THE ETHICS POLICE?:
THE STRUGGLE TO MAKE HUMAN RESEARCH SAFE

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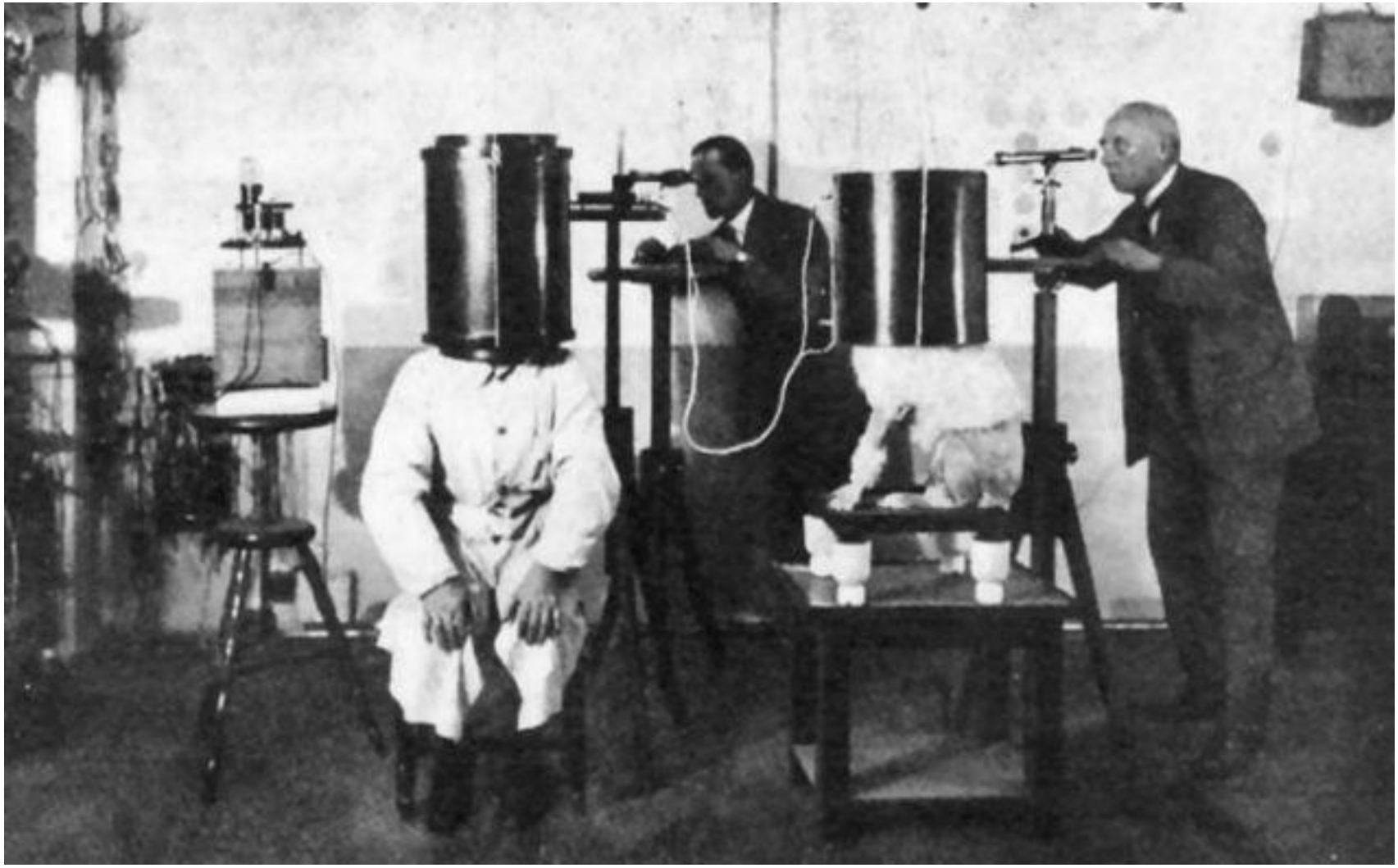


Background

- But recently, IRBs/RECs have been increasingly criticized
  - Discrepancies
    - Can impede research
  - Tensions with PIs
  - Are IRBs/RECs broken?
  - Unconstitutional?

Recent Controversies

Since IRBs/RECs were created, research ethics “scandals” and controversies have occurred:

- Kennedy-Kreiger study, involving exposure of lead to children
- Hopkins “checklist” hand-washing study
  - Any need to inform IRBs or patients at 67 institutions?
- SUPPORT Study
  - Randomizing newborns to two levels of oxygen
  - OHRP: consent forms were insufficient
  - Did clinical equipoise exist?
  - Debates continue
- Facebook experiment
  - Have users “signed away” all their rights to be involved in any research Facebook wants to do?

Policy debates

- In US: ANPRM/NPRM:
  - Centralize IRBs more?
  - Exempt certain areas of minimal risk research
  - Let PIs self-determine minimal risk status
  - How to handle biobanks?
- December 2014: NIH
  - CIRBs for all multisite studies?
    - How much should they be centralized, and how might that work?
  - Are other improvements needed, and if so, what?

Yet little empirical data exists

- Very few studies on views and experiences of IRBs/RECs
  - Several quantitative studies
    - Focusing on the form of IRBs/RECs (e.g, structure/process)
    - Not the content of decisions
  - But many questions remain:
    - How do IRBs/RECs make decisions?
    - What challenges do IRBs/RECs feel they face?
    - How do IRBs/RECs view these issues?

QUALITATIVE STUDY OF IRBS

Methods

- Contacted IRB leadership
- Every fourth institution of list of top 240 institutions by amount of NIH funding
- Response rate: 34/60 = 55%
- Asked 50% of these to distribute info to members and administrators
- Semi-structured, in-depth interviews

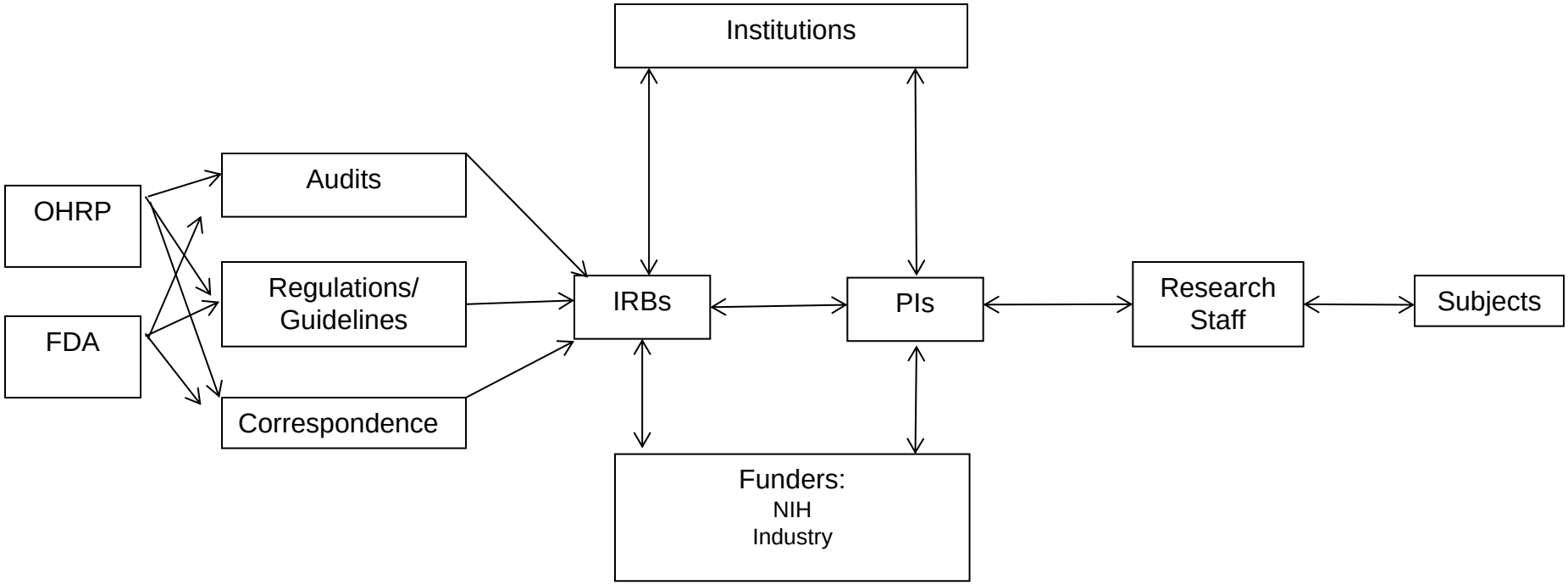
Characteristics of Qualitative Sample

	Total	**% (N=46)**
Type of IRB Staff		
Chairs/Co-Chairs	28	60.87%
Directors	1	2.17%
Administrators	10	21.74%
Members	7	15.22%
Gender		
Male	27	58.70%
Female	19	41.30%
Institution Rank		
1-50	13	28.26%
51-100	13	28.26%
101-150	7	15.22%
151-200	1	2.17%
201-250	12	26.09%
State vs. Private		
State	19	41.30%
Private	27	58.70%
Region		
Northeast	21	45.65%
Midwest	6	13.04%
West	13	28.26%
South	6	13.04%
Total # of Institutions Represented	**34**	

RESULTS

A wide range of issues concerning:

- Contexts of decisions
  - Who is on the IRB? How are they chosen?
    - Intra-IRB issues
  - Relationships with feds
  - Relationships with industry
  - Relationships with institutions
- Contents of decisions
  - Interpretations of principles and regulations
    - Assessing and weighing risks vs. benefits
    - Undue influence?
    - Is it research?
      - How good does the science need to be?
    - Informed consent
      - Is the form good enough?
- Relationships with researchers
    - Research integrity?
  - Additional issues in the developing world


Institutions
OHRP
Audits
FDA
Regulations/
Guidelines
Correspondence
IRBs
PIs
Research
Staff
Subjects
Funders:
NIH
Industry

Intra-IRB issues

- Very high degrees of commitment and dedication
- Some are “volunteered” for the IRB

Becoming members and chairs

Before appointment to IRB

Institutions vary

- Appointment may be due to variable reasons
- Individuals vary in prior education and experience:
  - In ethics
    - From some to none
  - In research
    - May have interest
  - May be chosen because of complex institutional factors:
    - Assignment “volunteered” by department as routine committee assignment
      - As remedial education/”punishment”
  - Turnover of chairs may occur because of:
    - Retirement
    - Scandal
    - Institutional wishes to change IRB
    - Roles may be fluid

Becoming Members and Chairs

Orientations

- Vary from little or none to some
  - “See one, do one”
- Learning “on the job”
  - Can take several months or years
- Often no attendance at national meetings
  - Because of limited resources

“Community” Members

- Finding Community Members
  - Challenges, given needs to understand science
- Retaining Community Members
  - IRBs vary in amount of resources to assist them
- Who They Are
  - Non-affiliated and/or non-scientific?
- What They Do
  - Input on protocols themselves
  - Only assessing consent forms
- Implications
  - Provide more support?
  - Have more then one?

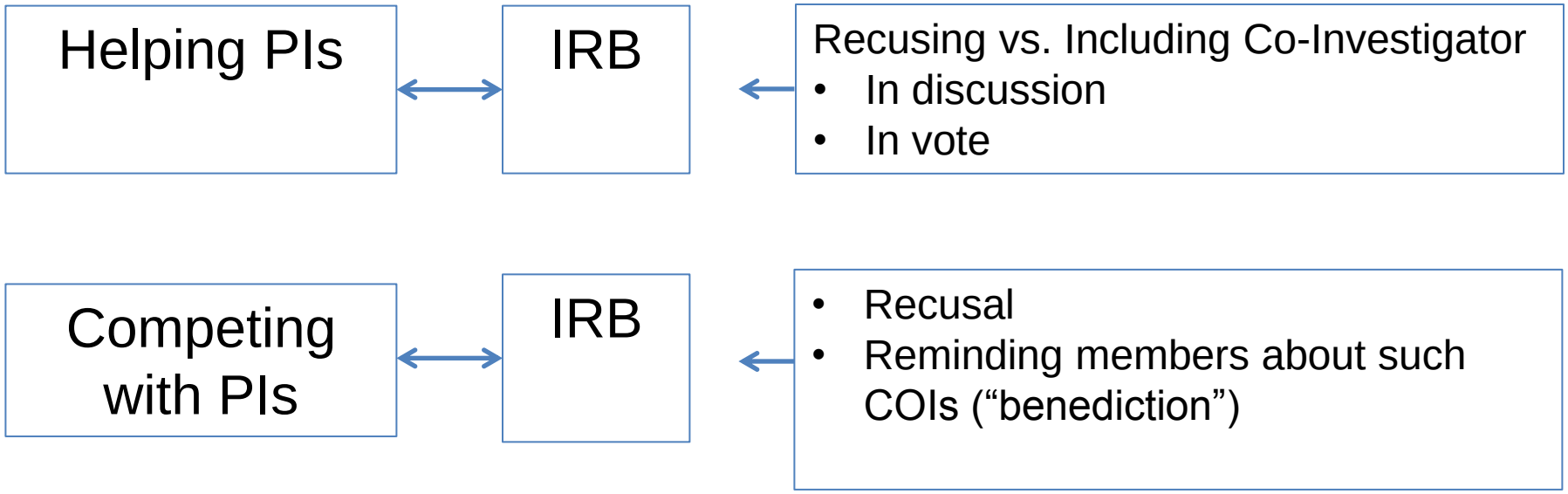
Contexts: Federal Agencies

- IRBs often caught in the middle between the feds and the researchers
- But often “blamed” by PIs as “the messenger”

Contexts: Institutions

- Amounts of support vary
  - Can increase after a “scandal” or audit, but can then return to prior levels
  - Differences in how to divide IRBs
    - Initial vs. continuing review
      - e.g., cancer vs. other
      - Separate IRB for normal volunteers?
    - Separate scientific review committees
- Compliance offices vs. IRBs

IRBs' and PIs' COIs



COIs (continued)

- Standard:
  - Not having even the appearance of a COI?
  - Direct and indirect financial COIs
  - Rather than financial and non-financial COIs
  - Clearer or more rigorous standards for recusal?
    - Okay to stay in the room for this discussion, if not for the voting?

THE CONTENTS OF DECISIONS:

Assessing and weighing potential risks and benefits of studies not yet conducted: Difficulties

Spectrums of Risk

- From major to minor
- "Significant" or not?
- From likely to unlikely
- From direct to indirect:
  - "Minimal risk"
  - "Minor increase over minimal risk"

Sources of Difficulties in Assessing Risks

- Because of inherent uncertainties of research (i.e., investigating "the unknown")
- Patients with ongoing, serious disease
- Therapeutic misconception
- Standards:
  - "Truly safe"?

Coercion and Undue Influence: Ambiguities and Dilemmas:

IRBs struggle with dilemmas concerning**:**

- *Content*
  - How much to give subjects
    - Pay subjects differently based on their income?
    - Will selection bias result?
    - Provision of free care as coercive?
    - What to give subjects (e.g., cash vs. vouchers
  - Added challenges in several situations:
    - Research on children
    - Research on students
    - Research in the developing world
  - When to compensate subjects
  - Whether, when, and how to inform potential participants about compensation
  - How to define undue influence:
    - Based on “gut feelings” and “common sense”
    - Can be subjective

Process of deciding about undue influence

- IRBs can take time to make these decisions
- Decisions often reflect compromises
- Underlying tensions arise:
  - “Undue inducement” is inherently subjective and difficult to assess in others
  - Questions arise of whether subjects should “volunteer” vs. do it for the money
  - Lack of a consistent standard:
    - Between IRBs
    - Even in one IRB over time

Is the science good enough? Assessing the Quality of Science

Potential problems with quality of science

- Quality of science can vary
- Quality of science can be:
  - Relatively low
  - Hard to measure
    - Especially possible benefits of eventual findings
  - Not great, but not egregious
  - Low risk, but low benefit
  - Low power
- Separate departmental sign-off can vary in quality
- Particular problems with studies with main goal not research per se:
  - To help industry sales
  - To serve as part of student education

IRB members' conflicting goals

As IRB members:
- Make science "good enough"
- Minimize risks
- Make risks commensurate with benefits

As scientists:
- Make science "as good as possible"
- Maximize benefits (i.e., social/scientific contribution)

Questions:

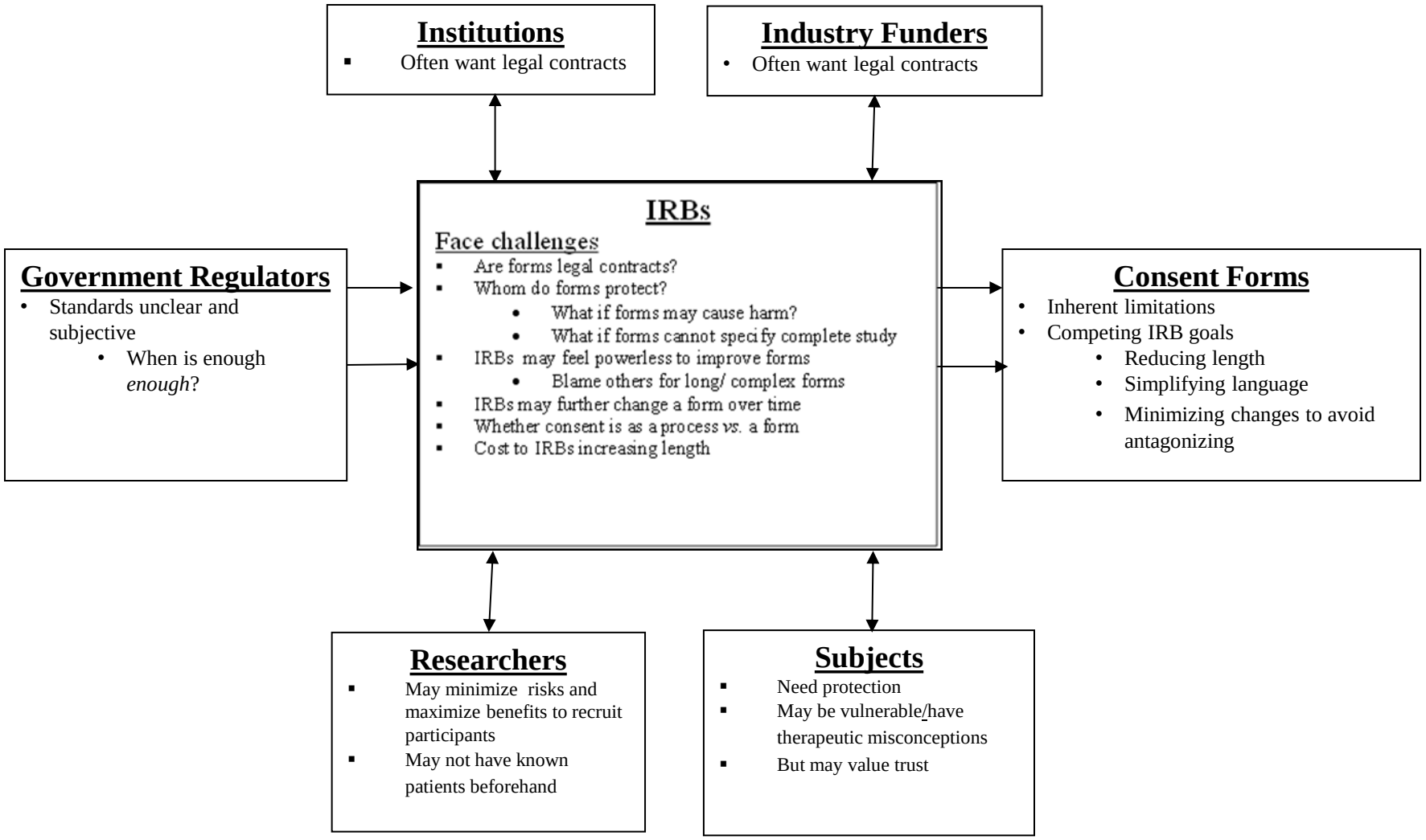
- What *role* to play?
- What *standard* to use?
  - Whether to make changes if study already approved elsewhere

Tensions:
- PIs may see the IRB as "overstepping" responsibilities
- IRBs may not consider costs to PIs
- RBs may not recognize these issues

Factors

IRB characteristics:
- How "pro research" the committee is
- Members/chairs are PIs

Are consent forms legal documents?



Variations between IRBs

- IRBs differ in their “colors” and “flavors”
- Vary from “nit-picky” to “user-friendly”

Locations of Variations

- Between IRBs
- Within a single institution
- Within a single IRB
- Within a single member

Causes of Variations

- Occasional perceived differences due to type of community (e.g., rural vs. urban)
  - Related to sexual issues (“other IRBs may be more prudish, and have trouble with HIV prevention studies among gay men, but we don’t”)
  - But very rare
- Differences that arise do not appear to reflect differences in values concerning research ethics
- Differences tend to concern procedural definitions, not community values

Causes of Variations

- Institutional differences
  - Types of studies the IRB has reviewed in the past
  - Past federal audits/“shut downs” of research
  - Differences in research intensiveness/size of institution/reliance on indirect costs
- Individual differences
  - Chairs and members make subjective interpretations
    - Rely on “gut feelings”, “intuition”, “sniff test”
    - Anxiety vs. psychological “comfort” (”peace of mind”)
    - Idiosyncrasies (“temperament”, “pet peeves”, “prudishness”)
    - “Nit-picky” vs. “user-friendly”/”pro-research”
    - “Good catches”: Effects of “many eyes seeing a protocol

Defending Variations

- Justifying differences
  - “Simply interpreting the regulations”
- A few acknowledge “minor differences”
  - As “fine-tuning”
  - But differences are often greater

RELATIONSHIPS WITH RESEARCHERS

Do IRBs Have Power?

- Power of chair and the IRB in the institution can vary
- Critical questions:
  - How much power do and should IRBs have?
    - What do these questions mean?
    - Who should decide?
    - Are IRBs the police, judge and jury?

IRB Perceptions of Their Power

- IRBs as having power
  - IRBs may acknowledge that PIs see them as having power
    - But may not acknowledge its full extent
  - IRBs may feel it is legitimate
    - It is based on overriding goals
    - They are trying to help PIs
  - IRBs may see problems but accept these as inevitable
  - IRBs may feel it is small because:
    - It's based on "the community's values"
    - But it may be based instead on institutional and/or personality factors.
- IRBs as not having power because:
  - They are "merely following the regulations"
  - They are themselves subject to higher administrative agencies
  - Their process is impersonal and not biased
  - Their process is "open"

IRBs' Perception of PIs' Views

- PIs may misperceive IRBs
- PIs may unfairly blame/inappropriately scapegoat IRBs
- IRBs cannot always publically respond to PI accusations
- PI claims that IRBs have power may not be fully valid

"OPEN DOORS"?: IRBS' RESPONSES TO TENSIONS WITH PIS

FORMS AND CONTENTS OF INTERACTIONS

- Protocol Reviews
  - IRBs vary in reviewer anonymity
  - Anonymity can reduce conflicts but make IRB seem a "faceless bureaucracy"

- IRB Meetings
  - Vary in whether PIs are invited and/or encouraged to attend
  - Presence of PIs can improve PI cooperation, but reduce candor in meetings

- Memos to PIs
  - Range in tone and content ("Using Southern Charm" vs. more bureaucratic).
  - More helpful memos can improve PI cooperation, but take more time

- PI Outreach Education
  - Varies in extent
  - Can improve PI cooperation, but take time and resources
- Toward best practices?
  - More “openness” and accessibility

Added challenges: Emerging economies:

Logistical Challenges

- Developing World
- IRBs/RECs
  - Quality of IRBs varies
  - Less resources
  - Less training
- Health system
  - More corruption

- US
- IRBs' low knowledge of:
  - Local context
  - Local regulations
  - Standard of care
- Local views of ethical issues
  - Different views of autonomy
  - Different risks/benefits of daily life
  - But how much such knowledge is enough?
- IRBs have difficulty knowing when they understand other cultures

Added challenges: Emerging economies:

Ethical Dilemmas for US IRBs

- How to interpret principles?
- How much to pay subjects?
- How much sustainability?
- Higher standards?

Added Challenges: Emerging economies

Responses:

Structural

- Capacity building of overseas IRBs
- Monitoring IRBs
  - Not always welcome
- Infrastructure changes?
- Communicate more w/ local IRBs?
- Negotiating compromises
- Needs for more communication
  - IRBs communicate poorly in part because they do so via PIs

Possible Federal Changes: Views of Local IRBs Regarding CIRB Reviews

Perceived Problems and Ambivalence Concerning CIRBs

- General wariness of CIRBs, and support for local IRBs

Perceived Advantages of Local IRBs

- Claims that local IRBs reflect community values
- Local knowledge of subjects
- Local knowledge of PIs
  - "Track records"/reputations
- Protecting "our own" subjects
- "Curbside consults" with PIs
- Desires for local autonomy, authority, and comfort
  - Against "being told what to do"
  - Wariness of centralized, federal bureaucracy

Perceived Problems with CIRBs

- Differences between CIRBs
  - Depends on who are members of the committee
- For-profit CIRBs may have conflicts of interest

Advantages of CIRBs

- Rarely acknowledged
- Streamlining work/Saving Time

Local Members as Biased in Their Views of CIRBs?

Other Possible Solutions

- More regional IRBs?

CONCLUSIONS

Possible changes to improve subject protection:

Federal level:

- Centralization?
  - May offer several advantages and disadvantages
- Future of other proposals in the NPRM?
  - Different rules for social science research?
  - Excuse certain minimal risk research?
    - But will PIs have COIs in making these determinations?

Other federal changes:

- More guidance and consensus
  - From OHRP, IOM, and/or others
- More case law/open, published precedents to establish consensus
  - Proprietary information can be redacted
- More consensus concerning areas where difficulties now arise
  - e.g., Is allergy skin testing minimal risk?
- Publishing decisions
  - Minutes or other summaries with proprietary information redcated
  - Similar to case law?
- External appeals process

- More regionalization?
- More external (unaffiliated and non-scientific) members
- Improved informed consent
  - Shorter summary documents to accompany longer forms
    - Yet many details need to be addressed
- Training of IRB personnel, using protocols about which consensus has been reached
  - Is this informed consent “good enough”?
  - Is the quality of the science of this protocol “good enough”?
- Will meet resistance
  - How then to proceed?

Institutional level:

- More resources
  - Compensating members
- Well-trained staff could make independent decisions about key issues
- Providing appropriate compensations to IRB members

Changes needed among BOTH IRBs and PIs

- IRBs and PIs would benefit from more fully understanding:
  - These tensions
  - The underlying causes

IRB Level: Needs for attitudinal changes

- Improving relationships with Pis
  - Better PR
    - Publicizing the benefits of IRBs
  - Some IRBs may misperceive PI complaints
  - Increased recognition of:
    - Ambiguous nature of regulations
  - Roles of interpretations
    - Acknowledgement of discretionary power?
  - Costs of variations

IRB Level:

- More transparency
  - Open doors
- Establishing institutional memory and a body of “case law”
- More and different training
  - Reaching consensus and standardization on definitions, interpretations, and applications of key terms and principles
    - Testing to demonstrate adherence to these standards
- Willingness to be studied
- Sharing “best practices”
  - LISTSERVs
  - National or regional meetings
    - Not always attended

Researcher Level: Needs for change, too

- Changing attitudes
- May misperceive IRBs
- Enhancing understandings Not “blaming the messenger”
- Avoiding inattentive and sloppy submissions to the IRBs

Public level

- Enhancing public education
- Enhancing media understandings
- Larger social/political questions:
  - How much should scientists be overseen?

Future research

- IRBs should be far more open enough to being studied
  - Many IRBs feel that they have nothing to gain
    - But that is incorrect
  - Some IRBs have required informed consent from all members

Broader implications

- How ethical principles get interpreted and applied differently in different settings
- How much of power is in the eyes of the beholder?
- Needs for more humanistic approaches

THE ETHICS POLICE?

The Struggle to Make Human Research Safe

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QUESTIONS?

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