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# More Than Cheating: Deception, IRB Shopping, and the Normative Legitimacy of IRBs

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## Introduction

Deception, cheating, and loopholes within the IRB approval process have received significant attention in the past several years. Surveys of clinical researchers indicate common deception ranging from omitting information to outright lying,<sup>1</sup> and controversy surrounding the FDA's decision not to ban "IRB shopping" (the practice of submitting protocols to multiple IRBs until one is found that will approve the protocol)<sup>2</sup> has raised legitimate concerns about the integrity of the IRB process. One author has described a multicenter trial as being withdrawn from consideration at one institution when rejection was imminent, in order to avoid informing other IRBs reviewing the protocol of the study's rejection (a requirement under the federal regulations for emergency research with an exception from informed consent).<sup>3</sup> This practice and IRB shopping seem at odds with the spirit, if not the "letter," of the regulations. While at first blush these practices seem to cast aspersions on the integrity of clinical researchers, the moral issues raised go deeper than the ethics of cheating. To the extent that these practices are common, or represent an IRB system that places unreasonable burdens on those seeking IRB approval, we should consider whether non-compliance reflects problems of normative legitimacy for the IRB system itself.

Common reasons for non-compliance cited by clinical researchers include perceptions of unreasonable requirements by IRBs, lengthy review times, requirements that threaten to undermine study design, and lack of clarity and/or controversy about what should be subject to IRB review.<sup>4</sup> As a recent review article examining empirical research on IRBs stated succinctly, "Empirical evidence collected in forty-three published studies shows that for review of a wide range of types of research, U.S. IRBs differ in the their application of the federal regulations, in the time they take to review studies, and in the decisions made. Existing studies show evidence of variation in multicenter review, inconsistent or ambiguous interpretation of the federal regulations, and inefficiencies in review<sup>5</sup> (though the problem of multiple IRBs reviewing multicenter trials may be improved by proposed changes to the regulations). Our own experience on IRBs (both as members [RS, TM] and as chair

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[RS]) points to other common complaints, including: expanding informed consent requirements that dictate forms so detailed and long that they actually hinder the informed consent process;<sup>6</sup> committees requiring changes to consent forms not for clarity, but to optimize the document; or requiring changes to the protocol that do not concern safety, benefits, or burdens, but rather attempt to improve study design. The issue of IRB requests for changes is of particular concern for multi-center trials, as changes that are not universal to all centers may undermine control of

partly because of the perceived arbitrary nature of IRB review itself: different IRBs will interpret federal regulations differently, and the same IRB might even interpret the regulations differently from meeting to meeting depending on who is in attendance. These phenomena are more than mere perception: several problems related to these have been documented in the literature. For example, a number of studies have shown wide variation in IRB assessment of the same protocol.<sup>9</sup> These studies documented variations in risk assessment which led to the following inconsistencies:

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variables.<sup>7</sup> There is also common misunderstanding of what might qualify for expedited or exempt review. This latter problem was at the center of controversy surrounding Gerald Schatten’s role in the discredited stem cell research of Korean scientist Hwang Woo-Suk. The University of Pittsburgh, based on information provided by Schatten, skipped a full review of Schatten’s research, designating it as exempt.<sup>8</sup>

We do not suggest that IRBs should be held to a standard or uniformity that is impossible to achieve, nor do we contend that any variability is intolerable. On the contrary, some variability is to be expected, to account for local input on ethical concerns, state laws, and institutional policies. Our concern lies with decisions that appear arbitrary or unclear to investigators that are never explained. To the extent that current practices reflect encouraged non-compliance because regulatory “pathologies” (described below) undermine compliance, the current system may be ineffective in shaping behavior because the burdens of compliance are too great or indiscernible or worse, fail to inculcate the recognition of normative legitimacy necessary for a regulatory system to effectively function.

For researchers, the IRB process can seem daunting. There is an almost mystical feel to the process itself. Protocols are submitted, months pass, and requests for changes are made, justified by institutional policies and federal regulations that are unfamiliar to most researchers. Few IRBs offer substantial help in preparing protocols for review. At the same time, there is little understanding on the part of researchers concerning what will pass scrutiny,

the type of IRB review required (e.g., expedited review done by the chair for minimal risk studies or full-committee review); requirements for informed consent, waived consent, and pediatric assent; length of time from initial submission to the IRB to approval; initial response; and the ultimate approval or disapproval of the same study. These variations raise numerous concerns, including whether human subjects are adequately protected, but from the perspective of a researcher, they only add to the perception of mystery and capriciousness of the IRB review system.

Below, we will argue that the current IRB system is flawed at a very fundamental level. These flaws raise questions concerning the ability of the IRB review process to provide known, and viable, guidelines to researchers. This, we argue, undermines the normative legitimacy of the IRB process, calling for changes that revise how we conceptualize the IRB process. As others have argued, the current IRB model is dysfunctional,<sup>10</sup> outdated and needs to be revised.<sup>11</sup> The current model is based upon a single researcher at a single institution, a far cry from many current trials that involve numerous investigators at numerous institutions, with wide variations in institutional policies and study populations. In addition, the current model, designed largely for clinical trials is poorly suited to review epidemiological and social scientific studies. These anachronistic features highlight the need for changes that update review for the complex nature of studies today.<sup>12</sup>

### Pathology of IRB Regulations

The findings in “Scientists Behaving Badly” are troubling and clearly changes are needed. The question then is what should we make of this widespread cheating? May we simply ignore it, or perhaps seek ways to increase oversight to deter such behavior? Or does such widespread cheating threaten the very core, the moral legitimacy, of the regulatory system for human subjects research in the United States? Legal scholars have long recognized a tie between the normative legitimacy of a regulatory system (law) and its ability to direct the behavior of its subjects.<sup>13</sup> This tie can take two forms: one controversial, and the other not. Both of these are relevant, in different ways, to the issue of “cheating” the IRB review process. The uncontroversial form is a version of “ought implies can,” requir-

study, for example, has examined the potential problems that “internal amendments” pose by introducing uncontrolled variance into multi-center studies.<sup>17</sup>

The jurisprudential literature also emphasizes the need for regulatory body/judicial consistency in the application of rules in order to avoid pathology that undermines the normative legitimacy of the regulatory system. Hart, for example, describes the need for “rules of recognition” that establish a consistent, known process of adjudication for when “primary rules” are broken.<sup>18</sup> In brief, this idea emphasizes the need for clarity and consistency within a court system applying the standards established by a legislative body. One illustrative example of this type of problem discussed in the scientific literature concerns federal risk and benefit categories for pediatric research.<sup>19</sup>

**Given the close relationship of the conditions that jurisprudential scholars recognize might undermine the normative legitimacy of law due to the reasons for non-compliance cited by researchers, and to features of IRB review outlined in the scientific and medical literature, we should consider whether the IRB system fails to meet the basic requirements of normative legitimacy for a regulatory system.**

ing that regulatory systems not require what subjects are *incapable* of doing. For example, H.L.A. Hart cites non-compliance due to a legal system’s inability to effectively communicate its requirements as one cause of “pathology” that might threaten the legitimacy of the system.<sup>14</sup> Simply put, a subject cannot conform to requirements that are contradictory or unknown to him. Here, complaints that IRB regulations lack clarity, or are contradictory, are relevant.

The controversial form ties the legitimacy of a regulatory system to its acceptance by subjects (as evidenced by compliance). Legal systems that do not enjoy the respect of subjects are often deemed to lack normative legitimacy. One classic work in this field directly relates the normative legitimacy of law to its acceptance by subjects (in the form of compliance).<sup>15</sup> Other works in jurisprudence emphasize the need for law to consider the viability of compliance: requirements that are unreasonably burdensome are unlikely to be effective in their purpose of directing behavior.<sup>16</sup> Here, complaints of lengthy review times, as well as complaints that IRB requirements sometimes undermine the validity of study design, are relevant. In addition, studies have shown that variation in IRB requirements for multi-center trials can negatively affect response rates and sample generalizability. One case

This study demonstrated variability in the application of the federal standards for risks and benefits in pediatric research among IRB chairs, with some decisions contradicting available data on risks or even the regulations themselves.

Given the close relationship of the conditions that jurisprudential scholars recognize might undermine the normative legitimacy of law due to the reasons for non-compliance cited by researchers, and to features of IRB review outlined in the scientific and medical literature, we should consider whether the IRB system fails to meet the basic requirements of normative legitimacy for a regulatory system. In describing the need for clear communication of standards in law, Hart outlines two principle devices which he acknowledges at first sight contrast. The first describes the need to predominantly use general classes and categories in order to avoid drowning in minutia and the implication that standards are narrowly focused on isolated cases. At the same time, Hart’s second device emphasizes the need to avoid such vagueness that the standards are indeterminate.<sup>20</sup> Each of these problems are present in current IRB regulations, both for the operation of the IRB itself and for researchers submitting protocols for approval. Problems of either type can lead to obstacles to appropriate use of IRBs by researchers, as

IRBs that do not function smoothly create difficulties for obtaining approval of protocols. This can lead, for example, to “IRB shopping” or attempts to circumvent the IRB process altogether (for example, by supplying misleading information to gain “exempt” status).

In the context of regulations that are too specific and delve into significant minutia, consider the example of a research protocol that might regularly enroll prisoners (it need not be directed at prisoners to fall under this schema). Such research must fall into one of four categories of research in order to proceed (45 CFR 46.306(a)(2) (A), (B), (C), (D)). The research must either (1) pose minimal risk to participants and focus on possible causes, effects, and processes of incarceration or; (2) pose minimal risk to participants and focus on the institutional structures of prisons or prisoners as incarcerated persons or; (3) must focus on conditions particularly affecting prisoners as a class (i.e., vaccine trials for hepatitis or drug addiction) or; (4) must focus on practices that have the intent and reasonable probability of benefiting the prisoner. In terms of problems posed to IRB operations, these regulations require IRBs to include a “prisoner representative” (someone familiar with the unique issues facing prisoners) on their board when initially reviewing protocols including prisoners, as well as for continuing review and the review of amendments. This is important, as it is difficult enough to meet federal regulations for membership diversity without this additional requirement. In terms of obstacles posed to researchers seeking approval, under category (3) and for category (4), if control groups are not expected to benefit, then such research must also be approved by the Secretary of Health and Human Services and published in the *Federal Register*. Needing prior authorization from the Secretary of Health and Human Services poses a significant hurdle to research.

In the context of regulations that are too vague, consider the example of adults with decisional impairments. For this population, vagueness within regulations occurs at a number of levels. First, the regulations do not define adults with decisional impairments, although it is widely accepted (among research ethicists, although not as widely understood among researchers themselves) that this term refers to adults with impairments that prevent them from understanding the decision to participate in research (rather than, for example, the presence or absence of a mental illness). The additional safeguards for this vulnerable population are also vague. For example, federal regulations require that IRBs *consider* including one or more members who are knowledgeable about and experienced in working with such individuals (45 CFR 46.107(a)). This leaves open the question

of whether IRBs which fail to include such members have adequately protected such persons. In addition, the regulations merely require that “additional safeguards” be in place to protect the rights and welfare of such persons (45 CFR 46.111(b)). It is this vagueness that poses the greatest challenge for researchers wishing to submit an “acceptable” protocol: there is great variability in how individual IRBs interpret this mandate (which may be complicated by variations in state law) and what is required to satisfy it. This can be particularly problematic for multi-center trials because the same protocol must pass multiple IRB reviews that can vary widely in their requirements.

These are but two examples of how current regulations concerning research involving human participants may reflect the types of “pathology” described by Hart above. Such pathologies suggest that the “misbehavior” of researchers in the IRB process might reflect a problem deeper than mere “cheating”: it may reflect a need to re-evaluate our approach to regulating human subjects research within the IRB system. This is not to condone cheating on the part of research investigators, nor is it to suggest that all instances of misbehavior are in some sense justified by pathologies within the regulatory system. We believe that reflection on how problems of cheating and misbehavior might be addressed through reforms to the IRB system, however, is clearly justified.

### Steps to Fix the IRB Process

If in fact the IRB approval process is too onerous, what can be done to correct this without sacrificing the underlying ideal of protecting participants’ safety and rights? As a first step we propose changes at the broadest level: the perspective taken by IRBs in the context of IRBs’ self-understanding of their role and purpose. At a national meeting of human research protection programs, IRB professionals debated the role of the IRB. Jeffrey Cohen, past director of the Division of Education and Development in the Office of Human Research Protections, argued that IRBs ought to focus on both protecting research participants and facilitating research, as IRBs possess unique knowledge for navigating regulatory schemas.<sup>21</sup> This view was criticized in favor of strictly protecting research participants. This insight — that IRBs possess unique knowledge regarding the regulatory requirements — should not be overlooked. If a well-intentioned researcher seeks to conduct her research in accord with the regulations, who better than the IRB to help facilitate this? As we stated above though, we must not sacrifice the underlying ideal of protecting participants’ safety and rights. Thus, we propose a third alternative: that the role of an IRB ought to be to facilitate *ethical* research.

If an IRB adopts the position that its role is *simply* to protect research participants, as suggested by guidance from FDA,<sup>22</sup> HHS,<sup>23</sup> and the regulations themselves,<sup>24</sup> the default position of that IRB is to err on the side of not approving research, as research not undertaken poses no threat of harm to participants. As we have argued elsewhere, it is not uncommon for IRBs to focus almost exclusively on issues of strict compliance<sup>25</sup> as reflected in the U.S. General Accounting Office study that found IRBs spend the majority of their time reviewing, modifying, and requesting changes to consent forms.<sup>26</sup> This of course can create an adversarial atmosphere and lead, perhaps indirectly, to the sorts of violations noted above.

Facilitating ethical research (in a context that limits harms to participants) might be modeled on the law's strategies for facilitating free action within limits related to potential harms to others.<sup>27</sup> Discussions of law's effective regulation of behavior have described the need to formulate standards in terms of presumptions of permission (emphasizing that what is not explicitly prohibited or required is presumed to be left to the participant's judgment).<sup>28</sup> Without this presumption, regulation of behavior may become so onerous that free action is significantly inhibited. A similar change in perspective could have positive ramifications for a number of tangible obstacles cited by researchers. For example, applied to the review of consent forms, if IRBs were to adopt a "presumption of adequacy" (requiring reason for changes) rather than, for example, seeking ideal or preferred language, burdens such as minor wording changes that require complex amendment at multiple sites (many where the protocol has already been approved) might be reduced. In fact, minor consent form wording changes are by far the most common revisions required by IRBs. While these changes may seem minor to IRB members, they do create burdens for researchers. This is not to imply that IRBs should not require wording changes that are seen as necessary for clarity or to achieve an appropriate reading level; rather, it is to change the presumption for requiring change to demonstrated need, rather than simple preferred language.

More fundamentally, the ideal of "facilitating ethical research" is more concordant with *all* of the ethical principles extolled in the *Belmont Report* (respect for persons, beneficence, and justice). When an IRB sees its role *solely* as the protection of research participants, and errs on the side of preventing harm, it sacrifices the principles of respect for persons and justice for the principle of non-maleficence. For example, potential participants might be prevented from deciding whether to participate in research that is delayed or not approved in the name of protection, thus vio-

lating respect for persons. Likewise certain populations might be (or already are being) systematically excluded from the benefits of research for the same reason. For example, in the past, children as well as pregnant women have been excluded from research, inhibiting the ability of these populations to benefit from new drugs and devices. Though the IRB system is not solely to blame for this, and in some cases clinical trial sponsors might exclude such populations to avoid legal liability, the result is well-known: many of the drugs used in pediatric medicine today have never been tested in the pediatric population and are thus used "off-label."

Conversely, an IRB that understands its role to be the facilitation of ethical research would work with researchers *and* participants to ensure that all of the principles extolled in the *Belmont Report* are balanced and upheld. This approach is concordant with a 2002 Institute of Medicine Report that recommended that IRBs should focus more on the ethical review of protocols, but in a collaborative manner that seeks to engage researchers in the conduct of ethical research.<sup>29</sup> Such an IRB might adopt a presumption of adequacy as discussed above that would respect the personhood of research participants in order to make their own autonomous choices, as well as ensure a fair distribution of the burdens and benefits of research. Vulnerable populations would no longer be excluded from participation in research, but would be able to choose for themselves whether or not to participate, with proper protections.

Recently, research ethics consultation has received much attention as well.<sup>30</sup> However, research ethics consultation differs from changing the focus on IRBs to one of facilitating ethical research in two important ways. First, facilitating ethical research is focused on IRBs in an attempt to prevent the undermining of their moral legitimacy. If nothing is done to fix the crisis in IRBs and research ethics consultation is sought, it is possible that merely pursuing research ethics consultation alone would further undermine the moral legitimacy of IRBs, as IRBs could come to be seen as irrelevant in the oversight of research. Secondly, research ethics consultation is focused solely on the ethical issues that arise in research, not on regulatory aspects, and is likely only warranted in particularly ethically challenging protocols.<sup>31</sup> Changing the culture of IRBs towards facilitating ethical research would potentially impact all human subjects research. This is not to say that research ethics consultation is not vital and important. Rather, we view it as distinct yet complementary to our recommendations.

Finally, the attitude of facilitating ethical research also captures the ideal that IRBs should be more

proactive in assisting researchers in developing protocols before they go to review. This could take several forms. IRBs can provide this themselves or can encourage the development of separate arms that will do this. At our own institution, for example, the Office of Research is developing “research advocates” who will work with investigators to ensure that their applications are clear and complete, as well as help investigators determine where and how to submit their protocols (i.e., the IRB, the IACUC, whether or not the study should be expedited, etc.). Such advocates will also assist an investigator in determining whether a study requires standard informed consent, or whether the study might qualify for a waiver of informed consent or perhaps a waiver of the requirement to document informed consent.

adequately provided on a volunteer, uncompensated basis (as they currently are at most institutions). Support in each of these areas should reflect the important financial priority that research programs represent to research institutions.

With the changes just described, we believe there is legitimate hope for a significant reduction in cheating of the IRB review process. Researchers do not begin their careers with disdain for research ethics and IRBs. In fact, medical students are positively disposed towards research ethics and report desires to conduct research in an ethical fashion.<sup>34</sup> Unfortunately, recent evidence indicates that early career scholars engage in numerous behaviors that either ignore, avoid, or outright violate policies aimed at protecting research participants.<sup>35</sup> What happens between medical school

**Regular, ongoing educational sessions that explain both the process and expectations for approval of protocols should be available at every research institution. Such programs should not be expected to be adequately provided on a volunteer, uncompensated basis (as they currently are at most institutions). Support in each of these areas should reflect the important financial priority that research programs represent to research institutions.**

## Conclusion

If IRBs are to provide the proactive assistance we have just described, some institutions will need to significantly increase support for IRBs, including the following: allowances for time committed by IRB members; increased staff support so that adequate assistance can be provided; and education of both IRB members and research investigators. Most IRB members volunteer their time, inhibiting their ability to devote significant effort to assisting other researchers with protocol development. Even time for substantial education is limited for a membership that must incorporate IRB duties into already busy schedules.<sup>32</sup> Likewise, at most institutions IRB support is notoriously underfunded and understaffed, a phenomenon long identified as a “root cause of compliance problems with research subject policy.”<sup>33</sup> If IRBs are to run smoothly, and further provide the assistance we call for above in preparing protocols for the approval process, much greater support for staffing is necessary. Finally, institutions must take seriously education of both IRB members and research investigators in order to facilitate the process. Regular, ongoing educational sessions that explain both the process and expectations for approval of protocols should be available at every research institution. Such programs should not be expected to be

and a young researcher’s early career that changes these attitudes and behaviors? One anonymous researcher has suggested in the literature that unethical behavior in research is *learned* — and argues that the key to facilitating ethical research is to ask how we might remove incentives for *senior* researchers to misbehave.<sup>36</sup> We believe that the most important component of removing such incentives is to improve the IRB review process.

As we described at the outset of this paper, a major reason that researchers do not comply with rules and policies of the review process is because compliance is simply too difficult. Many of the rules are unclear, IRB interpretations of these rules vary, and changes that complicate multi-institutional approval are sometimes related to “ideals” but are not necessary to protect research participants. These improvements should reflect a shift in perspective from *simple* protection of research participants towards facilitating *ethical research*. Such a shift would include a presumption of adequacy and streamlined regulations that, like the legal system, are designed to avoid the “pathologies” of specificity and/or vagueness that threaten the normative legitimacy of IRB review, as well as proactive assistance to researchers and substantial education of both researchers and IRB members.

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