

# Clinical Research in the Internet Era

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**Robert Martensen, MD, PhD**

Director, Office of History, National Institutes of Health &  
Lecturer, Department of Social Medicine, Harvard Medical School

# Medicine's Social Contract

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- In addition to possessing technical skills, the essence of being a biomedical professional—and of the research enterprise—lies in their ability to provide sound and ethical judgments in the face of uncertainty.
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# Questions

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What challenges and opportunities does the Internet pose to medicine's social contract for:

- 1) IRBs?
  - 2) Researchers?
  - 3) Research Subjects?
  - 4) Trial sponsors?
  - 5) IRB Administrators?
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# The Big Question

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- In an Internet era, how is it possible for Partners Health Care to stand out as a '**Trusted Source**' for researchers, participants, IRBs, sponsors, and overseers?
  - More generally, what does it mean these days to be a '**Trusted Source**' in human research at the individual and institutional levels?
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# Format of Presentation

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## **Background and Contexts**

discussions moderated by Pearl O'Rourke, MD

## **IRBs**

discussion

## **Researchers**

discussion

## Short Break

## **Research Subjects**

discussion

## **Sponsors and Administrators**

discussion

## **Lunch**

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# I: Background and Contexts:

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Some Factors that Resonate in  
the Present

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## **Social Contracts, Including Biomedicine's, Are Fragile**

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- ❑ Medicine has been a learned profession since European universities started granting medical degrees in the 1200s, but it did not gain a broad social contract until the early decades of the 20<sup>th</sup> century.
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## 'Old School' Ethical Norms Concerning Human Experimentation

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- Although IRBs and 'bioethics' did not exist in 1900, ethical norms did, and according to William Osler a prominent physician of the time, they held that physicians should only *experiment* on patients if the research were likely to benefit those individual patients.
  - Randomized clinical trials did not exist, and neither did the ethical norms that now authorize them morally.
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# Historical Contingencies, not God, Explain Biomedicine's Rise to Power

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- Biomedicine gained social support and privileges largely through its ability to prevent ravages of epidemics, improve surgical outcomes, and standardize physician education and credentialing.
  - Hospital underwent analogous changes as they displaced homes as the seats of vital diagnostic and therapeutic interventions.
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- Osler was updating the venerable Hippocratic norm that physicians should not experiment on patients, which was part of a broader imperative:

*Primum non nocere*

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- Medicine achieved social authority—a **strong social contract**—during a period when medical research generated treatments that either cured previously lethal diseases, such as safe appendectomies and antibiotics for bacterial infections, profoundly ameliorated their course, such as insulin for diabetes, or prevented epidemics through mass vaccination campaigns.
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## When the Profession Became Sovereign

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- As a profession, medicine became well-organized during the period 1900-1950, as did hospitals and the health insurance industry. Through the AMA and other professional groups, organized physicians gained substantial control over medical education, licensing, fee schedules, membership standards, and legal monopoly concerning prescriptions.
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# Hospitals Engaged in an Analogous Process

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- After WWII, hospital organizations also secured substantial privileges for their members, including public subsidies for expansion. In return, they agreed to legislation that specified they were to provide services to at reduced prices in their communities.
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# When Organized Medicine Called the Shots

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- In comparison with today's professional scene, which is mostly about atomized scramble and hustle by medical students and residents, specialty groups, practitioners, medical schools, researchers, hospitals, and laboratories, the medical profession in the early and mid-20<sup>th</sup> century advanced its interests through members' consenting to **'mutual coercion, mutually agreed upon.'**
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# Ethical Norms: the 1950s:

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- During medicine's 'Golden Era'—the 1950s and 1960s—a physician, according to the 1957 AMA 'Principles of Ethics,' was to limit his sources of *"professional income to medical services actually rendered by him, or under his supervision to his patients. His fee should be commensurate with the services rendered and the patient's ability to pay."*
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## Ethical Norms Shift During the 1980s: When Greed Became Good

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- ❑ The AMA's 1980 revision of its 'Principles of Ethics' makes no mention of physicians' business practices except to decry '*fraud or deception.*'
  - ❑ Whereas most hospitals used to scramble for resources to provide a broad service mission, many now say, '*No margin, no mission.*'
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## 'Old School' University & Faculty Norms

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- Well into the 1960s, research universities, with some notable exceptions, expressed little interest in establishing property interests in the work of their faculty members. Professorial cultural norms disdained 'for profit' behavior.
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# Recombinant DNA Technologies and the New Biomedical Entrepreneurs

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- With the revolution in molecular biology that began in the late 1960s, some research universities became interested in potential income from patents on biological processes.
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## The Line Blurs Between Academe and Industry From the 1970s Onward

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- Clever biotech firms, such as Genentech and Amgen, create working environments that appeal to researchers who previously would have eschewed corporate employment.
  - Universities do not prohibit outside activities by researchers, many of whom hook-up with biotech entrepreneurs.
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# 1980s Legislation & New University Behaviors

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- ❑ Passage of the federal Bayh-Dole Act (1980) and Technology Transfer Act (1986), for which research universities lobbied heavily, permitted universities to profit at little cost to themselves from biological patents generated by discoveries made in their laboratories.
  - ❑ Gradually, universities re-configure their priorities to reward entrepreneurial faculty members.
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# Changes in the Clinic & Hospital

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- For universities, Medicare and Medicaid, along with cost plus private insurance plans, brought vastly increased streams of clinical revenue beginning in the 1970s.
  
  - Ditto for their effects on inner-city hospitals.
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# The Situation at Present

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- ❑ Compared to the 1970s, medical schools have leveraged themselves to the hilt in building facilities for profitable procedurally-intense specialties, such as cardiology and transplant surgery.
  - ❑ In terms of research infrastructure, they have done the same for basic sciences with lucrative grant-funding or those with commercial promise.
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# The World We Live In

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- In broad terms, commercial conflicts of interest suffuse all aspects of U.S. health care, whether they are officially 'non-profit' or not.
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- We live and practice amidst a 'biomedical industrial complex' that conflates its own facts, interests, values, and voices with ideal 'health care'.
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# The Challenge of the Internet

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- ❑ Instead of professionally controlled speech, heteroglossia prevails.
  - ❑ Central authority and deference, which is what biomedicine spent a century accumulating, erodes.
  - ❑ Medicine's 'social contract' experiences profound new stresses.
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# The Democratization of Professional Knowledge

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- Nothing like the Internet in scale has occurred since the invention of inexpensive mass printing at the end of the 16<sup>th</sup> century.
  - Then, inexpensive texts of all kinds and growing literacy soon led to the questioning of established hierarchies in religion, politics, and medicine.
  - We are experiencing a social transformation as profound as the crises of authority and knowledge now known as the Reformation of early modern Europe.
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## A New 'Reformation' for Clinical Research?

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- The rise of the Internet—and algorithmic technologies in general—combined with the current valorization of private interests are revolutionizing scientific practices even as they challenge the 'Old School' norms that have prevailed in traditional IRBs.
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# Life in an Internet World

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- ❑ Private interests and governments tend to cherish secrets, but the Internet promotes transparency.
  - ❑ Disparate individuals can organize themselves easily.
  - ❑ Learned knowledge is widely available.
  - ❑ Authority of all kinds is questioned or subverted.
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# The 21<sup>st</sup> Century Crisis of 'Professionalism'

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- ❑ Biomedicine achieved its strong **social contract** in the 20<sup>th</sup> century through delivering astounding improvements to daily life and by presenting itself as a public service by groups of professionals who were not driven primarily by considerations of trade. They expected considerable social deference, and the public granted it to them.
  - ❑ Prior to the rise of the Internet as a mass phenomenon, biomedicine reconfigured itself as an entrepreneurial enterprise, as noted previously.
  - ❑ Now biomedicine, including IRBs, must adapt to an Internet world in which a newly empowered public has the ability to question virtually everything.
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## The Medical Profession: The Center Has Not Held

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- Meanwhile, the medical profession, which struggled to become unified during much of the 20<sup>th</sup> century, has almost fractured into sets of competing specialty fiefdoms, each jealous of its neighbors and preoccupied with protecting its turf.
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# The Poaching of the Commons

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- Not only has organized medicine fractured into groups, but every variety of player—specialties, researchers, patients, pharmaceutical and device firms, hospitals, and academic medical centers—seeks to poach from 'The Commons,' not accept constraints so that it is managed wisely.
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# The 'Social Contract' and Clinical Research

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- In terms of facts, interests, values and voices, what does it mean these days for IRBs, researchers, sponsors, and overseers to behave as providers of 'sound and ethical judgments in the face of uncertainty?'
  - How does one become a 'Trusted Source' when everyone degrades 'The Commons' & solidarity has mostly dissolved?
  - What can IRBs, researchers, sponsors, and overseers reasonably expect of each other and of research subjects in order to continue producing valid science?
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# Discussion

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## II: IRBs

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- This presentation considers IRBs as entities in themselves and also as vital components of a larger picture, which is that of Human Research Protection Programs.
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## Goals and Perspectives for This Session

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- ❑ Identify some Internet challenges *and* opportunities for IRBs.
  - ❑ Use recent observational social science research on IRBs to reflect on potential IRB adaptations to the Internet era.
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# Standard Account of the IRB Process

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- Extant analyses of IRBs by MDs and health researchers tend to assume that IRB members deliberate within a framework that has been called *legal positivism*. That is, members apply fixed regulations more or less accurately, resulting in objectively right and wrong decisions.
  - These analysts tend to aspire to the positivistic ideals of experimental methods. Their experimental style of reasoning, however, does not accurately characterize how IRBs make decisions.
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# How IRBs Work in Practice

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- Instead of operating to the tenants of positivism, this presentation suggests that IRBs in fact employ analogical reasoning, or what John Forrester calls *reasoning in cases*. That is, they operate according to a pragmatic tradition developed in Anglo-American law during the late 19<sup>th</sup> century.
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# Local Decisions: An Achilles' Heel?

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- When university and hospital-based IRB models were devised in the 1960s-early 1970s, organizers praised their ability to make decisions based on local factors. Situational decisions, in short, were widely considered a 'good thing.' Today, however, observers criticize the fact that different local IRBs tend not to agree with one another when they evaluate the same protocol.
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# 'Locality' as a Scientific Issue

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- Differing evaluations of a single protocol used at different sites in Baltimore led the authors to declare:

*Inconsistencies in these reviews raised questions as to the validity and efficiency of the IRB process...Validity can be defined as the 'extent to which any measuring instrument measures what it is intended to measure.' It is important that the IRB process reliably measure with adequate validity the degree of safety of scientific experiments in order to preclude harm to subjects.*

JM Hirshon, JD Krugman, MD Witting, et al. Variability In Institutional Review Board Assessment of Minimal-Risk Research. 9: 1417-20;1420.

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# 'Locality' and the Internet

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- 'Locality' worthy of discussion because the Internet easily exposes variation between one deliberative body and another. Biomedical litigators, for example, routinely shop jurisdictions by comparing the pattern of their verdicts. In short, local variations have become obvious.
  - The new transparency raises a basic notion of fairness: like should be treated alike by deliberative bodies operating in the public sphere.
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## Conventional Wisdom on 'Locality'

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- Authors of IRB audit studies conclude that variations come from two sources: dubious application of federal regulations and hasty judgments made by overburdened board members and administrators.
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## Conventional Remedies for 'Locality'

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- Critics of 'locality' suggest two remedies:
    - 1) More resources for better training and more staff time.
    - 2) Centralization of boards.
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## But the Standard Account May Be Wrong

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- Evidence from interviews with IRB chairs across the USA suggests that different decisions from one board to the next are a product of how boards deliberate, not of board members' mistaken judgments.
  - The importance of 'local precedents.'
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## What Are 'Local Precedents'?

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- 'Local precedents' are decisions that board members use to guide their evaluations of subsequent protocols. By drawing on them, members tend to read new protocols as permutations of studies that they have previously debated and settled. Instead of working from general rules to specific cases, they tend to work from case to case.
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## 'Local Precedents' as a Decision Process

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- ❑ IRBs may vary not because their judgments are 'mistaken' but because they strive to make locally consistent decisions over time.
  - ❑ In order to maintain consistency, they rely on 'local precedents.'
  - ❑ 'Local precedents' tend to be idiosyncratic to each board but stable within them.
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## 'Local Precedents' and Researchers

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- When a 'local precedent' has not been established, a PI may help shape the solution. Once precedents are set and decision making inertia is established, future PIs lose influence on the same issue.
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## Two Common Variations Between IRBs

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- ❑ IRBs disagree as to the amount of scrutiny a given protocol will require. Whether protocols are expedited depends on how risky IRB leaders consider the protocol to be for subjects' bodies and minds.
  - ❑ In full-board reviews, IRBs arrive at different overall decisions concerning approval. Requested modifications differ substantially across IRBs and can be contradictory.
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# Typology of Modifications

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- ❑ **Changes to logistics and supervision**, i.e. requesting that an MD be present while subjects perform a physical test.
  - ❑ **Alterations to research process**, i.e. suggesting that researchers collect different data.
  - ❑ **Revisions to consent forms** to make them more clear or precise to IRB members.
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## Some Implications of 'Local Precedents' for IRBs and Overseers to Consider

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- ❑ **Efficiency:** Variance in turnaround time is usually attributed to uneven distribution of *material resources* between IRBs. Without disputing their importance, *conceptual resources*, in the form of 'local precedents,' also play an important role.
  - ❑ Does an individual IRB have sufficient *conceptual resources*--established precedents--to manage its concerns?
  - ❑ Developing 'local precedents' is time consuming.
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# The Importance of the 'Case Stream' as a Conceptual Resource

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- Sociologist Carol Heimer links the speed of case-based decisions to the existence of precedents. She argues that thinking in cases requires a regular flow of instances that can be seen as examples of a prior case, and thus inefficiencies emerge in situations when *case streams do not exist... (such as) when something is being encountered for the first time.*

C Heimer. Cases and Biographies: An Essay on Routinization and the Nature of Comparison. *Annual Review of Sociology*. 2001:27:47-76:56.

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## A Role for 'Model Problems' as Conceptual Resources

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- Suppose IRBs had access to exemplar protocols and problems as sources of model decisions that allow them to address ethical concerns efficiently: to identify a subsequent protocol's essential problem amid all of its particulars, to identify its resonance with a prior case, and to render a consistent decision.
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## Implications of 'Local Precedents' for Partners' IRB Overseers

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- Developing *case streams* of decision-making precedents available on the Internet to all Partners' IRBs (and researchers) might enhance the efficiency of some of its member IRBs.
  - It's an example of how Partners' overseers can enhance their role as a 'trusted source' for their researchers and IRBs.
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## More Regulation or More Internet Coordination?

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- Given that IRBs make decisions based on cases, the challenge for a coordinated review system is not to craft more detailed federal (or Partners) regulations, but to train IRB members with a limited set of established precedents (cases) on which individual IRBs can base their decisions.
  - The Internet is superb for developing and managing such a conceptual resource.
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# III: Researchers, IRBs & the Internet

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What do researchers think of the traditional IRB process?

What do researchers want of IRBs?

What do IRBs want from researchers?

Proposed modest improvements.

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## What Do Researchers Want from IRBs?

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- ❑ Researchers want research subjects by the most expedient means possible consistent with the safety of the subjects.
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## The 'Traditional Review Process' for the Green Light to Procure Research Subjects

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- Clinical researchers come from diverse disciplines and do clinical research with wide ranges of risk and potential benefit. Protocols may be for 'one off' studies or pre-packaged documents for participation in a multi-center trials. Regardless of risk/benefit or protocol type, PIs typically submit it, wait weeks for a review, receive suggestions and corrections, revise and re-submit, wait for review, perhaps revise and re-submit and wait for additional review.
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## Typology of Common IRB Responses

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- ❑ Changes to logistics and supervision of the research, as in requesting that an MD be present while subjects undergo a physical test.
  - ❑ Alterations to the research design, such as suggesting researchers collect different data.
  - ❑ Revisions to consent forms.
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# What Do Researchers Say About the IRB Process?

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# ! Big Surprise !

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- A Litany of Complaints, with selected examples to follow....
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## "Death by a thousand duck bites,"

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is how Dr. Levine described colleagues' time-devouring attempts to satisfy picayune objections of review boards. Writing in the *Annals of Internal Medicine* a Stanford University team estimated that it took \$56,000 in administrative costs and over 10,000 pages of paper to tweak an already-approved research protocol that simply compared the progress made by patients who had attended two different types of addiction treatment programs.

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## Low Morale Among Trainees

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- Future scientists pay a price too. "Because the review process takes so long, my trainees cannot design and conduct their own projects during their allotted time in my lab," says Carol North, professor of psychiatry at the University of Texas Southwestern Medical Center. "Many talented would-be researchers are being turned-off from a research career."
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# Morale on the UK Side of the Pond

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- Nor is overweening ethics bureaucracy an American phenomenon. "Mindless regulation is halving the amount of research we can do," said Morris Brown of Cambridge University. Writing in *British Medical Journal* last year, he and his colleague(s) also implicated regulators who operated on the assumption that "they are protecting patients from rapacious researchers."

Stewart PM, et al. Regulation – The Real Threat to Clinical Research. *BMJ*, October 16, 2008.

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## Complaints of Excessive Red Tape

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- A report in *Science* last fall found that paperwork is among the biggest threats to pricing large clinical trials out of reach. Many say 'strangulating' red tape and capricious restriction foster mutual distrust between reviewers and researchers and encourage gaming by investigators.

*Science*, Oct 10, 2008.

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## Critics Allege IRBs Engage in Excessive Paternalism

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- In the wake of disasters, for example, mental health researchers are frequently denied timely access to victims lest they be "re-traumatized" by filling out a questionnaire. Some boards deliberate strenuously over whether a token gratuity, say \$25, will "coerce" people to enter studies against their better judgment.
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## Researchers Allege IRB 'Mission Creep' into Social Science

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- According to a 2005 report from the University of Illinois, which calls the practice 'mission creep,' IRBs now routinely review proposals that include conducting historical or journalistic interviews, observing behavior in public places, or using public databases. The time tax this imposes has caused trainees and professors to abandon studies, leading the American Association of University Professors to charge that ethics review often interferes with academic freedom.
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# The Consent Process

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- ❑ Researchers complain that obtaining consent has become onerous as well. In cancer drug trials, for example, prospective participants are routinely asked to sign complicated forms that can run to dozens of pages, often written in legalese. This ends up obscuring rather than clarifying the nature of the experiment.
  - ❑ The consent process is a 'biggie' for everyone & will be discussed later in today's program
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## □ Some Proposed Modest Reforms

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## Speeding up the Process: pre-review possibilities

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- ❑ Internet 'protocol navigators' that outline preparatory steps and provide 'acceptable precedents' organized by type of research and typical protocols.
  - ❑ Establish a Central Protocol Service Center that includes live advisors and Internet interaction.
  - ❑ Pre-review within the PI's home department, especially concerning research design and trial logistics.
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# Speeding Up the Process: at the initial review

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- Instead of an extended back-and-forth exchange of drafts and edits, why not provide an option to PIs that authorizes IRB staff to insert 'default edits'—*acceptable precedents*—as part of the initial review process?
  - Bring the computers and do the edits during the initial review. Researchers could choose or decline this service. Those who opt in would receive a review report right after the IRB meeting that focuses only on outstanding issues, if any.
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## At the Review: limiting review areas

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- Given that the primary purpose of IRB review is human subject protection, what is the logic for having IRB members discuss a protocol's research design, as when they suggest the PI gather different data?
  - Especially when the protocol has been pre-reviewed by the PIs home department, should not questions of research design be mute for the IRB unless they undermine safety or consent standards?
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## For the Social Sciences and Humanities: a limited role for IRBs

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- ❑ Social science protocols that include subject deception as an integral research methodology merit review, as do those that propose to use traceable identifiers on living subjects or those who have died within the recent past. Standard consent forms can be developed in these areas, which, when adopted, should lead to prompt issuance of waivers.
  - ❑ Why should IRBs mandate review of other social science protocols?
  - ❑ IRB policy concerning social science and humanities research can be easily posted on institutional websites.
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# Suggestions for Researchers

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- ❑ Know your institution's policies on human subject research, which are usually in its faculty or staff handbooks.
  - ❑ Know your IRB and make use of its resources early on, not as an add-on to your 'to do' list.
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## Suggestions for Researchers

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- ❑ Know your sponsors, as their behavior varies considerably.
  - ❑ Knowledge of the sponsor becomes especially important when the researcher is the local administrator of a large multi-center protocol that has been pre-packaged elsewhere.
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## IV: Research Subjects

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- How do they make choices?
  - Where do they get their information?
  - Medical Literacy: challenge & opportunity
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# How Do Subjects Make Choices?

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- The answer depends, in part, on how they see themselves in relation to the world.
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## Anthropology of Medical Choices

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According to anthropologist Mary Douglas, who studied thought styles in relation to medical choices:

*In all their behavior persons are continuously engaged in trying to realize an ideal form of community life and trying to persuade one another to make it actual.*

Mary Douglas, *Thought Styles* (London: Sage, 1996, p. 42)

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## Thought Styles and Choices

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- People evaluate every aspect of living and all choices—including choices of information sources—in terms of their relevance to their cultural ideal.
  - The same analysis they apply to medical choices applies to their choices in foods, religion, and probably furniture.
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## Four Distinct Kinds of Sub-Culture

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- ❑ Conservative hierarchy
  - ❑ Dissident enclave
  - ❑ Active individualism
  - ❑ Backwater isolation
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# Cultural Map

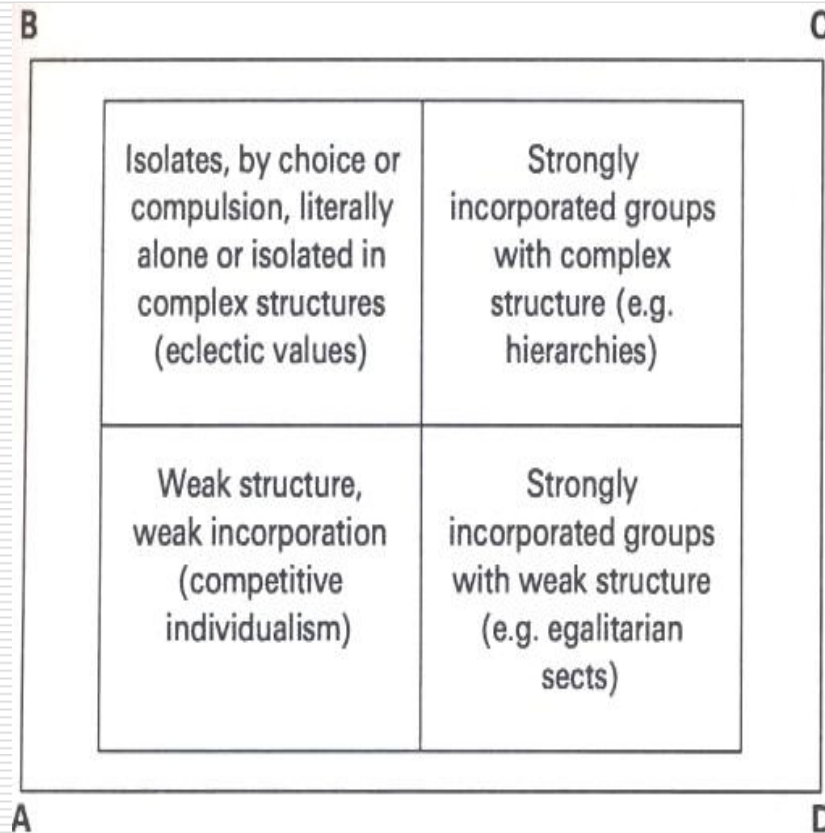
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## Cultural Map:

'Culture' as 4 groups: A) Active individualism; B) Backwater isolation; C) Conservative hierarchy; D) Dissident enclave.

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## A Active Individualism

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- Weak structures, weak incorporation.
  - Competitive individualism.
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## B Backwater Isolation

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- ❑ Isolates, by choice or compulsion, literally alone or isolated in complex structures (eclectic values).
  - ❑ Prefer to avoid the oppressive controls of the other forms of social life.
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## C Conservative Hierarchy

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- ❑ Based on hierarchical community, and so in favor of formality and compartmentalization.
  - ❑ Most IRB members and Sponsors live within this sub-culture, but not all researchers do.
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## D Dissident Enclave

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- ❑ Egalitarian structures and values based on equality within a group. It may have strongly incorporated groups with weak structures (e.g. egalitarian sects).
  
  - ❑ Free negotiation; hostile to other ways of life.
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# Mutual Antagonism

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- A choice is an act of allegiance and a protest against the undesired model of society. Hierarchy disvalues equality, fervor opposes cool judgment, heterodoxy is opposed to orthodoxy.
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# Principle of Cultural Opposition:

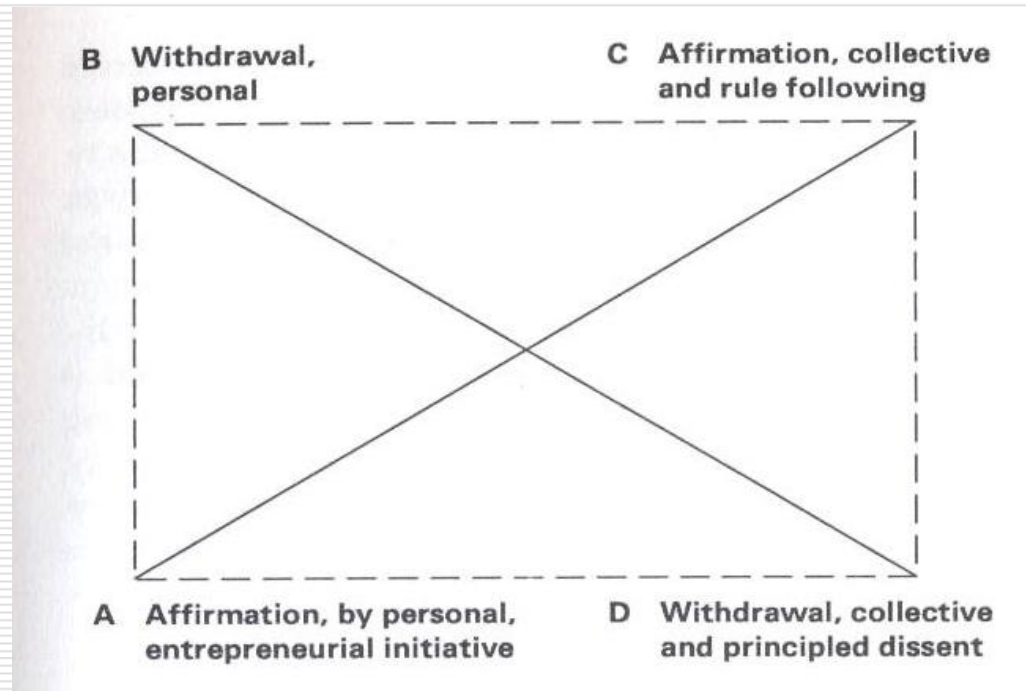
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- People may not know what they want, but they know what they don't like, and they are realistic about their opportunities.
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# Diagram of Opposed Cultural Bias

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- Diagonal A-C is the positive diagonal, the alliance of individual entrepreneurs with hierarchies, affirming authority; the diagonal B-D is the negative diagonal, the alliance of isolates with dissident enclavists, rejecting existing authority. (Mary Douglas, *Thought Styles* (1996, p. 45))



# Authority

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- In any community, some sectors will support authority. They are allies on the positive diagonal (A-C). Both types of cultural ideal accept authority, leadership, and domination. Appropriate use of force poses no problem for them; they are much more liable to worry about subversion, arbitrariness and anarchy.
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## Diagram of Opposed Cultural Bias

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- Diagonal A-C is the positive diagonal, the alliance of individual entrepreneurs with hierarchies, affirming authority.
  - Diagonal B-D is the negative diagonal, the alliance of isolates with dissident enclavists, rejecting existing authority.
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# Doubt and Protest

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- Anything the A-Cs approve will automatically be up for question by the sub-cultures on the negative diagonal (B-D). Isolates, by definition, will not be able to exert influence and will not expect to use force. Enclavists will combine together in protest against the domination of the mainstream society. Both are fertile grounds for protest about the use of power.
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## The Internet Favors Sub-Culture Recruitment

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- For example, there is nothing to stop a few isolates from banding together and forming an enclave, whether ethnic, religious, or a therapeutic community, as in a disease-based Web support group.
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# Where Do Subjects Get Their Information?

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- ❑ Subjects get their information from everywhere. Statements by researchers and protocols are part of the picture, but only part.
  - ❑ No controlled vocabulary exists; promotional rhetoric suffuses the Web.
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# Heteroglossia Reigns

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- ❑ When it comes to information for patients and research subjects, the Internet is heteroglossic.
  - ❑ No controlled vocabulary exists.
  - ❑ Promotional rhetoric and narrow self-interest suffuse the Web.
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# Heteroglossia, Promotional Rhetoric, and Chronic Illness

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- ❑ By definition, chronic diseases admit of no cures. Multiple diagnostic and treatment modalities are on offer.
  - ❑ 'Direct to consumer' marketing by interested parties undermines notions of a 'controlled vocabulary' of common and stable meanings.
  - ❑ Different parties may use the same words to convey different meanings.
  - ❑ Manipulation is the name of the new media game.
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# Medical Illiteracy Extensive:

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A substantial percentage of the public--20% to 30%, depending on the study--is 'medically illiterate' or 'marginally literate' in terms of usual health care information.

Unlike general illiteracy, medical illiteracy cuts across levels of socio-economic status, including formal education, income, and ethnicity.

Subjects for whom English is a second language pose additional challenges.

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# Medical (II)literacy & the Net

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The 'corrupted speech' of the Internet compounds the problem. Subjects will be consulting your protocols but also all kinds of disease and treatment information on the Web.

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# Addressing Functional Illiteracy

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- ❑ Internet-based informed consent procedures, which are gaining advocates among IRB leaders, need to be mindful of the prevalence of medical illiteracy.
  - ❑ 'Consent' is an educational opportunity, not a transitive verb, as in 'Nurse, consent the patient.'
  - ❑ Consent procedures modeled on the traditional model, which does not work well, will likely work even less well in a virtual context.
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# Person-to-Person Essential

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- ❑ Extensive person-to-person exchange--in addition to reading--is the only reliable means to assure that a subject's consent is informed.
  - ❑ One needs potential subjects to tell in their own words key aspects of the study to the study person before one can assume they understand what they're asked to consent to.
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## Proactive Assessments of Subject Comprehension are Vital

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- ❑ Given the extent of medical illiteracy, the traditional practice of assuming that a subject's lack of questions signifies his or her comprehension is an illusion.
  - ❑ Literacy needs to be assessed actively. To do so passively is not acceptable on moral or cognitive grounds.
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# Internet as Opportunity for Improved Consent Processes

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- The Net's ability to aggregate masses of information on the same topic from different sources provides IRB administrators an opportunity to design trial sites as *educational resources* for prospective subjects. For example, they could also provide a Web review of the merits and defects of other Web information on their subject.
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## Value of a Common 'Controlled Vocabulary' for Partners' Trials

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- In order to stabilize meanings, a key requirement for literacy, Partners can develop a 'controlled vocabulary' with standard definitions for use in all or most of its trials.
  - For prospective subjects, researchers, *and* sponsors, Partners would become a 'Trusted Source' in terms of a common language for its trials.
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## 'Controlled Vocabulary' and 'Established Precedents'

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- They represent two sides of the same coin, which is about practical enhancements of Partners' social contract with researchers and potential research subjects.
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# V: Sponsors & Administrators

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- 1) What Sponsors say to recruits.
- 2) Possibilities for Administrators.

# Direct Advertising the Beginning of Informed Consent

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According to the FDA, 'Direct advertising for study subjects (is) the start of the informed consent process,' and the OHRP has said that 'the information provided on these websites may constitute the earliest components of the informed consent process.'

FDA, 'Guidance for IRBs and Clinical Investigators: 1998 Update. Recruiting study participants: A. Media advertising. Oct. 2006.  
<http://www.fda.gov/oc/ohrt/irbs/toc4.html>

# The Internet & Sponsor Disclosure

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- ❑ Recruitment practices on the Web vary considerably by sponsor.
  - ❑ In a 2002 DHHS study of 22 sites (110 trials), only 29/110 mentioned potential benefits. 0/110 mentioned potential risks.
  - ❑ Dep't of Health & Human Services Office for Human Research Protections. Guidance on Institutional Review Board Review of clinical Trial Websites. When is IRB review of clinical trial websites required? Sept. 2005.  
<http://www.hhs.gov/ohrp/policy/clinicaltrials.html>
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## Misleading Speech Common

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- In the 2002 DHHS study, several sites referred to 'new drug treatments' rather than 'experiments' or 'unproven drugs.'
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## From a Hastings Center Report (2008)

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- Study in 2006 of sites of trials recruiting subjects for studies concerning Diabetes (171 trials) and unipolar Depression (184 trials).
  - Sites numbered 22 for Diabetes and 21 for Depression.
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# Information Characteristics

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- ❑ 11 parameters considered on trial sites, including:
  - ❑ drug or device;
  - ❑ whether site mentioned 'risk(s)' or 'side effects';
  - ❑ any incentive and \$\$ of financial incentive, if offered;
  - ❑ whether study was described as 'clinical trial';
  - ❑ number of visits involved in participation;
  - ❑ length of study;
  - ❑ any research procedures involving more than minimal risk;
  - ❑ source of sponsorship.

R Klitzman, I Albala, J Siragusa, et al. Disclosure of Information to Potential Subjects on Research Recruitment Web Sites. Hastings Center. IRB: Ethics & Human Research, Jan-Feb 2008.

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## Selected Results (Hastings 2008)

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- ❑ Basic study criteria often omitted:
    - ❑ Fewer than half reported study length.
    - ❑ Only 2% of Diabetes and 14% of Depression noted source of funding.
    - ❑ More than minimal risk in 67% of Diabetes and 77% of Depression studies. Most of these had for-profit sponsors and did not list # of visits or length of study.
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# Discussion (Hastings report 2008, p. 18)

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- ❑ 'We found that 38% of the sites...did not appear to provide balanced descriptions of the studies.'
  - ❑ 'Nearly 75% provided some description of incentives, yet roughly half of these failed to mention risks or what the study involved (i.e. length of study or # of visits).'
  - ❑ 'No sites used the term 'risk(s) and only one used the term 'side effects.'
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## Discussion continued (Hastings 2008, p. 18)

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- 'Many online recruiting sites include some--but not full--descriptions of what will be involved...Thus the information provided appears inconsistent with federal guidance and weighted toward encouraging research participation.'
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## For-profit Sponsors More Misleading

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□ Hastings report (2008, p 18):

'Sites that appeared out of balance were more likely to be sponsored by for-profit entities, and the majority did not explicitly describe the research sponsor.'

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# Trust at Stake

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□ Hastings Report (2008, p. 19):

'The source of funding...may well be important for potential study participants to be aware of, as it may affect the degree to which they trust investigators.'

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# Integrity of Information

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Hastings Report Recommendation to IRBs (p. 19):

- 'The goal should be balance in providing a realistic view of participation.'
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# Hastings Concern About 'Directory Listings'

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- 'By allowing 'directory listings' to bypass IRB review, the current guidance encourages sponsors and investigators to limit the amount of information provided in Web-based contacts..The fact that information about incentives is nonetheless often included...suggests how difficult it may be to persuade researchers...to refrain from 'selling' participation.'

(Hastings Report (2008, p. 19))

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## Partners: Challenge & Opportunity

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- ❑ Given the prevalence of 'corrupted speech' on Internet trial recruitment sites, Partners might *insist* on 'balanced presentations' by researchers and sponsors in their Web statements to prospective subject.
  - ❑ Observance of Federal guidelines should be a minimum.
  - ❑ All outreach efforts, including directory listings, would receive prospective review in Partners IRBs.
  - ❑ Surveillance and policing of Partners sites would be part of the process.
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