

## CASE AND COMMENTARY

### How Should Organizations Respond to Repeated Noncompliance by Prominent Researchers?

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#### Abstract

This article considers a case in which a prominent researcher repeatedly made protocol deviations year after year while the institutional review board and university leadership failed to adequately address his continuing noncompliance. This article argues that, in addition to reporting this researcher's pattern of noncompliance to the Office for Human Research Protections, as required by federal regulations, the university should implement a remedial action plan.

#### Case

Dr E is a physician-researcher and leading expert in his field whose work brings in millions of dollars in grant funding for the university. He and his collaborators regularly publish in top scholarly journals and garner national media attention. Despite Dr E's team's productivity and success over the past 15 years, its protocols' record of compliance with human subjects protection regulations has never been perfect and has recently gotten spottier. Deviations from institutional review board (IRB)-approved protocols so far do not appear to have violated subjects' welfare or safety. And for each known past deviation,<sup>1</sup> the IRB notified Dr E, as principal investigator, whose team responded by submitting protocol modification requests<sup>2</sup> to the IRB, which were all approved. IRB members remain concerned about what has now become Dr E's team's persistent, years-long pattern of deviating from protocol and then needing reminding about federal regulatory compliance obligations.

The IRB's chair, Dr J, has grown frustrated over the years by failed attempts to solicit assistance from university leadership in motivating Dr E to comply with requirements without recurrent prompting. In a letter to the university's new provost, Dr A, and board of trustees,<sup>3</sup> Dr J stated, "Dr E's team's pattern of disregard for compliance with federal human subjects protections concerns

IRB committee members deeply. We feel obligated to recommend to the university leadership that current trends, which are well documented, should not continue to be tolerated out of respect for subjects' vulnerabilities and out of respect for IRB board members' volunteer service to the university."

When Dr J wrote similar letters in the past, members of university leadership were divided about how to respond. The majority emphasized the importance of Dr E's team's prominent contributions to the field and to the university and reminded the others that violations have been minor. A few agreed with Dr J that continued tolerance of Dr E's team's repeated deviations, though minor in the past, could be perceived as sanctioning more serious noncompliance in the future that could imperil subjects and the university's reputation. Others suggested that Dr E's team's pattern of protocol deviations could be seen as undermining the university IRB's authority and the integrity of federal human subjects regulatory processes—but not enough to interfere. Proponents of this latter view conceded that Dr E should comply without prompting, but they pointed out that his team has, in the end, always responded to the IRB's requests and that the IRB is doing what it needs to do. They continue to hold that there's no need for university leadership to intervene in how the organization functions with respect to human subjects research governance.

As a new provost, Dr A looks into the matter further. Federal human subjects research protections require reporting of "continuing noncompliance,"<sup>4</sup> but IRBs have discretion about how to interpret and report an investigator's pattern of minor noncompliance.<sup>5</sup> Nevertheless, Dr A finds that IRBs are charged with assessing and addressing issues of research protocol deviations on behalf of any organization that receives federal funds for human subjects research. Dr A considers how she should urge the university's leadership to respond.

### **Commentary**

In this case, Dr E has been taking advantage of his status as a prominent researcher. In recognition of Dr E's prominent academic achievements and financial contributions to the university, the IRB considered Dr E to be so important as to be untouchable. While members of the university leadership differed in their opinions regarding the implications of Dr E's repeated noncompliance, they all agreed that there was no need for the university to intervene. In fact, some strongly believed that "there's no need for university leadership to intervene in how the organization functions with respect to human subjects research governance."

As the new provost, Dr A investigated the matter further and noted that federal regulations require reporting of continuing noncompliance<sup>6</sup> and that the IRB so far had not adequately addressed Dr E's pattern of protocol deviations on behalf of the university. Thus, it is particularly pertinent for Dr A to ask the question, "How should organizations respond to repeated noncompliance by prominent researchers?" In order to answer this question properly, one needs to understand our current system of protecting human subjects participating in research. We believe that the university should report Dr E's continuing noncompliance to the Office for Human Research Protections (OHRP), as required by federal regulations, and implement a remedial action plan to effectively prevent recurrence of protocol deviations.

### **Federal Human Subjects Protections**

Since 1974, the Federal Policy for the Protection of Human Subjects, also known as the Common Rule after 1991, has [relied on IRBs](#) to review and approve human research protocols as well as to provide continued oversight to ensure that the rights and welfare of human subjects participating in research are protected.<sup>6</sup> Under this system, for many years research institutions delegated authority and responsibility for protecting human research subjects to their IRBs, often without providing sufficient financial and administrative support. As a result, IRBs were overworked and undersupported.<sup>7</sup>

A paradigm shift toward less reliance on IRBs for oversight occurred in the late 1990s and early 2000s when it became clear that IRB oversight alone was [insufficient to protect human subjects](#) participating in research. Two young volunteers, Jesse Gelsinger and Ellen Roche, who participated in phase one clinical trials out of altruism, died on September 17, 1999, and June 2, 2001, respectively, as a result of egregious noncompliance by the investigators and IRBs.<sup>8,9,10</sup> In addition, a number of major academic institutions' federally funded research programs were temporally suspended due to persistent, serious noncompliance with federal regulations.<sup>8,11</sup> Since that time, institutions conducting research involving human subjects have established operational frameworks, referred to as human research protection programs, to ensure that the rights and welfare of research participants are protected and to meet ethical and regulatory requirements that are essential for the protection of human subjects.<sup>13,14</sup> In addition to IRBs, investigators, institutions, sponsors of research, research volunteers, and the federal government share responsibilities for protecting human research subjects.<sup>12</sup>

Under the current system, ultimate responsibility for human subjects protections resides at the highest level of the institution. The institution must assume the leadership role in ensuring the integrity of its human research protection program by providing adequate resources and establishing ethics education programs and a culture of research excellence and transparency as well as by continuous monitoring and quality improvement through program accreditation.<sup>12,13</sup> The belief that “there’s no need for university leadership to intervene in how the organization functions with respect to human subjects research governance” held by some members of the university leadership in this case is thus entirely inappropriate.

### **Recommendations for Scope of University Research Oversight Responsibilities**

We propose that the following ethical criteria be used to consider the nature and scope of the university’s responsibilities to various stakeholders in this case.

- Protecting the rights and welfare of human research subjects should be the university’s highest priority;
- The university should take the lead role in ensuring the integrity of its human research protection program;
- Serious or continuing noncompliance should not be tolerated regardless of an investigator’s seniority or level of research funding; and
- The university should take a proactive role in addressing issues of noncompliance that are beyond its IRB’s capability to resolve.

In subsequent paragraphs, we will focus our discussion on the third and fourth criteria.

We suggest that the provost, Dr A, recommend to the university leadership reporting Dr E’s continuing noncompliance to the OHRP, along with implementing a remedial action plan to prevent Dr E’s protocol deviations from recurring, in line with the Guidance on Reporting Incidents to OHRP.<sup>4</sup> The remedial action plan should include a university-wide educational training for all investigators, including Dr E and his staff, regarding the importance of complying with IRB-approved research protocols and the consequences of protocol deviations. In addition, the university should assign or hire a research compliance officer to work with Dr E, his staff, and the IRB to ensure that all contemplated research activities that are outside of IRB-approved protocols are submitted to the IRB for review and approval prior to their

implementation, except when deviations from protocol are performed to eliminate apparent immediate hazards to a subject.<sup>6</sup>

Having a research compliance officer, part-time or full-time, to work with Dr E, his staff, and the IRB to prevent any protocol deviations from recurring demonstrates that the university leadership will take a proactive role in addressing issues of noncompliance that are beyond the IRB's capability to resolve. It is an investment by the university that is well justified in view of Dr E's prominent contributions to the field and the university.

Reporting Dr E's continuing noncompliance to the OHRP will give a strong message to:

- Dr E that repeated protocol deviations, even minor protocol violations that do not cause actual harms to human subjects, cannot be tolerated;
- The research community at large that serious noncompliance or continuing noncompliance will not be tolerated regardless of an investigator's seniority and level of research funding; and
- The IRB that it has failed to carry out its responsibility to inform the university leadership of Dr E's continuing noncompliance and report it to the OHRP as required by federal regulations, given that Dr E's continuing noncompliance was so obvious and well documented.<sup>1,6</sup>

One could argue that there is no need to report Dr E's repeated protocol deviations to the OHRP. Although the Common Rule requires that continuing noncompliance be reported, it does not explicitly define what constitutes continuing noncompliance.<sup>4,6</sup> It does permit IRBs some latitude in interpreting and determining whether the investigator's pattern of minor noncompliance constitutes continuing noncompliance. Since the IRB so far has not determined that Dr E's repeated protocol deviations year after year constitute continuing noncompliance and, moreover, these deviations have not resulted in actual harms to human subjects, it would be simpler if Dr A would just follow the previous university policy and decide not to intervene. However, whether to report continuing noncompliance is not entirely up to the IRB's discretion, especially in this case, in which the IRB's decision was unduly influenced by Dr E's prominent researcher status. If there is any doubt, either Dr A or the IRB chair, Dr J, should consult the OHRP for advice. The OHRP considers the following to be examples of continuing noncompliance:

- The principal investigator (PI) makes the same mistake repeatedly, especially after the IRB has informed the PI of the problem;
- The PI has multiple problems with noncompliance over a long period; and
- The PI has problems with multiple projects.<sup>15</sup>

One could also argue that there is no need to assign a research compliance officer to work with Dr E, his staff, and the IRB to prevent future protocol deviations from recurring, since the university could not possibly afford to have a research compliance officer work with each investigator who is repeatedly noncompliant. We agree that having a research compliance officer work with Dr E, his staff, and the IRB is a substantial, albeit temporary, investment on the part of the university. However, if Dr E continues to make protocol deviations after the educational training, there are few options open to the IRB and the university other than temporarily to suspend his research protocols, which we believe is one option that the university would not want to take. Our proposed approach offers the best chance to ensure that Dr E's protocol deviations would not recur. In view of Dr E's prominent contributions to the field and the university, this investment in a remedial action plan is well justified.

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**Editor's Note**

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