Correspondence

Was the Institutional Review Board System a Mistake?

To the Editor—The statement by the Infectious Diseases Society of America (IDSA) [1] is the keenest analysis of the institutional review board (IRB) system ever published in a medical journal. It describes a regulatory regime swamped with pointless paperwork (eg, the Health Insurance Portability and Accountability Act [HIPAA]), multiple IRBs making irrec- oncilable decisions whose inconsistency reveals the absence of workable guidelines, duplicate adverse-event reporting, risk-averse interpretations of rules that hurt the very people (children) the system aspires to protect, and mission creep that leads IRBs to assert ever broader authority (eg, over hospitals’ attempts to improve the care they provide).

What ought a diagnostician make of symptoms like fruitless paperwork, bureaucratic imperialism, and arbitrary deci- sions? These are the indicia of a noto- rious malady—a regulatory agency fatally infected with the standard pathologies of government bureaucracies. Regulation is often necessary and often works satisfac- torily, but the IDSA statement raises pressing questions about whether the IRB sys- tem is fundamentally misconceived.

The most basic requirement for any reg- ulatory bureaucracy is to do more good than harm. The IDSA statement takes a pioneering step by raising the issue of the IRB system’s costs. It reminds us that research has saved and can still save “hun- dreds of thousands of lives” [1, p 328] and that the IRB regime delays, damages, and even destroys research. It does so—as the statement powerfully demonstrates—by demanding endless paperwork, by making decisions capriciously, by enforcing rules with mechanical rigidity, and by seizing authority over areas that IRBs have neither the time nor the competence to regulate.

What benefits has the IRB system pro- vided to justify such costs? As is customary in discussions of IRBs, the IDSA statement invokes the “unfortunate history of abuse of vulnerable subjects in research” [1, p 329]. We favor harsh punishments for unethical researchers. But the question is not whether there have been instances of shameful abuse, it is whether the risk of serious abuse is great enough to require that every instance of human-subject re- search be approved in advance by a bu- reaucracy operating without ascertainment standards, without due process, and with- out accountability.

We have never located a systematic at- tempt to answer that question, and the IDSA statement makes us wonder what the answer would be. For example, the statement points out that HIPAA cannot find justification in any examples of abuse. The statement points out that “investi- gator fraud or inattention to participant safety” [1, p 333] is rare.

In sum, we doubt the IRB system can be tweaked, or repaired, or reformed in ways that will cure the severe inherent problems with the IRB bureaucracy. We particularly question increasing the fund- ing of the agency—the Office for Human Research Protection—that has presided over the IRB system with no visible concern for the costs it imposes. IDSA’s im- pressive and important statement should lead us all to the essential, unanswered question—was the IRB system a mistake?

Acknowledgments

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Reference


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Reply to Whitney and Schneider

To the Editor—There is widespread and growing recognition of the need to change the oversight system for research and quality improvement efforts; important activities are “grinding to a halt” [1, 2]. The question is not whether change is necessary; it is the identification of needed changes and the development of strategies to build the momentum for change. The Infectious Diseases Society of America (IDSA) suggested pragmatic changes in 5 key areas of regulatory oversight, changes that would not necessarily require changes in federal laws or the Common Rule. Our reasons for this focus on pragmatic changes were that we accept the rationale for the basic structure of the current reg- ulatory system and that proposals for comprehensive changes in that system have not engendered momentum for change [3–5].

Whitney and Schneider [6] suggest that the data used to develop the IDSA policy
statement on regulatory burden imply the need for radical change, perhaps the elimination of the entire system of review by an institutional review board (IRB). They characterize the IRB as a “bureaucratic malady” gone wild. The reality is much less dramatic. In a very real sense, the IRB is all of us—researchers and lay people, trying to review research responsibly while complying with a dizzying array of regulations, requirements, interpretations, and guidance documents. Rather than “seizing authority” over new areas, IRBs have had large new responsibilities foisted upon them by misguided federal actions (eg, the general reliance on the IRB to deal with the unnecessarily complex permissions-based privacy protection system resulting from the Health Insurance Portability and Accountability Act [HIPAA] regulations).

The solution is not to transmogrify the IRB into the villain of the oversight system; it is to rethink how that system needs to be updated to reflect a research environment very different than the one that existed in the 1970s, when that system was created. The fundamental idea that proposals for research involving human subjects should be reviewed by an independent panel of other researchers and community representatives is sound. That does not mean that every data-gathering activity is research that requires IRB review, nor does it mean that multicenter research projects need to undergo redundant review by the IRBs of all participating sites. Our current use of this valuable resource of our fellow researchers and interested laypersons (ie, the IRB) is badly flawed.

The IRB is not a mistake; it is a key component of the system that inspires trust among prospective research participants. It is time to restore the balance in the system for oversight of research and quality improvement, not time to destroy that system.

Acknowledgments

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References


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Table 1. Prevalence of K65R and Q151M Mutations in Patients Experiencing Failure of Stavudine-Based First-Line Regimens in Various Settings

<table>
<thead>
<tr>
<th>Setting, reference</th>
<th>No of genotyped samples</th>
<th>Frequency of K65R, %</th>
<th>Frequency of Q151M, %</th>
<th>Subtype</th>
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</thead>
<tbody>
<tr>
<td>India [1]</td>
<td>138</td>
<td>5(^a)</td>
<td>11</td>
<td>Predominantly subtype C</td>
</tr>
<tr>
<td>Malawi [2]</td>
<td>50</td>
<td>10</td>
<td>Not reported</td>
<td>All subtype C</td>
</tr>
<tr>
<td>Malawi [6]</td>
<td>94</td>
<td>30(^b)</td>
<td>24</td>
<td>All subtype C</td>
</tr>
<tr>
<td>South Africa [4]</td>
<td>65</td>
<td>14(^c)</td>
<td>10</td>
<td>All subtype C</td>
</tr>
<tr>
<td>Thailand [5]</td>
<td>122</td>
<td>7</td>
<td>9</td>
<td>Mostly CRF01 AE</td>
</tr>
<tr>
<td>Uganda [3]</td>
<td>8</td>
<td>25</td>
<td>13</td>
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\(^a\) Two percent received stavudine, and 3% received zidovudine.

\(^b\) Thirty percent had both K65R and K70E mutations.

\(^c\) Some patients also received didanosine.

To the Editor—We read with interest the recent study by Kumarasamy et al [1] about the high frequency of significant mutations found after failure of first-line antiretroviral regimens. From an international perspective, 2 findings have particularly important ramifications on the future of human immunodeficiency virus (HIV) treatment in resource-limited settings: (1) the unpredictable nature of stavudine-induced HIV-resistance mutations in subtype C viruses, including a high prevalence of K65R and Q151M mutations in patients experiencing failure; and (2) the accumulation of nucleoside reverse-transcriptase inhibitor (NRTI)– and non-nucleoside reverse-transcriptase inhibitor (NNRTI)–resistance mutations during the period before treatment failure is diagnosed.

This study adds to findings from other studies [2–6] that have found a relatively high prevalence of K65R and Q151M mutations in patients with non-B subtype HIV infection who experience failure of stavudine-based first-line regimens (Table 1). In addition to the expected accumulation of thymidine analogue mutations, the high prevalence of K65R and Q151M mutations is all of us—researchers and lay people, trying to review research responsibly while complying with a dizzying array of regulations, requirements, interpretations, and guidance documents. Rather than “seizing authority” over new areas, IRBs have had large new responsibilities foisted upon them by misguided federal actions (eg, the general reliance on the IRB to deal with the unnecessarily complex permissions-based privacy protection system resulting from the Health Insurance Portability and Accountability Act [HIPAA] regulations).

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