autonomy

- Patients have the right to make decisions about their own bodies

The Principle of Beneficence

- The action should help the patient (consistent with the patient's values)

The Principle Non-Maleficence

- The action should not harm the patient

The Principle of Justice

- The process and allocation of resources are fair

FDA Responds to Public Advocacy, February 2015

Dr. Peter Lurie,
Associate FDA Commissioner

Individual Patient Expanded Access Applications: Form FDA 3926

- 45 minutes to complete (compared to 100 hours)

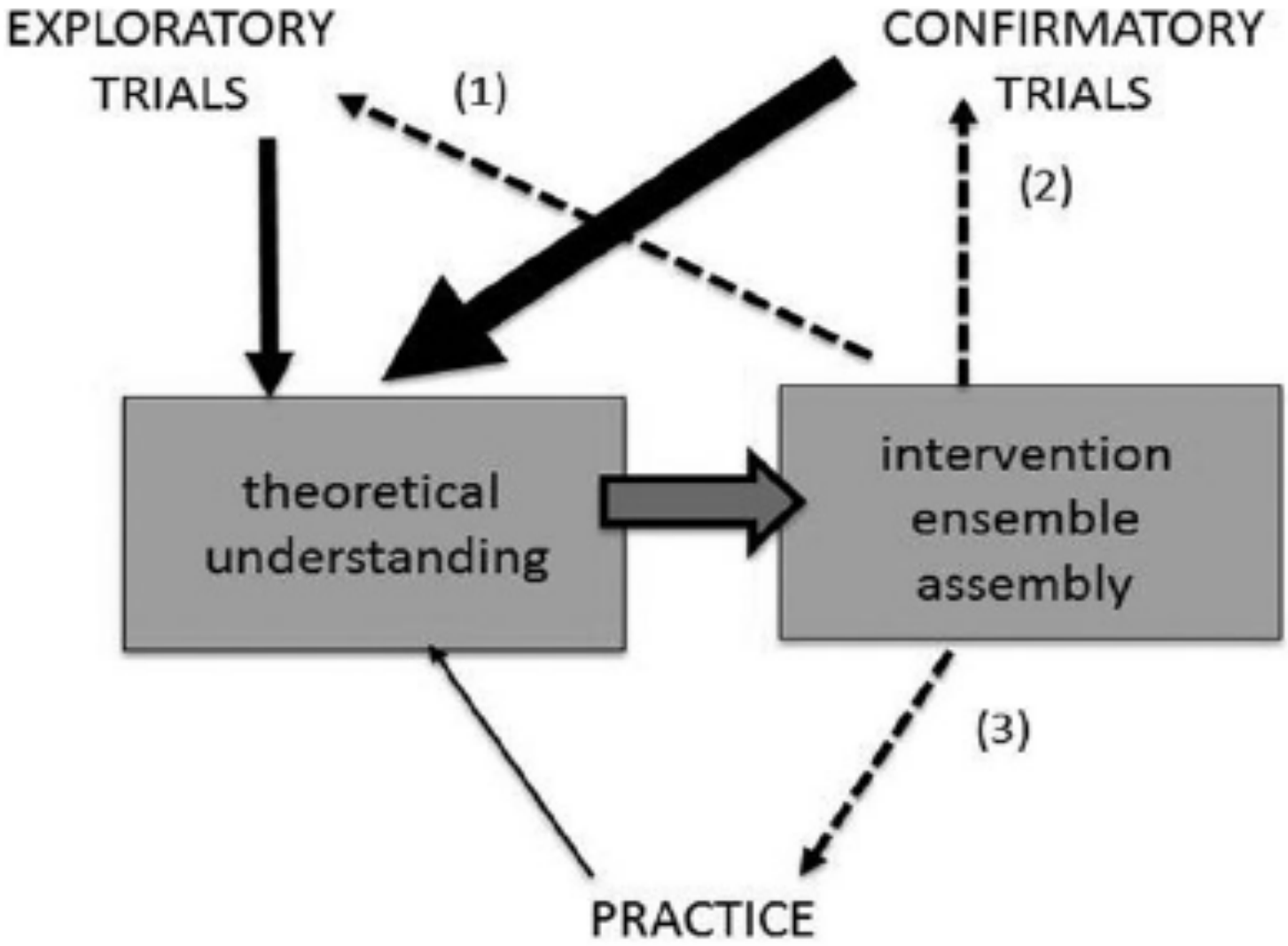
Company Creates Bioethics Panel on Trial Drugs

Art L. Caplan
Richard Perry/
The New York Times

By Katie Thomas - May 7, 2015

Johnson & Johnson has appointed a nationally known bioethicist to create a panel that will make decisions about patients' requests for lifesaving medicine, responding to an emotional debate over whether companies should allow desperately ill people to have access to the drugs before they are approved.

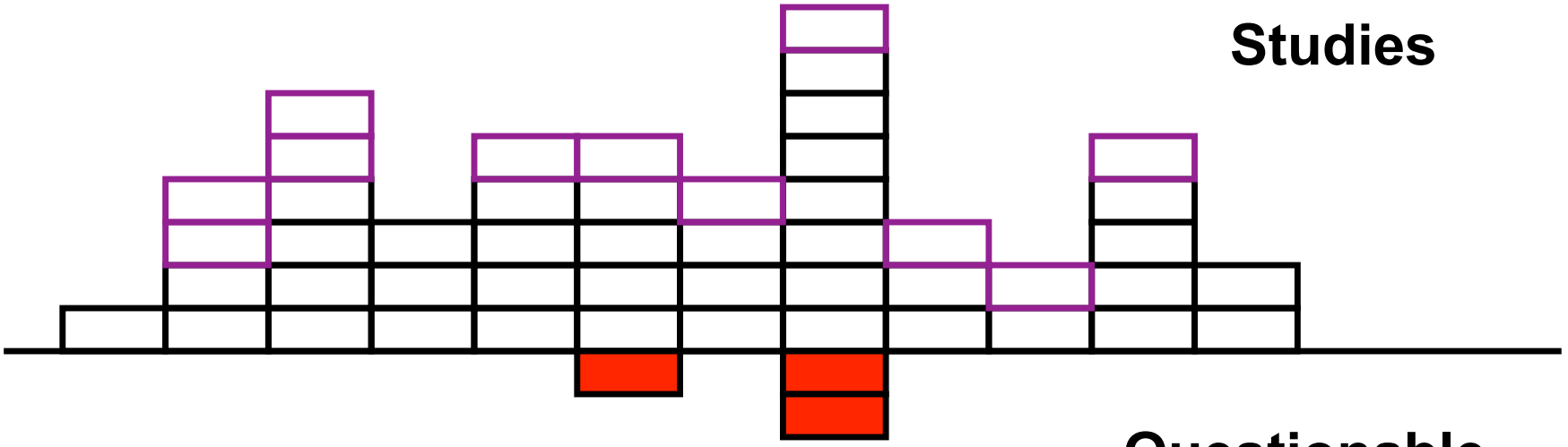
http://www.nytimes.com/2015/05/07/business/company-creates-bioethics-panel-on-trial-drugs.html



Jonathan Kimmelman and Alex John London, "The Structure of Clinical Translation: Efficiency, Information, and Ethics," *Hastings Center Report* 45 (2015): 1–7. DOI: 10.1002/hast.433

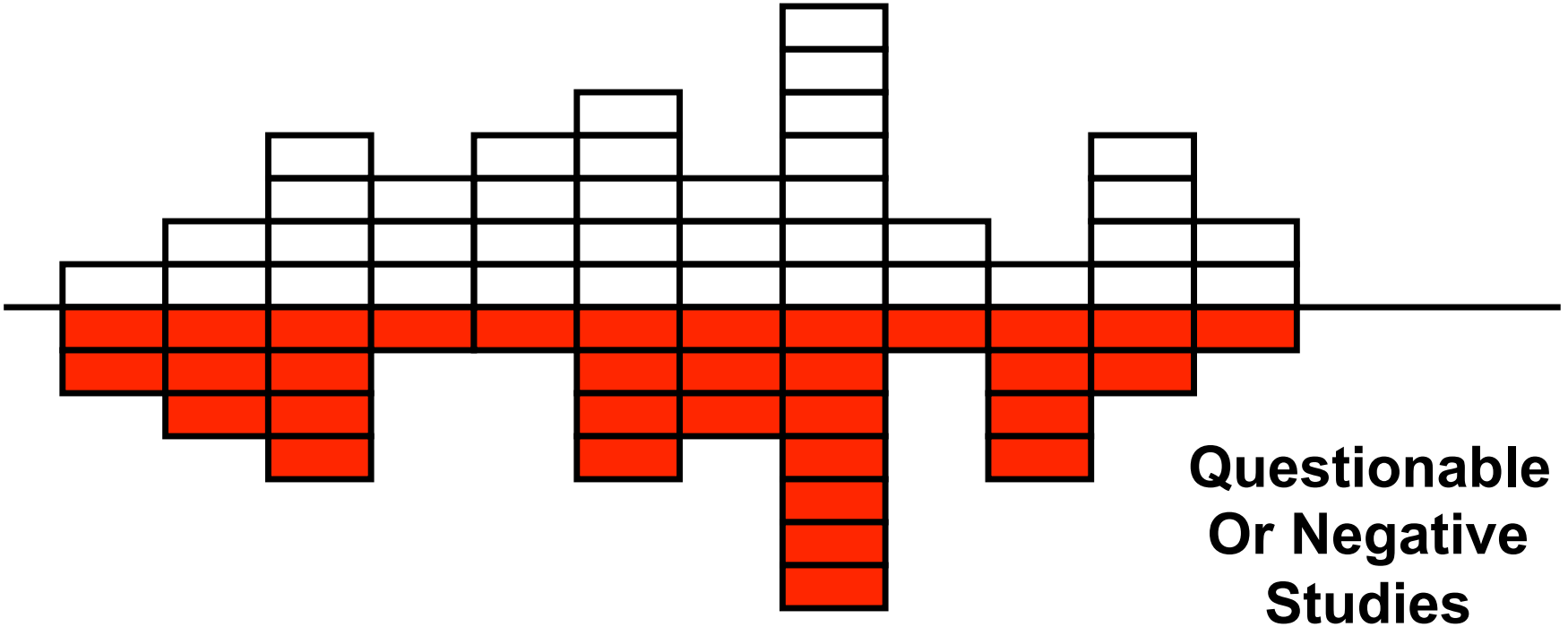
The Published Literature

courtesy of Dr. Howard Brody, UT Galveston
and Dr. Shahram Ahari, URMC



The Scientific Record (FDA)

courtesy of Dr. Howard Brody, UT Galveston
and Dr. Shahram Ahari, URMC



NEJM Resident Bulletin Quote of the Week

"The purpose of our trial — Steroids or Pentoxifylline for Alcoholic Hepatitis (STOPAH) — was to determine whether prednisolone or pentoxifylline administered for a 28-day period reduced short-term and medium-term mortality among patients admitted to a hospital with severe alcoholic hepatitis. . . . In our study, the reduction in 28-day mortality observed among patients treated with prednisolone did not reach the conventional threshold of statistical significance, and no significant differences were observed in 90-day or 12-month outcomes . . . Pentoxifylline did not improve survival in patients with alcoholic hepatitis."

M.R. Thursz and Others, Original Article, "Prednisolone or Pentoxifylline for Alcoholic Hepatitis" April 25, 2015

So what can you do?

Regardless of your role, remember the importance of perspective in how one approaches and ethical issue.

Processes are best designed by considering the various in advance of, and independent from, individual requests.

Share information, both good and bad …

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