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Approval Sheet

Institutional Review Board Members' Experiences of Justice Issues during Research Ethics Review

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B.S. in Nutrition and Health Sciences
Oregon State University
2015

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health at Emory University
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Abstract

Institutional Review Board Members' Experiences of Justice Issues during Research Ethics Review

By Forrest Brady

The global health research field is growing rapidly, often engaging in human subjects research among populations that are underserved, underrepresented, and marginalized. Institutional Review Boards (IRBs) are groups constituted to review and monitor biomedical research on human subjects(Center for Drug Evaluation and Research, 2019), and are granted much power over whether research is approved, denied, or if more information is needed. However, little is known about the experiences of global health justice issues among IRB members during research ethics review.

This thesis was a cross-sectional, quantitative study conducted to describe the experiences of global health justice issues in research proposals reviewed by IRBs. The aim of the study was: (1) understand if IRBs experience global health justice issues, (2) if IRBs experience global health justice issues, understand what guidance they use in addressing them, and (3) understand if IRBs experience moral ambiguity or concern as a result of the global health justice issues in proposal review. A survey was developed and offered to all subscribers of Public Responsibility in Medicine and Research's (PRIM&R) blog, *Ampersand*, past or presently serving on an IRB. Data were analyzed using descriptive statistics and four typologies were created to attempt to explain IRB member experiences.

Findings were limited due to a low survey response rate, but seem to suggest that IRB members: (1) experience justice issues during research ethics review; (2) lack sufficient guidance for how to address global health justice issues; and (3) may experience concern and moral ambiguity as a result of insufficient guidance.

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PREFACE

List of Acronyms

APE	Applied Practice Experience
CIOMS	Council for International Organizations of Medical Sciences
ESC	Ethical, social, and cultural
FACE	Focus Area for Compassion and Ethics
HELP	Human Engagement Learning Platform
HIC	High-income country
HRPP	Human subjects protections program
IACUC	Institutional Animal Care and Use Committee
IRB	Institutional Review Board
LMIC	Low- and middle-income country
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principle investigator
PRIM&R	Public Responsibility in Medicine and Research
R&D	Research and development
REB	Research Ethics Board
REC	Research Ethics Committee
RECS	Research ethics consultation services
REDCap	Research Electronic Data Capture
TFGH	Task Force for Global Health
UNAIDS	The Joint United Nations Programme on HIV/AIDS

INTRODUCTION

A study conducted by the Human Engagement Learning Platform for Global Health (HELP) at Emory University to understand and address key ethical issues and challenges in global health was the genesis for this thesis. The findings from the qualitative landscape analysis of Task Force for Global Health (TFGH) Program Directors highlighted the need for a study exploring similar ethical issues and challenges among a different population, Institutional Review Board (IRB), Research Ethics Committee (REC), and Research Ethics Board (REB) members, which became my remote Applied Practice Experience (APE). This thesis attempts to describe experiences of justice issues among IRB, REC, or REB members, administrators, and chairs in global health research proposal review through analysis of data collected via a survey developed during my APE. For brevity throughout this thesis, I will use “IRB” as a short-form for all similar committees.

BACKGROUND

Defining Global Health and Research Ethics

A commentary published in the *Lancet* by Koplan et al. from the Consortium of Universities for Global Health Executive Board defines global health as: ". . . an area for study, research and practice that places a priority on improving health and achieving equity in health for all people worldwide. Global health emphasizes transnational health issues, determinants, and solutions; involves many disciplines within and beyond the health sciences and promotes interdisciplinary collaboration; and is a synthesis of population-based prevention with individual-level clinical care"(Koplan et al., 2009).

Regarding global health and research ethics, bioethicists Soloman and Singer state: “Research ethics must be more deeply rooted in the context of global health. It must more forthrightly address the social, political, and economic forces that widen global inequities in health, and it must ultimately be concerned with reducing inequities in global health and achieving justice in health research and health care.”(Benatar & A Singer, 2000)

When justice in research ethics emerged in United States documentation for research practices, it was conceptualized as "fairness in distribution" or "what is deserved" and was ultimately documented as fair selection of research participants(Office for Human Research Protections, 2016a). However, bioethicists report that global health research focusing on health and social justice should also include aspects like engaging research participants in study design, improving health and well-being of marginalized populations, and increasing research capacity of host communities(Benatar & Singer, 2010; London, 2005; Pratt, 2021; Pratt & de Vries, 2018).

Institutional Review Boards (IRBs), Research Ethics Committees (RECs), and Research Ethics Boards (REBs) are groups formed within institutions globally to protect the rights and welfare of human participants in research conducted by members of that institution. IRBs have the power to approve, deny, or ask for more information about research studies. However, views on IRB purpose and use are conflicting. In an editorial published in the *Journal of the American Medical Association,* the authors criticized IRBs, even calling the structure dysfunctional and “more concerned with protecting the institution than research participants”(Fost & Levine, 2007; Gunsalus et al., 2006). IRBs have also been criticized for stepping outside their jurisdiction for study protocol requirements beyond what is required by regulation, but not adding any additional protection to participants(Gunsalus et al., 2006; White, 2007).

Exploring IRB Member Experiences with Justice Issues

In 2019, the Human Engagement Learning Platform (HELP) for Global Health at Emory University, in collaboration with the Focus Area for Compassion and Ethics (FACE) at the Task Force for Global Health (TFGH), conducted a qualitative landscape analysis of seven global health program directors and senior leadership at the TFGH to identify prominent ethical challenges that arise in their programmes and to explore ways that global health leaders experience, engage with, and attempt to resolve these ethical challenges. This study resulted in three main findings(Grek, Landskroener, & Lavery, 2019):

1. TFGH program directors face a range of complex and significant ethical issues and challenges in their programs and these often result in an experience of uncertainty that the authors have called "moral ambiguity".
2. The program directors' perceived need for assistance to address these ethical issues and challenges falls on a spectrum from immediate need to no perceived need.
3. Program directors recognized TFGH's unique status in the global health community and the opportunity it might afford to shape the evolution of global health ethics beyond TFGH.

The TFGH study doesn't speak directly to how IRB members might experience justice issues in proposal review, but the first two findings may have relevance to this thesis. As the third finding is specific to the TFGH, I will only address the first two findings.

Moral ambiguity is conceptualized as the uncertainty about the best ethical way forward when there is tension or conflict among multiple stakeholder interests(Grek et al., 2019). It is plausible that IRB members also experience moral ambiguity as a result of justice issues in proposal review. A 2013 study in the *Journal of Empirical Research on Human Research Ethics*

claimed their research as the first to study how IRBs view and make decisions about social risks. They found that IRBs struggle with challenges relating to social risks leaving them feeling unclear about how to proceed and that IRBs may feel conflicted concerning "how to define, interpret, apply, assess, and weigh these concerns and certain terms in the federal regulations"(R. L. Klitzman, 2013b). These experiences could be similar to the experiences of moral ambiguity among TFGH directors.

Regarding IRB experiences, there is research on conflicts with principle investigators (PIs) and power dynamics(R. Klitzman, 2011; R. Klitzman, 2012), decision-making about the quality of science behind the protocol for review(R. Klitzman, 2013a), research integrity in low- and middle-income countries (LMICs) (R. L. Klitzman, 2012), perspectives and experiences making decisions about the informed consent process(Kane & Gallo, 2017; R. L. Klitzman, 2013a; Simon et al., 2011), decision-making about coercion and undue influence(R. Klitzman, 2013b), and the decision-making process in general(Pritchard, 2011), but there is a dearth of research on experiences of justice issues in protocol review. If IRB members experience ethical challenges like those seen in the findings from the TFGH study, the implications and impact of these experiences is not well understood.

If the TFGH program directors have a spectrum of perceived need for assistance, it can be hypothesized that IRB members experiencing justice issues may also differ in their perceived need for assistance with global health justice issues that arise during proposal review. In an Office for Human Research Protections (OHRP) exploratory workshop held to address local context in single IRB review for multi-site research, it was stated that IRBs have varying levels of expertise with issues of local context such as knowledge about culture, socioeconomic status, race and ethnicity, burden to particular populations, and benefit to research community and thus

may not have mechanisms to deal with these issues at local sites ("OHRP Exploratory Workshop on single IRB review - September 2020," 2020).

In 2016, The National Institutes of Health (NIH) published a mandate that nonexempt, multisite research funded by the NIH is to be reviewed by a single IRB ("NOT-OD-16-094: Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research,"), meaning that a single IRB conducts the ethical review of studies according to the federal guidelines on behalf of all research locations, while local IRBs are left to other regulatory tasks. The purpose of this mandate was to avoid duplication of IRB efforts, minimize conflicts, and expediate the review process. The mandate was reported as successful for clinical trials, but may be problematic with areas of global health research like community-based research(Angal, Petersen, Tobacco, & Elliott, 2016). Public comment raised a number of concerns including the fact that single IRBs may not have the appropriate awareness on the sociocultural contexts of the research, local laws, demographics, and populations at risk of exploitation(Robert Klitzman, Pivovarova, & Lidz, 2017).

Sources of Guidance for IRB Review

One of the first, and arguably most important, documents in the history of medical research ethics to outline standards for human-subject research is the Nuremberg Code, developed in 1947 in Nuremberg, Germany by American judges on the Nuremberg Trial for Nazi doctors(Shuster, 1997). The Nuremberg Code outlines ten principles, primarily focusing on voluntary informed consent, risk-benefit analysis, and the participant's freedom to withdraw from the study if desired("The Nuremberg Code (1947)," 1996; Rice, 2008). While it has never been adopted fully by any country, the Nuremburg Code was highly influential in medical ethics(Grodin & Annas, 1996).

The Declaration of Helsinki followed the Nuremberg Code and was adopted by the World Medical Association for physicians in 1964 “as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data”(World Medical Association, 2013). The Declaration of Helsinki was developed in part from the Nuremberg Code principles and focuses on research investigators’ ethical obligations to research participants(Shuster, 1997). Both the Nuremberg Code and Declaration of Helsinki were examples for the current U.S. system protecting human research subjects, which requires informed consent and review of research protocols by an IRB(Shuster, 1997). This U.S. system started with the National Research Act.

The National Research Act was signed into law in 1974, and The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was created to develop ethical guidelines for research involving human subjects. This came shortly after the unethical and immoral practice of the US Public Health Service Tuskegee Syphilis Studies came to public attention. In his book, *The Ethics of Research with Human Subjects: Protecting People, Advancing Science, Promoting Trust*, David Resnik argues that “the history of the ethics of research with human subjects indicates that the regulations and ethical guidelines have evolved in response to egregious abuses of human subjects and ethically questionable research”(David B. Resnik, 2018). As one of The Commission’s acts, Institutional Review Boards were developed in 1974 under the premise that deciding whether research fulfills ethical standards should not fall solely on research investigators (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978).

The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research was also tasked with identifying the ethical principles most relevant to

biomedical and behavioral research involving human subjects and creating guidelines to ensure research conduct was in compliance with the principles. As the product of four years of discussion and deliberations by the Commission, this set of ethical principles, the Belmont Report, was published in 1979(Office for Human Research Protections, 2016a). The Belmont Report has three overarching research ethics principles that create a framework for the drafting of IRB regulations; respect for persons, beneficence, and justice. These three principles were considered comprehensive enough to capture the range of ethical values likely to arise in ethics review of research involving human subjects and are used as the guiding principles for human subjects research(Emanuel E, 2008).

The respect for persons principle provided a way to focus on the autonomy or self-determination of research participants, which The Commission thought could be ensured by enacting appropriate procedures for obtaining informed consent. Beneficence revolves around the ideas of "do no harm", maximizing possible benefits, and minimizing possible harms through use of relevant data and study design(Office for Human Research Protections, 2016a). The principle of justice involves fair procedures and outcomes in research subject selection(Office for Human Research Protections, 2016a). Considerations for justice in research are dominated by selection of human subjects regulations; The Belmont Report's third principle, justice(Eldridge, Robinson, Corey, Brems, & Johnson, 2012; Menikoff, 2013). The Belmont Report has been criticized for its lack of definite steps and failure to address practical moral problems (Emanuel E, 2008). Broader issues of global health justice may be out of scope of the Belmont paradigm.

The current, primary source of guidance for IRBs in the United States is the Federal Policy for the Protection of Human Subjects or the U.S. 'Common Rule', published in 1991, and

then revised and published again as the “final rule” in 2018. The final rule was designed to accommodate for the increasing diversity of types of studies (observation, clinical, cohort, etc.) supported by the Common Rule and coordinate policies across federal departments and agencies(Department of Homeland Security, 2017). The significant revisions to the Common Rule include updated protocols for informed consent, creation of new exempt research categories, updated IRB review procedures for US-based institutions engaging in cooperative research within the United States, and removal of the requirement for continuing review for certain ongoing research studies(Department of Homeland Security, 2017).

The Federal Policy for the Protection of Human Subjects has five subparts. Subpart A, The Federal Policy, is referred to as the “Common Rule” and is the core substance of the Federal Policy. The Common Rule discusses compliance with policy, all issues related to IRBs (membership, functions, role, approval, etc.), and procedural and regulatory practices for research. The Federal Policy also includes specific subparts (subparts B-D) that deal with research issues specific to pregnant women, human fetuses, and neonates (subpart B), prisoners (subpart C), and children (subpart D). Subpart E stipulates that institutions supported by a federal department or agency are required to comply with the Common Rule, and thus research involving human subjects requires IRB review in accordance with the Common Rule.

For the purposes of this research, I assumed that the justice issues that arise among IRB members surveyed are predominantly covered by subpart A, the Common Rule. During data collection, I did not take steps to specify whether the global health justice issues presented involved populations covered under subparts B-D of the Federal Policy, as the survey needed to be brief and was meant as a basis for the development of future research studies. IRB procedures are vastly different with research among protected populations, and it is conceivable that in

survey responses a respondent may relate the global health justice issue of interest to an experience reviewing research protocols for one of the populations in subparts B-D. The existence of subparts B-D adds to the broad scope of justice issues that may present in global health research, but this thesis will not discuss additional implications of working with these populations in the context of global health research.

The U.S. Common rule is highly influential within the international research community and has forged the evolution of research ethics guidance models around the world. This includes revisions to the Declaration of Helsinki, most recently amended in 2013, Council for International Organizations of Medical Sciences (CIOMS), and The Joint United Nations Programme on HIV/AIDS' (UNAIDS') guidance documents for ethical considerations in HIV research.

The Belmont Report provided the ethical architecture for the Common Rule, which made the principles in the Belmont Report concrete, outlining basic provisions for IRBs, informed consent, and Assurances of Compliance for all participating departments and agencies through its subparts(Office for Human Research Protections, 2016b). However, the concept of justice adopted from the Belmont Report is perceived narrowly. Literature on justice issues in global health research is dominated by fair subject selection of the protected populations that make up subparts B through D of the Federal Policy for the Protection of Human Subjects.

This is exemplified by literature on the exclusion of pregnant women in vaccine trials for infectious diseases like Zika virus, influenza, Ebola, and COVID-19 claiming it is unjust to exclude the interests of pregnant women in vaccine development because pregnant women may experience delays in treatment recommendations or are excluded from vaccination campaigns during outbreaks(Krubiner et al., 2021; Taylor et al., 2021). Literature also discusses the

underrepresentation of incarcerated individuals in health research, claiming that without ethically conducted research in prisons, medical intervention development targeted toward these populations is slowed(Ahalt, Haney, Kinner, & Williams, 2018).

Further, much global health research is conducted among underserved populations and in LMICs. The Common Rule lacks stipulations for populations outside of subparts B-D, like persons with limited English proficiency(Glickman et al., 2011), racial minorities, and indigenous peoples(Jacobs et al., 2010). There is research questioning whether lack of guidelines protecting populations like those outlined above leaves institutions vulnerable in their ability to protect marginalized populations and in deciding the appropriate response to justice issues among these populations(B. Bozeman, Slade, & Hirsch, 2009). It is further suggested that if the structure of IRBs remains unchanged, IRB failure is likely in the face of issues that do not conform with what is routinely seen in proposal review and could result in significant threats to participants' well-being(B. Bozeman et al., 2009).

From 2013 to 2018, U.S. investment in medical and health research and development (R&D) grew by 35.7%, with 2018 spending reaching $194.2 billion dollars(Research America, 2019). With this growth in medical and health R&D, there has been huge investment in global health research initiatives. Institutions are required to follow the Common Rule if they accept U.S. federal funds. Many more institutions also formally agree to apply the Common Rule to non-federally supported research.

It has been more than forty years since IRBs and the Belmont Report were created and thirty years since the Common Rule was first published. Much of the literature proposing reform to Institutional Review Board procedures revolves around the bureaucratic and organizational structure of the system (Emanuel & Menikoff, 2011; Fost & Levine, 2007; Grady, 2015). An

article published in 2009 in the *American Journal of Public Health* takes criticism a step further to discuss the rules followed by IRBs and resulting impact on IRB performance and impact on communities(B. Bozeman et al., 2009). The authors call attention to systemic issues and inadequacies with implementation of institutionalized science ethics, proposing that organizational flaws among IRBs are not paid due attention (B. Bozeman et al., 2009). Studies on the impact of IRB rules and guidelines are few and far between, especially for global health justice issues. However, Bozeman et al. (2009) discuss the Kennedy Krieger Institute Lead Paint Study on alternative, less expensive lead reduction methods for housing and how the IRB for the study followed appropriate rules for research review and approval, and yet, the study still resulted in legal questions surrounding its ethics, with arguments that the less expensive treatment is also less effective, exploits participants, and is counterintuitive to providing the best care possible(B. Bozeman et al., 2009).

Often, there is a focus on preventing potential harms to populations during data collection, like preserving identity and confidentiality(Leyva-Moral & Feijoo-Cid, 2017) or preventing trauma from emotional and sensory reliving of experiences during data collection(Btoush & Campbell, 2009). However, it is possible that steps can be taken to protect populations more holistically during the IRB review process, and little research questions what these steps might be (B. Bozeman et al., 2009). An understanding of the justice issues that arise in global health research proposal review is first needed, but there is a dearth of research on this topic. This thesis works to fill that gap.

Moral Ambiguity

It is recognized that uncertainty exists among IRB members about the decision-making process(Pritchard, 2011) and that moral ambiguity exists in the global health field, but it is not

understood if global health justice issues in proposal review result in moral ambiguity for IRB members due to the lack of guidance. Depicting moral ambiguity in global health, the TFGH study found that program directors encounter varying complex and significant ethical issues and challenges in their programs which often result in uncertainty or moral ambiguity, and current ethical guidance in global health appears to be inadequate to address the problems reported(Grek et al., 2019). Additionally, an ethics and global health course at Harvard Medical School discusses the institutionalization of global health, the resulting moral ambiguity, and prompts students to consider how fealty to hierarchical structures and systems with standard operating procedures may undermine social justice, health equity, and human rights(Sayeed & Taylor, 2020).

It is further recognized that in the global health field, experiences of moral ambiguity can be detrimental to one's physical and emotional health. A 2019 article published in the *British Journal of Psychiatry* examined ethical dilemmas and the resulting impact on medical professionals and researchers during the provision of psychosocial support for complex humanitarian emergencies. The authors raise concerns that "moral conundrums" can be particularly emotionally and morally challenging, impacting mental health and decision-making(Cherepanov, 2019).

Significance

Tools have even been created outside of the Federal Policy to help IRB members in the decision-making process(Anderson & DuBois, 2012). However, the physical and mental toll uncertainty takes on IRB members is not well-documented. If proposal review results in experiences of moral ambiguity among the very people appointed to review and monitor research for moral and ethical wrongdoings, solutions are needed.

It is critical that governing institutions recognize, acknowledge, and guide IRB appointees through experiences of moral ambiguity. IRBs existing in a state of moral ambiguity and distress is a dangerous position for both IRB members and for institutions. Experiences of moral ambiguity, distress, and unease could indicate deeper systemic issues in the design of regulations and protocols for global health research. Without clear direction and guidance on how to manage global health justice issues in the context of research ethics review, IRBs' ability to promote and defend justice in research is sub-optimal.

Broader issues of global health justice may be out of scope of the Belmont paradigm. Populations that may need protections are not accounted for in the Common Rule and broader social implications of the research, as the Federal Regulations state that IRBs should not consider "long-range" effects of the research(Cho et al., 2008) despite the importance of ethical, social, and cultural (ESC) contexts for global health research.

With the requirement for federally funded research to be reviewed by IRBs, the Common Rule dominates global health research guidance, oversight, and monitoring of research both within the United States and internationally.

Seeking approval for research is a stepwise procedure. Research ethics consultation services (RECS) can be used as an adjunct to IRBs to address justice issues beyond the regulatory framework(Havard, Cho, & Magnus, 2012), but not all institutions have RECS. If an institution does not have RECS available and if research teams submit proposals with justice issues to IRBs, even with the final rule's revisions to the Common Rule, the scope of the guidance provided in the Common Rule may be too narrow to address the justice issues(Department of Homeland Security, 2017; Otrompke, 2012). This could mean that

globally, the persons tasked with protecting the rights and welfare of research participants lack the necessary guidance to make informed judgements on research proposals.

IRBs are meant to protect populations affected by the research, but the global health research community knows very little about IRB members' experiences with global health justice issues. Only after understanding if justice issues exist in proposal review, if guidance is sufficient to resolve justice issues, and how IRB members feel about justice issues can one then suggest opportunities to better protect the peoples impacted by research through IRB ethical review.

Opportunities may include policy changes, a requirement for IRB member composition to be representative of study participant population(Barry Bozeman & Hirsch, 2005), standardization of IRBs, improved technical understanding of existing guidelines, more collaboration and deliberation on research review(Ahalt et al., 2018), new or revised guidelines, trainings and education for IRBs and research teams, updated protocol templates requiring additional contextual information on the research population, a change in the structure of research proposals and protocols altogether, or even organizational reform(B. Bozeman et al., 2009).

This thesis attempts to describe IRB members' experiences of global health justice issues outside of what is seen in the literature and outlined in available guidelines. These issues include different standards of care in HICs vs. LMICs, differences in sociocultural context and understanding between the research team and the research participants, the broader impact of the research on the host communities and not just research participants, data and specimen ownership and stewardship, and fairness of partnerships in proposed research. This will be done through three aims. First, understanding if IRBs experience global health justice issues. Second,

if IRBs experience global health justice issues, understanding what guidance they use in addressing them. And third, understanding if IRBs experience moral ambiguity or concern as a result of the global health justice issues seen. Together, these three aims attempt ***to describe the experiences of global health justice issues in research proposals reviewed by IRBs***.

METHODS

Study Design

This exploratory pilot study was conducted May 2020-March 2021 at Emory University's Rollins School of Public Health through a cross-sectional, quantitative survey. The survey was open for 12 weeks, from September 7th, 2020 to November 15th, 2020.

Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Emory University(Harris et al., 2009). REDCap is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources(Harris et al., 2009).

Sampling Frame

The survey was offered to all personnel serving on an IRB including past or current members, administrators, and chairs who were 18 or older, English-speaking, and subscribers of Public Responsibility in Medicine and Research's (PRIM&R) blog, *Ampersand*. Sampling frame was comprised of the entire membership of PRIM&R (roughly 4,000 members).The web-based survey was distributed to subscribers of *Ampersand* through a blog post linking to the anonymous, web-based survey via REDCap. The sample size was dependent on response rates.

After the initial blog post was run in *PRIM&R This Week* and posted on *Ampersand*, the blog post was re-linked approximately 7 weeks later to further drive data collection.

Sampling Rationale

PRIM&R is a membership driven non-profit organization and functions like a "trade" association composed of individuals involved in research and research administration from institutions globally. PRIM&R works to ensure ethical standards in research and provides resources to the research oversight community including IRBs, REBs, and RECs and has a large reach through their membership community, including members from more than 1,000 institutions in more than forty countries(PRIM&R, 2021). It can be assumed that most IRB members, administrators, or chairs are members of PRIM&R and subscribe to *Ampersand* blog. Other members of PRIM&R include Institutional Animal Care and Use Committees (IACUC) staff, those involved in biomedical, behavioral, social science research from public, private, federal, academic, and industrial institutions, personnel from the Research Integrity branch at the National Institute of Health (NIH), and human subjects protections programs (HRPPs) personnel(PRIM&R, 2021). Many PRIM&R members attend PRIM&R meetings, which serve as an opportunity for interdisciplinary conversation and collaboration between IRB members and the rest of the PRIM&R community yielding a broad array of perspectives on the research ethics field. PRIM&R's blog, *Ampersand*, was chosen as the method of survey dissemination due to their broad reach and large number of members involved in IRBs.

Instrument Development

The survey instrument and questions on ethical challenges experienced were informed by the landscape analysis conducted by HELP to understand ethical issues and challenges experienced

by TFGH program directors. The ten broad and pervasive categories of ethical challenges uncovered are outlined below(Grek et al., 2019).

1) Ethical misalignment between funders, implementation partners, and host country partners
2) Funding and budgets functioning as constraints on ethical decision-making
3) Concerns about the limited impact of programs on improving host country capacity
4) Concerns about missed opportunities to benefit host country communities
5) Ethical shortcomings of current guidance and practice conventions
6) Data governance/stewardship/management issues
7) Challenges with navigating complex sociocultural contexts
8) Ethical challenges related to photography in the context of global health programs
9) Reputational risks and challenges related to maintaining the trustworthiness of the program
10) Accountability for unintended consequences

These categories of ethical challenges uncovered by HELP yielded a place to start survey development and were adapted to the global health justice issues the research team suspected IRB members and chairs may experience in their review of research proposals.

After an initial development, a virtual, informal focus group discussion was conducted with three members of PRIM&R, who also currently serve on an IRB, to compile feedback on the initial survey draft with a hope of better understanding the intricacies of proposal review. Data were collected on the specific issues that present during proposal review and feedback was given on whether or not the survey draft was properly designed to learn about these issues effectively. Based on the feedback questions and response options were refined and revised. The final survey instrument contained twenty-three questions, of which, two were open-ended.

Survey Structure

The survey instrument was divided into four sections: demographic information about the respondent, features of respondent IRBs, experiences with ethical issues and concerns, and guidance used in proposal review.

Survey Section 1: Demographics

Age and gender were collected as demographic data for each participant. It was decided in the conceptualization of the survey that a focus on IRB characteristics and experiences of justice issues would be more important than extensive demographic data on the participant.

Survey Section 2: Features of IRBs

Information was collected on IRB country, current IRB membership status, role, years of experience serving on an IRB, number of protocols reviewed monthly as primary/principle reviewer, number of protocols reviewed requiring full-board review, type of IRB institution, number of protocols reviewed by institution per year, and percentage of protocols reviewed where majority of data collection is conducted outside of IRB country. Number of protocols the institution reviews per year was meant to serve as a proxy for institution size, and the percentage of proposals reviewed in which the majority of data collection is conducted outside of the country where the IRB is located, was meant to gauge the global reach of the respondent's institution and research conducted there.

Survey Section 3: Experiences with Ethical Issues and Concerns

Using the ten findings from the TFGH qualitative research, nine broad categories of global health ethical issues were developed; proposed budget for study completion, proposed benefits to host community, data and specimen ownership, data and specimen stewardship, attention to sociocultural context of research, research team knowledge, skills, and relationships

for navigation of sociocultural contexts, institutional liability or reputation, fairness of partnerships, and foresight/planning for unintended consequences of the research.

After considerable deliberation and consultation, a 5-point Likert scale with response options of never (0% of the time), Rarely (1-33%), Sometimes, (34-66%), Often (67-99%) to always (100% of the time) was chosen to assess the frequency with which respondents encounter and feel concern about the nine issues and challenges. This scale was chosen for the instrument because it was thought that there would be a larger sample size, and thus more data to analyze. I thought a greater spread from the 5 point scale (vs. a 3 point scale) would result in more descriptive data when assessing frequency. Percentages were assigned to each response option to add ordering to the measured frequencies and help specify and assign meaning as discussed in the book, *Superforecasting: The Art of Science and Prediction,* by Tetlock and Gardner(Tetlock, 2016). As the survey was administered via the web, percentages also helped balance the Likert scale to make it more like an interval scale(Bishop & Herron, 2015) for analysis.

To further explore the nature of respondents' concern and determine whether IRB members experience moral ambiguity similar to the TFGH findings of moral ambiguity among global health program directors, participants were asked if they ever approve applications that fulfill the IRB requirements, but leave them feeling uneasy or distressed, the percentage of the time they are left with that feeling, and the most common sources for their ethical unease or distress. A response indicating approval of applications but residual feelings of unease or distress would imply uncertainty about the best ethical way forward, and thus moral ambiguity.

Survey Section 4: Guidance

To assess guidance seeking behavior of IRBs on the previously listed justice issues and concerns, questions were included on sources of guidance utilized when dealing with the issues

outlined in the survey, the most helpful sources of guidance, and the ability of the guidance to help resolve justice issues.

Determining typologies

Definitions of IRB member experiences with global health research justice issues were developed using the 5-point scale associated with the response options to the questions on encountering ethical issues and feeling concern. There is literature that states that collapsing categories can be used as a way to increase cell sample size when there aren't many responses in one of the categories(DiStefano, Shi, & Morgan, 2020), but because my data are scarce across the board, I wanted to maintain what little granularity I had. Additionally, because there were 18 items in the survey that required individual responses using the Likert scale, literature supports the treatment of a Likert scale as interval data(Carifio & Perla, 2008; Carifio & Perla, 2007), and I decided to leave the scale as was originally designed.

Four categories were created. To my knowledge, categories like these have not been previously developed or defined, and thus definitions were developed based on a comparison between the response option score (1-5) for the frequency with which the issue is encountered, and the frequency the respondent feels concern about the issue (table 1).

Table 1. Operational definitions for data on experiences with global health justice issues

Category	Operational Definition
Do not encounter the issue and ***do not*** feel concern	If encounter is reported as "never (1)" and feel concern is reported "never (1)"
Do not encounter the issue, but feel concern	If encounter is reported as "never (1)" and feel concern is reported as "rarely (2)", "sometimes (3)", "often (4)", or "always (5)"
Encounter the issue and feel concern	If encounter is reported as either "rarely (2)", "sometimes (3)", "often (4)", or "always (5)" AND feel concern is reported as either "rarely (2)", "sometimes (3)", "often (4)", or "always (5)"
Encounter the issue, but ***do not*** feel concern	If encounter is reported as "rarely (2)", "sometimes (3)", "often (4)", or "always (5)" AND feel concern is reported as "never (1)"

Conceptual typologies are an analysis tool often used in social and political sciences. To create conceptual typologies, I used the "guidelines for careful work with typologies" published by Collier et. al who state that "conceptual typologies make a fundamental contribution to concept formation"(Collier, LaPorte, & Seawright, 2012). Using the categories developed in table 1, the typologies I present have two dimensions: encounter and feel concern, as shown by the 2 x 2 matrix in Table 2. In the matrix, I attempt to conceptualize the component categories of the dimensions with terms that evoke relevant concepts that may apply to the issue or respondent.

Table 2. Conceptualization of IRB experiences with justice issues in global health proposal review

		Survey respondent feelings of concern about justice issues	
		Feels Concern	**Does not feel concern**
Survey respondent encounters or does not encounter the justice issue	**Encounter**	Affected	Unaffected
	Does not encounter	Aware	Unaware

After all issues for each respondent were sorted into one of the four types, respondents were also broadly sorted into a typology of experience.

Ethical Considerations

Ethical approval for this study was obtained from Emory University Institutional Review Board in the United States (IRB00020524), and electronic-consent was obtained from each respondent via REDCap prior to the start of the survey.

Statistical Analysis

To describe the pattern of experiences with global health justice issues, descriptive statistics including frequencies, proportions, means, and range were generated using Excel version 16.45. The low response rate yielded uninterpretable standard deviations and confidence intervals, and range was reported instead. Individuals who did not fully complete the survey (n=4) were excluded from the analysis.

To analyze the nine ethical issues and challenges presented in the survey, a point value ranging from 1-5 was attributed to response options; “never (0%)” being 1 to “always (100%)” being 5. Means were taken for each issue to determine an average frequency at which the survey participants reported encountering and feeling concern about the issues.

A paired t-test was used to determine if the frequency the respondent reported encountering the issues differed from the frequency they reported experiencing feelings of

concern. The frequency of "encounter" and the frequency of "feel concern" from each respondent are not independent, and as such, were treated as a pair(Xu et al., 2017), similar to a pre- and post-treatment comparison. With a small sample size, I recognize that the logic behind a paired t-test is not sound to operationalize, and a p-value is not a reliable measure of statistical significance. However, I still wanted to practice and use a statistically accepted method to analyze my results. A p-value of ≤ 0.05 was considered statistically significant, showing a difference between the frequency of encountering the issues and feeling concern about the issues.

I anticipated doing a cross-comparison with demographics and types, but given the limited sample size and the data received, I decided that comparisons wouldn't yield interpretable results and did not perform them. See the limitations section (page 49) for a deeper discussion of analytic strategy regarding small sample size.

FINDINGS

Although PRIM&R has a large membership community and *Ampersand Blog* has a wide audience of subscribers, response rate was low, with 11 individuals starting the survey and only 7 individuals fully completing it. Thus, the results are based on a sample of n=7. With this limited sample size, it is difficult to confidently characterize the types of experiences. However as this is an exploratory pilot study, the data will still be used to attempt to characterize the difference in the types of global health justice issue experiences among IRB members for use in future study development.

My findings are broken down into six sections: respondent demographics coupled with characteristics of IRBs, global health justice issues and concerns, typology of experiences, guidance, moral ambiguity, and additional relevant issues for consideration noted from open-response questions.

Sections 1 and 2: Respondent Demographics and Characteristics of IRB Work

Respondent demographics and characteristics of each respondent's IRB institution and work are shown in Table 3. Of the 7 respondents, 71.4% (n=5) identify as female, 14.3% (n=1) identify as male, and 14.3% (n=1) selected "prefer not to answer" when asked their gender. 42.9% (n=3) of respondents were between 56 and 65 years of age, with respondents selecting age bins ranging from 26-35 years to 56-65 years.

The majority (71.4%) of respondent IRBs were located in the United States, with one (14.3%) respondent located in Canada and one (14.3%) respondent located in Peru. 57.1% (n=4) reported their primary role as and IRB member and the remaining 42.9% reported their role as administrator. All respondents reported that they are currently serving in their role. Only one respondent reported serving on multiple boards.

Respondents were sampled from 4 different institution types, with the most common being universities. Years of experience serving on an IRB ranged from 3-5 years to 11+ years, with the majority (42.9%) of respondents reporting serving for 11+ years. The average number of protocols reviewed per month where the respondent was the primary/principle reviewer ranged by each respondent ranged from 0 to 100, with a total sample mean of 25.5 protocols per month. Of the proposals reviewed per month as the primary/principle reviewer, the mean that required full board review was 2.2 proposals per month, and the percentage that required full board review ranged from 0% to 83%. When asked the percent of proposals where the majority of data were collected in a country outside of the country where their IRB was located, 1 respondent answered none, 1 respondent answered 1-5%, 3 respondents answered 6-20%, and 2 respondents answered 41-60%.

Table 3. Demographic characteristics of survey participants, characteristics of survey participant work with their IRB, and characteristics of the IRB the survey participant serves

Characteristics		Respondents (n=7) Frequency / mean n (%) / mean (range)
PARTICIPANT DEMOGRAPHIC CHARACTERISTICS		
Age		
	18-25	0
	26-35	1 (14%)
	36-45	2 (29%)
	46-55	1 (14%)
	56-65	3 (43%)
	65+	0
	Prefer not to say	0
Gender		
	Male	1 (14%)
	Female	5 (71%)
	Prefer Not to Say	1 (14%)
CHARACTERISTICS OF WORK DONE FOR IRB/REB/REC		
Currently Serving on an IRB		
	Yes	7 (100%)
	No	0
Primary IRB Role		
	Member	4 (57%)
	Chair	0
	Co-chair	0
	Administrator	3 (43%)
	Other Role	0
Serves on more than 1 IRB/REB/REC		
	Yes	1 (14%)
	No	6 (86%)
Years of Experience		
	0 to 2	0
	3 to 5	2 (29%)
	6 to 8	0
	8 to 10	2 (29%)
	11+	3 (43%)

Mean protocols reviewed per month as principle/primary reviewer	25.6 (0-100)
Mean protocols requiring full board review per month	2.2 (0-6)
CHARACTERISTICS OF IRB, REB, REC	
Institution type*	
Hospital-based	2
University	6
NGO	1
Government Agency	1
Private organization/philanthropy	0
Commercial IRB	0
Other	0
Country of IRB	
United States	5 (71%)
Canada	1 (14%)
Peru	1 (14%)
Percent proposals where majority of data collection is in a country outside of country where IRB located	
None	1 (14%)
1-5%	1 (14%)
6-20%	3 (43%)
21-40%	0
41-60%	2 (29%)
61-80%	0
81-99%	0
100%	0
# protocols institution reviews per year	
0-50	1 (14%)
51-100	0
101-200	2 (29%)
201-300	0
301-400	0
401-500	0
501+	4 (57%)

Section 2: Experiences with Global Health Justice Issues and Concerns

*Institution type was a select all that apply question

Table 4 shows a side-by-side comparison of the distribution of responses for the nine justice issues presented in the questionnaire. The table is ordered top to bottom from most frequently encountered/felt concern to least frequently encountered/felt concern.

The adequacy of the proposal's attention to the sociocultural contexts of the research is most frequently encountered with 2(28.6%) individuals reporting they rarely encounter the issue, 2(28.6%) reporting they sometimes encounter the issue, 2(28.6%) reporting they often encounter the issue, and 1(14.3%) reporting they always encounter the issue (table 4). The issue least frequently encountered is the adequacy of the proposed budget for ethical completion of the study with 4 (57.1%) reporting they never encounter the issue, 2 (28.6%) reporting they rarely encounter the issue, and 1 (14.3%) they sometimes encounter the issue (table 4). Two issues (the adequacy of the foresight/planning for potential unintended consequences of the research reflected in the proposal and data and specimen ownership) had the same mean frequency.

The issue with the highest reported frequency of concern was also the adequacy of the proposal's attention to the sociocultural contexts of the research. No individual reported never feeling concern, 3 (42.9%) individuals reporting rarely feeling concern, 3 (42.9%) individuals reporting sometimes feeling concern, no individuals reporting often feeling concern, and 1 (14.3%) individual reporting always feeling concern. The adequacy of the proposed budget for ethical completion of the study was the issue encountered with the least average concern with 5 (71.43%) reporting they never feel concern, 2 (28.6%) reporting they rarely feel concern, and no participant reporting sometimes, often, or always. There were three instances where the average frequency of concern was tied between issues.

Table 4 shows that while the issues ranked with highest and lowest average frequency for encountering and feeling concern match, average frequency of encountering and feeling concern

for other issues do not match in ranking. Institutional liability, or the reputation of your institution being damaged, as a result of the proposed research is ranked 7th for average frequency encountered, but is tied for 2nd for feelings of concern.

Table 4. Side-by-side comparison of the distribution of responses (frequency and percent) for the 9 ethical issues presented in the questionnaire ordered by the issue that is averaged to be most frequently encountered or felt concern about to least frequently encountered or felt concern about

		Frequency *Encounter* Issues							Frequency *Feel Concern* About Issues				
		Never (0%)	**Rarely (1-33%)**	**Sometimes (34-66%)**	**Often (67-99%)**	**Always (100%)**			**Never (0%)**	**Rarely (1-33%)**	**Sometimes (34-66%)**	**Often (67-99%)**	**Always (100%)**
	Issue/Concern	n (%)	n (%)	n (%)	n (%)	n (%)		**Issue/Concern**	n (%)	n (%)	n (%)	n (%)	n (%)
1	**Adequacy of the proposal's attention to the sociocultural contexts of the research**	0	2 (28.6%)	2 (28.6%)	2 (28.6%)	1 (14.3%)	1†	**Adequacy of the proposal's attention to the sociocultural contexts of the research**	0	3 (42.9%)	3 (42.9%)	0	1 (14.3%)
2	**Research teams' knowledge, skills, and relationships for navigation of the sociocultural contexts of the research**	1 (14.3%)	1 (14.3%)	2 (14.3%)	2 (28.6%)	1 (14.3%)		**Research teams' knowledge, skills, and relationships for navigation of the sociocultural contexts of the research**	0	2 (28.6%)	4 (57.1%)	1 (14.3%)	0
3	**Data and specimen stewardship**	2 (28.6%)	2 (28.6%)	2 (28.6%)	0	1 (14.3%)	2‡	**Data and specimen stewardship**	2 (28.6%)	2 (28.6%)	2 (28.6%)	0	1 (14.3%)
4§	**The adequacy of the foresight/planning for potential unintended consequences of the research reflected in the proposal**	1 (14.3%)	4 (57.1%)	1 (14.3%)	1 (14.3%)	0		**The adequacy of the foresight/planning for potential unintended consequences of the research reflected in the proposal**	0	4 (57.1%)	3 (42.9%)	0	0

† Issue is tied with subsequent issues
‡ Issue is tied with subsequent issues
§ Issue is tied with subsequent issues

	Data and specimen ownership	2 (28.6 %)	2 (28.6%)	2 (28.6%)	1 (14.3%)	0		**Institutional liability, or the reputation of your institution being damaged, as a result of the proposed research**	0	4 (57.1%)	3 (42.9%)	0	0
5	**The fairness of the partnerships and collaborations associated with the proposed research**	2 (28.6 %)	2 (28.6%)	3 (42.9%)	0	0	3	**The fairness of the partnerships and collaborations associated with the proposed research**	2 (28.6%)	2 (28.6%)	3 (42.9%)	0	0
6	**Adequacy of the proposed benefits for host community capacity building**	3 (42.9 %)	2 (28.6%)	2 (28.6%)	0	0	4 **	**Data and specimen ownership**	3 (42.9%)	2 (28.6%)	2 (28.6%)	0	0
7	**Institutional liability, or the reputation of your institution being damaged, as a result of the proposed research**	3 (42.9 %)	3 (42.9%)	1 (14.3%)	0	0		**Adequacy of the proposed benefits for host community capacity building**	3 (42.9%)	2 (28.6%)	2 (28.6%)	0	0
8	**Adequacy of the proposed budget for ethical completion of the study**	4 (57.1 %)	2 (28.6%)	1 (14.3%)	0	0	5	**Adequacy of the proposed budget for ethical completion of the study**	5 (71.43%)	2 (28.6%)	0	0	0

** Issue is tied with subsequent issues

Section 3: Typology of Experiences

While the data are limited, they suggest there are different categories of experiences among IRB, REB, and REC members and administrators. In this section, I describe the results of my attempt to categorize respondent responses to justice issues (table 5) and the respondents themselves (table 6) into the 4 categories of experiences defined in the methods section (table 1).

Adequacy of the proposal's attention to the sociocultural contexts of the research is the only issue with 100% of respondent responses in agreement, placing it into type 3 (table 5). The remaining issues have one or more respondents whose combination of response options place them into more than one type. Two issues have the least agreement: Adequacy of the proposed budget for ethical completion of the study and adequacy of the proposed benefits for host community capacity building. These two issues have at least one respondent response sorted into each type (table 5).

Overall, type 3 has the most responses (65%), followed by type 1 (16%), then type 2 (11%), and lastly, type 4 (8%) (table 5).

Table 5. Number (n) and percent (%) of respondent responses categorized into typologies 1-4 for each issue presented in the survey and total number (n) and percent (%) of responses in each type

	Type 1 (Unaware) - Do not encounter the issue and *do not* feel concern	**Type 2 (Aware) - Do not encounter the issue, but do feel concern**	**Type 3 (Affected) - Do Encounter the issues and do feel concern**	**Type 4 (Unaffected) - Do Encounter the issue, but *do not* feel concern**
			Frequency	
Issue/Concern	n (%)	n (%)	n (%)	n (%)
Adequacy of the proposed budget for ethical completion of the study	3 (42.9%)	1 (14.3%)	1 (14.3%)	2 (28.6%)
Adequacy of the proposed benefits for host community capacity building	2 (28.6%)	1 (14.3%)	3 (42.9%)	1 (14.3%)
Data and specimen ownership	2 (28.6%)	0	4 (57.1%)	1 (14.3%)
Data and specimen stewardship	1 (14.3%)	0	5 (71.4%)	1 (14.3%)
Adequacy of the proposal's attention to the sociocultural contexts of the research	0	0	7 (100.0%)	0
Research teams' knowledge, skills, and relationships for navigation of the sociocultural contexts of the research	0	1 (14.3%)	6 (85.7%)	0
Institutional liability, or the reputation of your institution being damaged, as a result of the proposed research	0	3 (42.9%)	4 (57.1%)	0
The fairness of the partnerships and collaborations associated with the proposed research	2 (28.6%)		5 (71.4%)	0
The adequacy of the foresight/planning for potential unintended consequences of the research reflected in the proposal	0	1 (14.3%)	6 (85.7%)	0
TYPE TOTAL	10 (16%)	7 (11%)	41 (65%)	5 (8%)

One individual had a statistically significant difference (p=0.04) between the frequency with which they encountered issues compared to the frequency of their reported concern about the issues. After examining the data, that individual was placed in type 2: do not encounter the issues, but do feel concern (Table 6). The remaining 6 individuals were found to have no statistically significant difference between the frequency with which they encountered issues

compared to frequency they felt concern, and were categorized into type 3: do encounter the issues, but do feel concern (Table 6).

Table 6. Distribution of survey respondents across the 4 typologies of experiences

Typology	Frequency n (%)
Type 1 (Unaware)	0
Type 2 (Aware)	1 (14.3%)
Type 3 (Affected)	6 (85.6%)
Type 4 (Unaffected)	0

Section 4 Guidance

Respondents reported seeking guidance from the CIOMS, published scientific literature, specific national guidelines like the Canadian TCPS-2 Guidelines or Indian Council of Medical Research Guidelines, previous reviews, current IRB deliberations, both non-IRB and IRB colleagues, the PI/investigator, the local IRB for the proposal, and the Common Rule (table 7).

The most commonly reported sources of guidance were IRB colleagues, the PI/investigator(s) for the proposed research, IRB deliberations (i.e., the meeting itself), and other specific national guidelines or regulations (e.g., Canadian TCPS-2 Guidelines, Indian Council of Medical Research Guidelines, etc.). The least commonly reported source of guidance was the Declaration of Helsinki (table 7).

Table 7. Sources of guidance for the ethical issues outlined in the survey instrument

Source of Guidance	**Frequency**	
	n	**%**
IRB colleague	5	14%
The PI/investigator(s) for the proposed research	5	14%
In IRB deliberations (i.e., the meeting itself)	5	14%
Other specific national guidelines or regulations (e.g., Canadian TCPS-2 Guidelines, Indian Council of Medical Research Guidelines, etc.)	5	14%
The U.S. "Common Rule" Regulations (including sub-parts, if relevant)	3	9%
Previous IRB reviews	3	9%
Non-IRB colleague	3	9%
The local IRB for the proposal	3	9%
Published scientific literature	2	6%
The CIOMS Guidelines	1	3%
The Declaration of Helsinki	0	0%

While respondents reported seeking guidance from ten different sources, only five sources of guidance were selected as most useful. Two (29%) respondents reported IRB colleagues and 2 (29%) reported IRB deliberations as most useful, while 1 (14%) respondent each reported CIOMS guidelines, the PI/investigator(s), and the local IRB as most useful (table 8).

Table 8. Most useful source of guidance reported by respondents for reviewing and making decisions about the issues presented in the survey instrument

Most Useful Source of Guidance	**Frequency**	
	n	(%)
IRB colleague	2	29%
IRB deliberations	2	29%
The CIOMS Guidelines	1	14%
The PI/investigator(s) for the proposed research	1	14%
Local IRB for the proposal	1	14%
The U.S. "Common Rule" and subparts	0	0%
The Declaration of Helsinki	0	0%
Other specific national guidelines or regulations	0	0%
Previous IRB reviews	0	0%
Published scientific literature	0	0%
Non-IRB colleague	0	0%

Following the question on most useful source of guidance, respondents were asked level of agreement that the source of guidance indicated as most useful for making decisions about the nine categories of ethical issues helped to resolve concerns about the issues. Four (57%) individuals selected agree, 1 (14%) selected neither agree nor disagree, 1 (14%) selected disagree, and 1 (14%) selected strongly disagree.

Section 5: Moral Ambiguity

Of 7 respondents, 6 (86%) reported that they approved applications that fulfilled the necessary requirements, but left them feeling uneasy or distressed, ethically. All (n=7) respondents reported an average of 1-5% of applications approved left them with that feeling.

Table 9 shows the breakdown of most common sources of ethical unease or distress among respondents' approved proposals. Proposed budgets for ethical completion of the study, data and specimen ownership, and attention of proposal to sociocultural context of the research were not reported as common sources of ethical unease or distress.

Table 9. The most common sources of ethical unease or distress as reported by survey respondents

Issue/Concern	Frequency (percent) n (%)
Proposed budgets for ethical completion of the study	0
Impact on host communities	2 (18%)
Data and specimen ownership	0
Data and specimen stewardship	2 (18%)
Attention of proposal to sociocultural context of the research	0
Research team's ability to navigate sociocultural contexts of the research	2 (18%)
Institutional liability or damage to the reputation of your IRB as a result of the proposed research	2 (18%)
Partnerships and collaborations associated with the proposed research	1 (9%)
Foresight/planning for potential unintended consequences of the research reflected in the proposal	2 (18%)
I do not feel ethical unease or distress	0
Other	0

Section 6: Additional Relevant Issues for Consideration - Open-response Answers

Two respondents (29%) noted additional issues for consideration through answers to open-ended questions. The remaining respondents did not provide any additional context or issues for consideration.

The first respondent brought up three points, but did not indicate if the issue listed was a justice issue encountered, a concern felt, or both:

1) *"The relationship between my IRB review and the role of the in-country REC review"*

2) *"Concern that IRB members, as a whole, do not conduct in-depth reviews, they rely on the one or two who are always detailed"*

3) *"In the absence of local guidance, issues like data stewardship are left to the discretion of the IRB"*

Upon being asked if there is anything else the researchers should know, the second respondent noted:

> *"It's difficult to draw the line on where IRB concerns should end for studies determined to be exempt. Our role at the IRB for these studies is to make the determination without imposing unnecessary burdens on researchers, but often these studies are conducted by teams without much experience in the host community. While the risks associated with these studies are low, there's sometimes room for improvement in subject protections."*

DISCUSSION

This section is divided into three sections to best discuss IRB member experiences with justice issues in the context of my findings: discussion of typologies, difficulties with typologies, and variety in experiences.

Discussion of Typologies

Four different types were created: "affected", "unaffected", "aware", and "unaware" (table 2). Participants in this study were only placed into the "affected" and "aware" types (table 6), but respondent responses to individual issues span the 4 types (table 5). In this section, I discuss IRB member experiences that may place them within a certain type and the possible implications. Following discussion on typologies, I briefly cover implications of variety in findings, challenges of developing typologies, and end with a discussion on moral ambiguity findings.

Typology 3: Affected

In the ideal world of research, IRB members encounter justice issues in proposal review, but do not feel concern because they have the appropriate guidance, knowledge, resources, and support to resolve concerns. "Affected" was the most common type from this data (tables 5 and

6). This is the type where respondents and responses were placed if both encountering and feeling concern about the justice issue were reported. As it seems that IRB members should have no concerns or minimal concerns during proposal review, this finding lends a bit of unease on my part, and could 1) suggest that IRB members are missing one or more of the tools that help resolve global health justice issues, or 2) suggest that investigators do an excellent job anticipating potential implications for research participants and address them proactively. In this subsection, I address my findings in the context of this type and the applicability and usefulness of available tools.

Strikingly, no respondent listed the Common Rule as the most useful guidance source for making decisions about the justice issues (table 8) , even though most respondent IRBs were reported as US-based (table 3).

Further, two surprising sources of guidance were IRB colleagues and the local IRB for the research. Both were also listed by some respondents as most useful in resolving the justice issues outlined. While no respondent selected the Common Rule as most useful, interestingly, almost half of respondents did not agree that the other guidance sources selected as most useful helped resolve justice issues.

This combination of findings is difficult to interpret and explain because there is an emphasis on the importance of regulatory frameworks, like the Common Rule, as overarching guidelines for research review(Breault, 2006). My findings instead show potential gaps in the current regulatory framework and suggest either 1) the current regulatory paradigm for global health research review is not sufficient or 2) is too static for IRB members to resolve complex justice issues. Both indicate a need to re-evaluate provision of guidance for global health research review. Previous research examining alignment of IRB discussions with the Common Rule ethical framework has found that IRBs did not always cover all criterion mandated by the Common Rule in their deliberations(Lidz et al., 2012). I cannot help but wonder if this is because

the criterion covered by the Common Rules is not applicable to the breadth of research IRBs review, especially that of global health research.

Without more comprehensive data, I cannot make any definite recommendations for specific modifications to the regulatory framework for any of the typologies, but I can lay out a few potential directions that could be taken with further research results.

To start, the demand of the regulatory framework for particular attention to specific vulnerable populations leads to a lack of attention to other marginalized or minority groups and thus, a dearth of guidance on populations that also require special attention and resources during research(Levine et al., 2004). Revised, new, or additional guidance may provide protections for research among marginalized, underserved, and minority populations outside of those specified in subparts B-D of the Common Rule.

A comparison of experiences between IRB members serving in North America (HICs) to those serving on non-North American countries (primarily LMICs) may be of particular importance to explore for further modifications to guidance. If, with further research, experiences with global health justice issues occur mostly in countries outside of the United States, provision of guidance for international global health research may need to be updated or specialized guidance for global health and international research review should be provided.

John Hopkins University developed the Johns Hopkins Fogarty African Bioethics Consortium to address the need for global bioethics to keep pace with the growth of global research in LMICs(John Hopkins Bloomberg School of Public Health), and it would be informative to explore the justice issues addressed in the Consortium, but from the perspective of IRB members, to understand how experiences with justice issues between researchers, researched populations, and IRB members align.

Bozeman et al. state “The typical professional and policy response to calamities involving human participants in research is to layer on more ethical guidelines or strictures.”(B. Bozeman

et al., 2009) Along this note, two directions to resolving the gap in the current regulatory framework that are not centered around guidance are the availability of specialized trainings focusing on relevant and current global health research review and more deliberative engagement in proposal review processes. Supporting literature suggests there is a need for more sensitivity and awareness about justice issues, and that clarification can assist IRBs to make decisions that require them to define, interpret, assess, and weigh issues(R. L. Klitzman, 2013b).

Further research may want to pay particular attention to the justice issues I found to have the highest level of agreement in typology and the corresponding IRB or participant characteristics. Adequacy of the proposal's attention to the sociocultural contexts of the research was most frequently experienced with respondent responses unanimously placing it into the type 3 typology. This level of agreement indicates that it is perhaps one of the more troubling justice issues in proposal review. In reference to settling conflicts among IRB members regarding justice issues, a blogger on *Ampersand* equates the role of an IRB administrator to a tightrope walker; always trying to balance protections for stakeholders(Hahn, 2010). A system where IRB members can report troublesome justice issues without judgement or fear of repercussions could yield relevant data to inform restructuring, revisions, and development of trainings and guidance as global health research evolves.

Typology 2: Aware

As the conceptualization of this typology implies, feelings of concern without encountering justice issues in proposal review indicates knowledge about, or at the very minimum, "awareness" of, the justice issues. This was the type with the second highest frequency (tables 5 and 6).

Within the scope of this study, I did not explore the reasons for not encountering the justice issues; however, I will still outline the characteristics of the one respondent whose responses placed her into this typology and what they could mean in the context of this type.

The participant in this typology is the youngest of all study participants. In comparison to the other participants, she reported fewer years of experience serving on an IRB, but a number of research proposals cross her desk (average of 10 per month). The size of the institution and scope of IRB review at her institution are large and she likely reviews global health research. Knowing these data, one next may ask why her responses categorized her as “aware”.

Potential explanations include 1) Characteristics like age, years of experience, institution size, and number of proposals reviewed per month could result in little exposure to the justice issues outlined. I hypothesize that while this explanation could align with my respondent, the size of her institution and probable review of global research minimize the likelihood of this explanation; 2) IRB guidelines lack stipulations about the global health justice issues outlined in the questionnaire, thus IRB members do not see them as within their purview. They do not report encountering them, but do feel residual concern due to the inability to acknowledge or address the issues. 3) The structure of research applications does not solicit information from proposals that allow IRB members to discern the justice issues, and thus they report not encountering justice issues.

Like the “affected” type preceding this subsection, increased training and improved, comprehensive guidelines are needed. Because I already covered the need for guidance in typology 3, I would like to further discuss what training might look like in this subsection.

Literature shows that among research studies posing greater than minimal risk, IRBs do not always explore whether the application adequately addresses the risks or minimization of the risks(Lidz et al., 2012). The exact reasons why this occurs are not clear; however, it could be because of points 1 or 2 in the previous paragraph. Training may inform IRB members about justice issues not outlined in the current regulatory framework. Qualitative research findings from a study conducted on social risks support this, stating that “IRB chairs, members, staff, policy makers, and researchers may benefit from educational efforts targeted at addressing these

realms, including the complexities and ambiguities involved in definitions and applications of these terms, to increase awareness and sensitivity about these issues."(R. L. Klitzman, 2013b) The development of an adaptable training package to address justices issues in the context of the needs of individual institutions seems like a feasible option once research on IRB member experiences is available.

Point 3 indicates a need for updated research applications. A revised research proposal template might require investigators to display awareness about the justice issues that endanger human subjects, like sociocultural contexts of the research and the larger impact of the research. This might look like a section in the proposal specific to justice issues and mechanisms to mitigate them. A solution like this serves a double purpose; IRB members can more clearly discern justice issues and research teams may be more prepared to address justice issues if arise during research with IRBs on standby to assist if needed.

Typology 4: Unaffected

I see two potential reasons why an IRB member may experience problems with justice issues in proposal review and remain unconcerned: 1) IRB members may not feel concern because they consider the justice issues that arise in proposal review as outside their ability to resolve, and yet the issues still do not elicit concern; or 2) IRB members encounter justice issues in proposal review, but view them as out of their scope of practice, believe someone else may deal with the issues, and do not feel concern.

Ensuring representation of the communities and stakeholders who might be at risk of injustices could result in more cultural humility and empathy towards research populations. The single IRB review requirement for multi-site research makes it increasingly important to appoint IRB members representative of research populations(Barry Bozeman & Hirsch, 2005) and promote community representation through collaboration. In their manuscript, Angal et al. call for collaboration between single IRB and tribal ethics review boards on community-based study

approaches in Tribal Nations where single IRB review may undermine tribal governance and oversight(Angal et al., 2016).

This leads me to my next point; single IRB review is not one size fits all. In my findings, the open-ended response stating that "in the absence of local guidance, issues like data stewardship are left to the discretion of the IRB" exemplifies this perfectly. Interestingly, Angal et al. also bring up data ownership, mentioning historical instances where non-tribal research teams produced publications that resulted in stigmatizing misrepresentation of the tribes because tribal partners could not advocate for the endorsement of study data as tribal property(Angal et al., 2016).

Angal et al. offer valuable insight on collaboration as a solution to harmful research outcomes, stating that joint reviews for certain study types allows for the exchange of information and maximize IRB ability to assess proposals for justice issues(Angal et al., 2016). However, it is likely that effective cross-collaboration within the global health research community requires revised guidelines and deeper systemic changes to IRB structure.

An alignment in experiences of justice issues, like data stewardship, between IRB members and research populations, indicates a need to further explore experiences of IRB members to identify justice issues that could be averted in proposal review and enact steps to prevent harms like those that Angal et al. describe.

Typology 1: Unaware

It is heartening to find that no respondent was typed as "unaware" in this study. However, I hypothesize that because I did find individual responses that were typed as "unaware", a study with a larger sample size may reveal a number of individuals in this type. For this reason, I will still briefly discuss implications of the "unaware" type, but not go into detail about possible solutions because of the comprehensiveness of the previous three sections and limitations in the design of the survey instrument.

Returning to the Task Force for Global Health qualitative landscape study results, if TFGH program directors report experiencing justice issues like those presented in the questionnaire, but IRB members do not, there may be a disconnect between program managers or research teams and IRBs. The question is then, how and where does this disconnect happen? While the reasons for not encountering justice issues could have similar explanations as those found under type 2, "aware", possible reasons for not feeling concern are more difficult to explain, and easy answers for this typology are not available.

Before delving into possible reasons, I first need to highlight a logical loop in this type not accounted for in the survey design. The survey should have included general awareness or knowledge about the issues as global health justice issues. With this study's data, it is unknown if 1) IRB members report not encountering the issues and are simultaneously *unaware* of the issues, resulting in no concern; or 2) IRB members *are aware* of the justice issues, report not encountering the issues, and even with awareness do not feel concern.

Lack of awareness is easier to interpret. If an IRB member is unaware of an issue, they are not likely to feel concern or recognize if they encounter it. In this scenario, my interpretation and recommendations still revolve around guidance, training, and application structure like outlined under the previous subsections. Feelings of concern may arise as awareness grows.

Awareness accompanied by a lack of concern has more than one potential explanation. The easy explanation is that IRB characteristics such as number of protocols reviewed per month, scope of global health work, or institution size and type do not put IRB members in situations where they review proposals with global health justice issues, and thus have no reason for concern about the proposals they review. The more complicated explanation is similar to the third point in the previous typology; the structure of research applications does not allow for IRB members to discern the justice issues, thus they report not encountering justice issues and being unconcerned, even though they are aware. A third, and even more complicated, explanation

revolves around the scope of IRB practice, as defined by regulatory frameworks. If IRB members view the justice issues presented as out of their scope of practice, the issues are not within their purview, and they may not report encountering them. As a result of viewing the issues outside of their purview, IRB members also do not report feeling concern.

All scenarios under the "unaware" typology are a cause for concern among the research community, and we should be asking what harms happen to research populations if justice issues in proposal review go unnoticed by the IRB reviewer.

Difficulties with Typologies

In this section, I would like to further explain the process of assigning typologies and what I learned. Categorizing, labeling, and assigning value through a conceptualization of categories was not easy. A typology is supposed to be multidimensional, clear, exhaustive, and descriptive, but with a limited sample size, it felt arbitrary, like it was lacking any reason or a system. I followed the template produced by Collier et. al, who state that the goal is to encourage scholars to be more "rigorous" and "creative" with concepts and contribute to the evaluation of explanatory claims(Collier et al., 2012). Small sample size limited my ability to back my exploratory claims or discern granularity in types. However, I can guess that if individual responses to justice issues fall into all of the different typologies of experiences, IRB members also fall into each of the typologies of experiences. It is likely that the sample size for this study was too small for there to be evidence of this phenomenon. These typologies may serve as a conceptual starting point and identify points of focus for future studies to map the variation in experiences of justice issues and begin to think of what the variation could mean.

Variety in experiences

I would also like to speculate about the variability in these data. There was not always an alignment between how frequently the sample population encountered an issue and how frequently they felt concern. For example, institutional liability, or the reputation of their

institution being damaged, as a result of the proposed research was reported as more frequently "felt concern about" than "encountered". This may have to do with the fact that almost half of survey respondents are administrators who may have different concerns about justice issues than members. While IRB administrators may still review proposals, their primary role is to oversee and manage the IRB system and operations, including ensuring that applications are in compliance with federal, state, and institution laws. This may mean that they experience a greater frequency of concern about institutional liability. Further, IRB administrators hold a great deal of power, especially if the IRB committee is in disagreement about an ethically challenging situation(Hahn, 2010).

The primary role of an IRB member is to review research. While they may encounter and feel concern about administrative issues like institutional liability, they may not teeter between obligations to different stakeholders in the research community in the same way as IRB administrators, and thus may experience justice issues differently. In future research, I recommend either creating two different surveys, one targeted to IRB member experiences of justice issues and one for IRB administrator experiences of justice issues, or cross-comparing the same justice issues between administrators and members. Similar to the TFGH study findings, it seems that IRB personnel may also experience a spectrum of justice issues as well as perceived need for assistance.

Adequacy of the proposed budget for ethical completion of the study and adequacy of the proposed benefits for host community capacity building show further variation. Responses to these two issues were spread across the different typologies, showing that there may be conflicting experiences. This could be a further result of the different roles (i.e. administrator vs. member), but there are also other potential explanations for differing experiences. For example, IRBs in different regions may require individualized or specialized guidance and training for

proposal review. It also could indicate that IRBs need to specialize in areas of research like global health to better serve the research teams they work with.

Moral ambiguity

In addition to the typologies, it is important to discuss findings on moral ambiguity. Responses to the open-ended questions (findings section 6) indicate that IRB members can experience moral ambiguity during proposal review, especially in instances requiring communication and collaboration between IRBs and in-country review teams or research teams. This may imply that the roles of local and single IRBs are not clearly defined. Like the preceding sections, solutions could include modifications to guidance and training procedures.

Difficulties determining a set point for "where IRB concerns should end" for exempt studies, implies the IRB member experiences uncertainty about best methods for minimizing justice issues among research populations, while also limiting burden to research teams.

Without additional contextual information accompanying open-ended question responses, my ability to suggest implications is limited, but the very existence of concerns for minimal risk studies indicates a problem. If IRB members are uncertain where their concerns should end, the concept of "minimal risk" may need to be narrowed, standardized, or more clearly defined.

Defining minimal risk is not a new discussion topic(D. B. Resnik, 2005). Minimal risk standards in guidelines span different international research regulations, which have varying definitions. In addition to a revised definition, it may be beneficial for the review of global health research to reach an international consensus on the definition(Kopelman, 2004). Currently, survey procedures, interview procedures, observation, and even research involving benign behavioral interventions that maintain anonymity are exempt under the revised Common Rule(Office for Human Research Protections, 2016b). These data collection methods are frequently used in global health research, and if one IRB member experiences moral ambiguity,

it is likely others do too, indicating a need for re-evaluation and/or elaboration on exemption categories outlined in the revised Common Rule.

LIMITATIONS

The instrument for data collection was designed using qualitative data that was related to this study, but not explicitly created for the development of the global health justice issues among IRBs. Further, the design of the survey instrument was centered around justice issues known to exist in global health research, but did not restrict participants to those proclaiming experience in global health research review. Thus, not all findings may be directly applicable to the global health field.

PRIM&R members and *Ampersand* subscribers were used for the source population; however response rates were low, yielding a small sample (n=7). The small sample size posed limitations for analyzing the data. For example, determining definite classifications for typologies of respondents was a challenge. Ability to perform a statistically sound analysis, operationalize the logic of paired t-testing, and report significance given p-values was impaired. I recognize and understand that a p-value of 0.05 from the analysis of 9 data points is not robust enough to make any definite conclusions, but also did not see any better way to conduct the analysis with the limited sample size. Further, the data did not allow for stratification to compare between different groups in the sample, an analysis I previously planned to conduct.

The PRIM&R reader population is mainly concentrated at institutions in North America, and thus the results may not be representative of the opinions of IRBs in LMIC countries, who might have different views of justice issues in global health research. Further, while questions asked about global health justice issue experiences, all individuals in the targeted population may not work primarily with global health research proposals. This may limit the depth of the data obtained on global health specific questions. However, this population was chosen in order to

elicit a broad range of responses from both global health and non-global health IRB members, chairs, and administrators.

To keep the survey concise and minimize non-response, the survey was limited to 23 questions, and not all questions of interest to the research team were asked. The format of survey (web-based), limited number of questions, and close-ended question format may have impacted the richness of data. For example, it is impossible to know the unwritten reasons that might exist as to why different issues or individuals fall into different typologies. However, this was an exploratory pilot study, and the results can be used to develop more comprehensive, large-scale studies among global IRBs.

Conclusion

In this thesis, I explored how Institutional Review Board, Research Ethics Board, and Research Ethics Committee members, chairs, and administrators experience global health justice issues in the research proposals they review through analysis of results from a web-based survey. Nine ethical issues were presented. Over half of the issues were reported as common sources of ethical unease or distress. Four typologies of experience were developed and defined. Each of the respondents and nine ethical issues presented in the survey instrument were analyzed and sorted into the four typologies. The majority of responses to the ethical issues were conceptualized as "affected" and "aware". However, almost half of participants indicated that the guidance they marked as most useful in reviewing and making decisions about the issues was either neutral or not helpful with resolving concerns about the ethical issues.

If this is a fair representation of the experiences that exist in the IRB population at large, regardless of if individuals encounter the issue presented, most IRB members experience concern about global health justice issues. This being the case, there are three implications that follow. 1) Current guidelines and protocols may not be efficient in resolving issues and may need to be re-

evaluated; 2) IRB procedures for review may need re-structuring, including modification of required information in research proposals; and 3) IRB training on resolving the global health justice issues that present is inadequate, and curriculum may need to be adapted.

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APPENDICES

Appendix A

The survey administered to PRIM&R members and *Ampersand* subscribers is provided below.

The Human Engagement Learning Platform (HELP) for Global Health

— An Assessment of how IRBs, REBs, and RECs Experience and Manage Global Health Research Ethics Challenges —

1) What is your age?
    a) 18-25
    b) 26-35
    c) 36-45
    d) 46-55
    e) 56-65
    f) 65+
    g) Prefer not to say

2) What is your gender?
    a) Male
    b) Female
    c) Non-binary/ third gender
    d) Prefer to self-describe
    e) Prefer not to say

3) What country is your IRB/REB/REC located in?

4) Are you currently serving on an IRB/REB/REC?
    a) Yes
    b) No

5) [If yes to 4] What is your role?
    a) Member
    b) Chair
    c) Co-chair
    d) Administrator

e) Other role
f) Prefer not to say

6) Do you currently sit on more than one IRB?
   a) Yes
   b) No

7) [If yes to 6] If you currently sit on more than one IRB/REB/REC and have different roles on each, check all that apply.
   a) Member
   b) Chair
   c) Co-chair
   d) Administrator
   e) Other role
   f) Prefer not to say

8) How many years of experience do you have serving on an IRB/REB/REC?
   a) 0-2
   b) 3-5
   c) 6-8
   d) 8-10
   e) 11+

9) On average, how many protocols do you review as the principal/primary reviewer per month?

10) On average, of the protocols you review as the principal/primary reviewer per month, how many require full-board review?

11) What type of institution does your IRB/REB/REC serve? If you currently sit on IRB/REC/REBs at multiple institutions, please check all that apply.
   a) Hospital-based
   b) University
   c) NGO
   d) Government agency
   e) Private organization/philanthropy
   f) Commercial IRB
   g) Other
   h) Prefer not to say

12) On average, how many protocols does your IRB/REB/REC review per year?
    a) 0-50
    b) 51-100
    c) 101-200
    d) 201-300
    e) 301-400
    f) 401-500
    g) 501+
    h) Don't know

13) Of the protocols you review, please approximate the percentage in which the **majority** of data collection is conducted in a country other than the country in which your IRB/REB/REC is located.
    a) None
    b) 1-5%
    c) 6-20%
    d) 21-40%
    e) 41-60%
    f) 61-80%
    g) 81-99%
    h) 100%
    i) Don't know

14) Please indicate how often, if at all, **you encounter** the following issues in your work with the IRB/REB/REC:

	Never (0%)	Rarely (1-33%)	Sometimes (34-66%)	Often (67-99%)	Always (100%)
Adequacy of the proposed budget for ethical completion of the study					
Adequacy of the proposed benefits for host community capacity building					
Data and specimen ownership					
Data and specimen stewardship					
Adequacy of the proposal's attention to the sociocultural contexts of the research					
Research teams' knowledge, skills, and relationships for navigation of the sociocultural contexts of the research					
Institutional liability, or the reputation of your institution being damaged, as a result of the proposed research					
The fairness of the partnerships and collaborations associated with the proposed research					
The adequacy of the foresight/planning for potential unintended consequences of the research reflected in the proposal					

15) Please indicate how often, if at all, you **feel concerned** about the following issues in your work with the IRB/REB/REC:

	Never (0%)	Rarely (1-33%)	Sometimes (34-66%)	Often (67-99%)	Always (100%)
Adequacy of the proposed budget for ethical completion of the study					
Adequacy of the proposed benefits for host community capacity building					
Data and specimen ownership					
Data and specimen stewardship					
Adequacy of the proposal's attention to the sociocultural contexts of the research					
Research teams' knowledge, skills, and relationships for navigation of the sociocultural contexts of the research					
Institutional liability, or the reputation of your institution being damaged, as a result of the proposed research					
The fairness of the partnerships and collaborations associated with the proposed research					
The adequacy of the foresight/planning for potential unintended consequences of the research reflected in the proposal					

16) Are there any other ethical issues or concerns relevant to your review of research that aren't listed in the previous question?

17) Where do you seek guidance while reviewing any of the issues in questions 14-16? Please check all that apply.

a) The U.S. "Common Rule" Regulations (including sub-parts, if relevant)
b) The Declaration of Helsinki
c) The CIOMS Guidelines
d) Other specific national guidelines or regulations (e.g., Canadian TCPS-2 Guidelines, Indian Council of Medical Research Guidelines, etc.)
e) Previous IRB/REB/REC reviews
f) Published scientific literature
g) Non-IRB/REB/REC colleague
h) IRB/REB/REC colleague
i) The PI/investigator(s) for the proposed research
j) In IRB/REB/REC deliberations (i.e., the meeting itself)
k) The local IRB/REB/REC for the proposal

18) Of the sources of guidance listed in the previous question, which is the most useful to you for reviewing and making decisions about the issues in questions 14-16?

l) The U.S. "Common Rule" Regulations (including sub-parts, if relevant)
m) The Declaration of Helsinki
n) The CIOMS Guidelines
o) Other specific national guidelines or regulations (e.g., Canadian TCPS-2 Guidelines, Indian Council of Medical Research Guidelines, etc.)
p) Previous IRB/REB/REC reviews
q) Published scientific literature
r) Non-IRB/REB/REC colleague
s) IRB/REB/REC colleague
t) The PI/investigator(s) for the proposed research
u) In IRB/REB/REC deliberations (i.e., the meeting itself)
v) The local IRB/REB/REC for the proposal

19) Please rate your level of agreement with the following statement:
I feel that the guidance I have indicated in question 18 helps me to resolve the concerns I have about the issues in questions 14-16.

(1) Strongly disagree
(2) Disagree
(3) Neither agree nor disagree
(4) Agree
(5) Strongly agree

20) When considering issues such as those described in questions 14-16, do you ever approve applications that fulfill the necessary IRB/REB/REC requirements, but leave you feeling uneasy or distressed, ethically?

a) Yes
b) No
c) Unsure

21) [If yes to 20] Approximately what percentage of the applications you approve leave you feeling uneasy/distressed, ethically?
    a) None
    b) 1-5%
    c) 6-20%
    d) 21-40%
    e) 41-60%
    f) 61-80%
    g) 81-99%
    h) 100%
    i) Don't know

22) What are the most common sources for your ethical unease or distress? Check all that apply.
    a) Proposed budgets for ethical completion of the study
    b) Benefit to host communities
    c) Data and specimen ownership
    d) Data and specimen stewardship
    e) Attention of proposal to sociocultural context of the research
    f) Research team's ability to navigate sociocultural contexts of the research
    g) Institutional liability or damage to the reputation of your IRB/REB/REC as a result of the proposed research
    h) Partnerships and collaborations associated with the proposed research
    i) Foresight/planning for potential unintended consequences of the research reflected in the proposal
    j) I do not feel ethical unease or distress

23) Is there anything else we should know?