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## Is the Customer Always Right? Department of Health and Human Services' Proposed Regulations Allow Institutional Review Boards to Place Customer Service Ahead of the Welfare of Research Participants

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**IS THE CUSTOMER ALWAYS RIGHT? DEPARTMENT OF HEALTH  
AND HUMAN SERVICES' PROPOSED REGULATIONS ALLOW  
INSTITUTIONAL REVIEW BOARDS TO PLACE CUSTOMER  
SERVICE AHEAD OF THE WELFARE OF RESEARCH  
PARTICIPANTS**

INTRODUCTION

“[C]oast through your next study.”<sup>1</sup> Coast Institutional Review Board (IRB), a for-profit company, offered a coupon, including this statement informing potential customers that they could “coast” through any study review, on its website for a free IRB review of a research protocol.<sup>2</sup> True to its word, Coast IRB allowed customers to coast through IRB review.<sup>3</sup> In 2009, Coast IRB unanimously approved a study involving a fictitious medical product from a fictitious investigator at a fictitious company.<sup>4</sup> This bogus medical product was derived from a real product that the Food and Drug Administration (FDA) pulled from the market after it killed human research-subjects.<sup>5</sup> In fact, two other IRBs rejected the fictitious study, while claiming that the study was “the worst thing I have ever seen” and was “a terrible risk for the patient.”<sup>6</sup> In August 2011, just two years after the Coast IRB incident, Essex IRB fell into a similar trap.<sup>7</sup> Essex IRB, another for-profit IRB,

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1. Coast Institutional Review Board’s coupon enticed customers to use its services by implying its review of the study will be easy for the customer. *Institutional Review Boards That Oversee Experimental Human Testing for Profit: Hearing Before the Subcomm. on Oversight and Investigations of the Comm. on Energy and Commerce*, 111th Cong. 2–3 (2009) [hereinafter *Hearing on IRBs*] (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce). This hearing has not been discussed in any legal journal articles regarding IRBs.

2. *Id.*

3. See e.g., Alicia Mundy, *Sting Operation Exposes Gaps in Oversight of Human Experiments*, WALL ST. J. (Mar. 26, 2009), <http://online.wsj.com/article/SB123811179572353181.html>.

4. See *id.*

5. *Hearing on IRBs*, *supra* note 1, at 2 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

6. *Id.*

7. Inspectional Observations, U.S. Dep’t of Health and Human Servs. Food & Drug Admin., Form FDA 483 (Mar. 14–21, 2011), [http://www.circare.org/fdawls/essexirb\\_fdafoia\\_2011-6068.pdf](http://www.circare.org/fdawls/essexirb_fdafoia_2011-6068.pdf).

approved a similar bogus study using the *same* fictitious investigator from the 2009 sting operation.<sup>8</sup>

IRBs are the formal entities, regulated by the Department of Health and Human Services (HHS), responsible for reviewing research involving human subjects.<sup>9</sup> All federally funded human subjects research and all FDA regulated studies must be approved by an IRB.<sup>10</sup> An IRB's primary purpose is to "protect the rights and welfare of human research subjects" by approving, modifying, or rejecting human research studies.<sup>11</sup> IRBs have a duty to assure research-subjects that all study risks are fully disclosed, that all risks will be minimized to the extent possible, and that all risks are appropriate in relation to any anticipated benefits.<sup>12</sup>

Originally, the Office for Protection from Research Risks (OPRR) allowed only IRBs located in or supported by institutions to review federally funded studies.<sup>13</sup> These institutionally supported IRBs, composed primarily of members from the research institution, are referred to as "local IRBs."<sup>14</sup> Subsequently, in 1996, OPRR changed its position to allow IRBs that are unaffiliated with the institution engaged in research to review federally funded studies.<sup>15</sup> These unaffiliated IRBs are referred to as "independent IRBs."<sup>16</sup> Currently, the Office of Human Research Protections (OHRP)—which replaced OPRR in 2000<sup>17</sup>—allows an institution to choose whether to use its local IRB or to rely on the review of another, qualified IRB.<sup>18</sup> However, on July 26, 2011, HHS and the Office of Science and Technology Policy (OSTP) issued proposed regulations for "Streamlining IRB Review of Multi-Site Studies," which suggest mandating a central IRB for multi-site studies in order to strengthen protection for research subjects.<sup>19</sup> A "central IRB" is a single IRB

8. *Id.*

9. U.S. DEP'T OF HEALTH & HUMAN SERVS., *Chapter 1: Institutional Administration*, in INSTITUTIONAL REVIEW BOARD GUIDEBOOK 1 (1993), available at [http://www.hhs.gov/ohrp/archive/irb/irb\\_chapter1.htm](http://www.hhs.gov/ohrp/archive/irb/irb_chapter1.htm).

10. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512–13 (proposed July 26, 2011); Institutional Review Boards, 21 C.F.R. § 56.103(a) (2012).

11. U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 9, at 1.

12. U.S. DEP'T OF HEALTH & HUMAN SERVS., *Chapter 3: Basic IRB Review*, in INSTITUTIONAL REVIEW BOARD GUIDEBOOK, *supra* note 9, at 2.

13. David Forster, *Independent Institutional Review Boards*, 32 SETON HALL L. REV. 513, 517 (2002).

14. *Id.* at 515.

15. *Id.* at 517–18.

16. *Id.*

17. Office of Public Health and Science, 65 Fed. Reg. 37,136 (June 13, 2000).

18. Protection of Human Subjects, 45 C.F.R. § 46.114 (2011).

19. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512, 44,521 (proposed July 26, 2011). The proposed regulations cover seven topics: "Ensuring Risk-Based Protections, Streamlining IRB Review of Multi-Site Studies, Improving Informed Consent, Strengthening

that reviews a study that will take place at multiple research sites and whose review will supplant the local IRB's review on the study.<sup>20</sup>

This note will argue, by analyzing the proposed regulations and their implications for research-subjects' protection, that forcing a research site to use a central IRB does not strengthen protection for research subjects.<sup>21</sup> Due to the challenges imposed on a local IRB to approve and monitor the many institutions in a multi-site study, these proposed regulations are effectively forcing institutions to use an independent IRB.<sup>22</sup> Since the majority of independent IRBs are for-profit IRBs,<sup>23</sup> these regulations will push IRB review to for-profit companies, companies like Coast IRB and Essex IRB. For-profit IRBs do not operate in the best interests of the research subjects because they have greater incentives, namely income, to approve research proposals, as illustrated in the Coast IRB and Essex IRB cases.<sup>24</sup> Additionally, for-profit IRBs have a conflict of interest because their sole source of income is the fees paid by the sponsors, the companies backing the study, writing the research protocol, and investing in this protocol's approval.<sup>25</sup> As a result, under the proposed regulations, research subjects face a greater risk of participating in potentially harmful studies.<sup>26</sup>

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Data Protections to Minimize Information Risks, Data Collection to Enhance System Oversight, Extension of Federal Regulations, and Clarifying and Harmonizing Regulatory Requirements and Agency Guidance." *Id.* at 44,512.

20. *Id.* at 44,522.

21. This note will focus on biomedical and pharmaceutical clinical trials. Distinguishing between biomedical and behavioral research is necessary in order to know which activities need to be reviewed. THE NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, THE BELMONT REPORT 10 (1979), available at [http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b\\_09\\_02\\_Belmont%20Report.pdf](http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf) (stating "problems relating to social experimentation may differ substantially from those of biomedical and behavioral research"). Additionally, social scientists see social science research as fitting poorly into the "medically-driven IRB protocol templates and language." Caroline H. Bledsoe et al., *Regulating Creativity: Research and Survival in the IRB Iron Cage*, 101 NW. U. L. REV. 593, 596-97 (2007). Furthermore, FDA regulation of devices requires the use of local institutional review committees in the same facilities as where the testing of the device is to occur. *See also* Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,521 (proposed July 26, 2011) (stating that the proposed regulations not apply to FDA-regulated device studies). Therefore, this analysis does not pertain to behavioral research or medical device research.

22. *See infra* text accompany notes 133-63.

23. Compare Ruth Macklin, *How Independent Are IRBs?*, IRB: ETHICS & HUMAN RESEARCH, May-June 2008, at 15, 19 (2008) (stating that there are some not for profit independent IRBs, but that information on them is scarce), with *Commercial Institutional Review Boards*, CITIZENS FOR RESPONSIBLE CARE AND RESEARCH, <http://www.circare.org/info/commercialirb.htm> (last visited Apr. 19, 2013) (listing forty-nine active commercial IRBs).

24. *See infra* text accompanying notes 221-42.

25. *See infra* text accompanying notes 221-32.

26. *See infra* text accompanying notes 213-45.

The first section examines the history of research-subjects' protection, the proposed regulations, and the current legal issues involving IRB review. The second section explains why the proposed regulations will essentially push IRB review to independent IRBs and why independent IRBs do not act in the research-subjects' best interests. The final section makes suggestions for improving research-subjects protection if the ultimate HHS regulations include this central IRB provision.

## I. UNDERSTANDING INSTITUTIONAL REVIEW BOARDS AND THE PROPOSED REGULATIONS

### A. *History of Regulating Research-Subjects' Protection*

Both the International community and the United States developed regulations to protect research subjects in response to subject abuse in "scientific" experiments. The Nuremberg Code, which was enacted in 1949 in response to Nazi experimentation on concentration camp prisoners,<sup>27</sup> developed the basic principles of ethical conduct for research involving human subjects and specified ten "Directives for Human Experimentation."<sup>28</sup> In 1964, the World Medical Association adopted similar recommendations in the Declaration of Helsinki.<sup>29</sup> Among other requirements, the Declaration of Helsinki mandates that research ethics committees be "independent of the researcher, the sponsor, and any other undue influences."<sup>30</sup> Although the United States adopted many of these directives when creating its own research-subjects' protection regulations,<sup>31</sup> the United States has not expressly adopted

27. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011); THE NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, *supra* note 21, at 2.

28. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011); *The Nuremberg Code*, NATIONAL INSTITUTES OF HEALTH, available at <http://history.nih.gov/research/downloads/nuremberg.pdf>. The ten directives mandate voluntary consent, experiments be for the good of society, experiments have anticipated results that justify the performance, experiments that avoid unnecessary physical and mental pain, experiments that will not knowingly result in subject death or disabling injury, experiments whose importance outweighs risks to subjects, protection against remote possibilities of injury or death, experiments conducted only by qualified personnel, subject autonomy to end a study at any point, and scientist agreement to terminate an experiment if it is likely to result in injury, disability, or death of the subject. *Id.*

29. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011).

30. *World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Humans*, WORLD MEDICAL ASSOCIATION, para. 15, <http://www.wma.net/en/30publications/10policies/b3/17c.pdf> (last visited Apr. 19, 2013).

31. *Compare The Nuremberg Code*, *supra* note 28 (requiring voluntary consent and continued observation after initial approval), with Protection of Human Subjects, 45 C.F.R. §

all of the provisions of the Nuremberg Code and the Declaration of Helsinki.<sup>32</sup> Furthermore, United States courts have varied in their application of the Nuremberg Code to cases involving injured research subjects.<sup>33</sup> In contrast, courts have consistently concluded that the Declaration of Helsinki does not apply in the United States.<sup>34</sup>

Before the United States developed its own research-subjects' protection regulations, astounding research abuses occurred on United States soil: deliberately denying treatment to men with syphilis,<sup>35</sup> injecting plutonium into unsuspecting hospital patients,<sup>36</sup> purposefully infecting children with

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46.116 (2011) (mandating subject's legally effective informed consent for subject's involvement in research experiment), and Protection of Human Subjects, 45 C.F.R. § 46.109(e) (2011) (requiring continuing review of a study at least once a year).

32. Compare *The Nuremberg Code*, *supra* note 28 (necessitating the risk to never exceed the humanitarian importance of the problem to be solved by the experiment), and *World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Humans*, *supra* note 30, para. 24 (requiring subjects be adequately informed of sources of funding, any possible conflicts of interest, and any other relevant aspects of the study), with Protection of Human Subjects, 45 C.F.R. § 46.101 (2011).

33. Compare *Grimes v. Kennedy Krieger Inst., Inc.*, 782 A.2d 807, 835 (Md. Ct. App. 2001) (finding the Nuremberg Code to be the "most complete and authoritative statement of the law of informed consent to human experimentation" and that "absence of judicial precedent makes codes, especially judicially-crafted codes like the Nuremberg Code, all the more important"), with *Robertson v. McGee*, No. 01-CV-60-C, 2002 U.S. Dist. LEXIS 4072, at \*9 (D. Okla. Jan. 28, 2002) (stating that the court agrees that there is "no private right of action for an alleged violation of international law" under the Nuremberg Code). Resorting to international law is unnecessary when there is a standard in the Code of Federal Regulations. *Id.* at \*9–\*10.

34. *Sykes v. United States*, No. 1:10-CV-688, 2011 U.S. Dist. LEXIS 94815, at \*9, \*45 (D. Ohio July 22, 2011) (holding that there was no private right of action for alleged violation of the Helsinki Declaration in a case where a human subject allegedly died from pharmaceuticals given in a clinical trial because the Code of Federal Regulations governs human subjects research in the United States). See also *White v. Paulsen*, 997 F. Supp. 1380, 1383 (D. Wash. 1998); *Hoover v. West Virginia Dep't. of Health & Human Services*, 984 F. Supp. 978, 980 (D. W.Va. 1997); *Abdullahi v. Pfizer, Inc.*, No. 01 Civ. 8118, 2005 U.S. Dist. LEXIS 16126, at \*31 (D. N.Y. Aug. 09, 2005).

35. From 1932-1972, the United States Public Health Service documented the natural history of syphilis, using 399 black sharecroppers infected with syphilis, in the Tuskegee Syphilis Study. CARL H. COLEMAN ET AL., *THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS* 41 (2005). Not only did the physicians deny treatment to the men with syphilis, even after the effective treatment of penicillin became available, but they also went to "extreme lengths to ensure that they would not receive therapy from other sources." *Id.* at 41.

36. From 1944-1974, the federal government funded radiation experiments where physicians "inject[ed] plutonium into unsuspecting hospital patients" and released radiation into the environment. *Id.* at 44. Several patients died from acute radiation effects. *Id.* In addition, the government did not maintain adequate records in order to keep the public from learning about these programs. *Id.* at 45.

hepatitis,<sup>37</sup> and injecting live cancer cells into elderly patients.<sup>38</sup> Following these highly publicized cases of research abuse, United States federal agencies enacted the 1974 Research Act.<sup>39</sup> In 1979, the National Commission published its own guidelines for research-subjects' protection in the Belmont Report.<sup>40</sup> The Belmont Report provided a framework to guide the resolution of ethical problems arising in human-subjects' research.<sup>41</sup> In addition to the Belmont Report, in 1981, the FDA created provisions requiring IRB approval during the FDA clinical investigation procedure, which include IRB review of clinical investigations and of continuing review.<sup>42</sup> Continuing review is the process of periodically reviewing a study after the initial approval.<sup>43</sup> Subsequently, in 1991, fourteen federal departments joined with HHS to adopt uniform rules, known as the Common Rule, for the protection of research subjects.<sup>44</sup> The Common Rule covers all federally conducted or supported human-subjects research.<sup>45</sup>

The Common Rule documents IRB member requirements: a minimum of five members with varying backgrounds, a minimum of one member with a primary scientific area of concern, a minimum of one member with a primary nonscientific area of concern, and a minimum of one member not affiliated with the institution.<sup>46</sup> The Common Rule requires IRB member diversification in order for its members to have sufficient experience and expertise to

37. From 1956–1971, Doctor Saul Krugman “fed extracts of stools from [hepatitis] infected [institutionalized] children” as well as injected children with the hepatitis virus in order to study the hepatitis virus. *Id.* at 39.

38. In 1963, the NIH and the Public Health Service funded a study where physicians “injected live cancer cells into twenty-two indigent, chronically ill, and debilitated [and unsuspecting] elderly patients at the Brooklyn Jewish Chronic Disease Hospital.” *Id.* at 39.

39. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011). This Act created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission). *Id.*

40. *Id.*

41. THE NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, *supra* note 21, at 3.

42. Protection of Human Subjects, 46 Fed. Reg. 8,958 (January 27, 1981) (codified at 21 C.F.R. § 56.101); 21 C.F.R. § 56.103(a) (2012).

43. 21 C.F.R. § 56.103(a) (2012).

44. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011). The Common Rule adopted 45 C.F.R. Part 46 Subpart A of the HHS regulations. *Id.* A total of seventeen federal agencies now follow some form of the Common Rule. U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-09-448T, HUMAN SUBJECTS RESEARCH: UNDERCOVER TESTS SHOW THE INSTITUTIONAL REVIEW BOARD SYSTEM IS VULNERABLE TO UNETHICAL MANIPULATION 6 (2009).

45. Protection of Human Subjects, 45 C.F.R. § 46.101(a) (2011).

46. 45 C.F.R. § 46.107(a), (c), (d). The FDA's IRB member requirements match those of the Common Rule. *See* Institutional Review Boards, 21 C.F.R. § 56.107 (2012).

safeguard the rights and welfare of research subjects.<sup>47</sup> Additionally, the Common Rule mandates that IRBs provide continued review of studies at least once per year.<sup>48</sup> The last major addition to research-subjects' regulations came in 2009 when HHS required each IRB reviewing research conducted or supported by HHS to be registered with HHS.<sup>49</sup>

*B. Proposed Regulations: "Enhancing Protection for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators"*

When the current regulations were developed, research generally took place at single sites, predominantly universities, colleges, and medical institutions.<sup>50</sup> Presently, however, a substantial portion of research occurs in multi-site studies at centers unaffiliated with these academic research institutions.<sup>51</sup> Multi-site studies, studies where a single research protocol is conducted at numerous research sites, are particularly common in clinical trials.<sup>52</sup> This change in research dynamics is partially due to the shift in clinical trial funding from the government to pharmaceutical companies<sup>53</sup> and to the need of these trials to generate sufficient participant numbers and generalizable results.<sup>54</sup> Research-subjects' protection regulations, on the other hand, have not evolved along with the proliferation of multi-site clinical trials.<sup>55</sup> While the Common Rule does not require separate approval from every local IRB in a multi-site study, in many of these studies each institution's local IRB will review the research protocol independently, resulting in duplicative reviews of

47. Protection of Human Subjects, 45 C.F.R. § 46.103(b)(3) (2011).

48. 45 C.F.R. § 46.109(e). The IRB has the discretion to determine the frequency of continuing review. *Id.* However, in determining this frequency, the IRB is to consider the degree of risk. *Id.*

49. 45 C.F.R. § 46.501. This registration must be renewed every three years. *Id.* at § 46.505(a).

50. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011).

51. *Id.* at 44,521; Trudo Lemmens & Benjamin Freedman, *Ethics Review for Sale? Conflict of Interest and Commercial Research Review Boards*, 78 MILBANK Q. 547, 548–49 (2000) (stating that research of new drugs is increasingly taking place at pharmaceutical research centers or physicians' offices independent of academic research centers).

52. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,521 (proposed July 26, 2011).

53. Lynn A. Jansen, *Local IRBs, Multicenter Trials, and the Ethics of Internal Amendments*, 27 IRB: ETHICS & HUM. RES. 7, 7 (2005).

54. William Burman & Robert Daum, *Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts*, 49 CLINICAL INFECTIOUS DISEASES 328, 330 (2009).

55. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011).



study protocols.<sup>56</sup> Further delaying the research process, investigators must resubmit any IRB protocol changes made by a local IRB to all reviewing IRBs.<sup>57</sup> For these reasons, critics have argued that the highly regulated IRB review structure hinders the research process by creating inefficiencies and adding bureaucratic complexity with duplicative IRB review.<sup>58</sup> These critics have claimed that research is unnecessarily delayed, since there is no evidence that research subjects are protected by the multiple reviews.<sup>59</sup> Conversely, the absence of evidence, especially in the absence of any research focusing on the safety of these reviews, is not a reasonable argument to change regulations. Duplicative reviews of studies provide additional scrutiny of research protocols for the primary goal of protecting research subjects. Until more research is performed, there is no evidence to demonstrate that removal of these additional reviews will benefit research subjects. However, in response to the critics, HHS proposed new human subjects research protection regulations.<sup>60</sup>

### 1. Proposed Regulations

On July 26, 2011, HHS and OSTP proposed regulations to strengthen protection for research subjects and to match the “evolving human research enterprise [and] the proliferation of multi-site clinical trials.”<sup>61</sup> HHS and OSTP requested comments to the proposed regulations be submitted before October 26, 2011.<sup>62</sup> As of the date of this note, the proposed regulations are closed for commenting, and HHS has yet to release final regulations.<sup>63</sup>

The proposed regulations mandate “that all domestic sites in a multi-site study rely upon a single IRB as their IRB of record for that study,”<sup>64</sup> meaning the regulations require the use of a central IRB for multi-site studies. This is a change from the current regulations, which give institutions a choice in

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56. *Id.* at 44,521, 44,522.

57. *Id.*

58. *Id.* at 44,513.

59. *Id.*

60. *Id.* at 44,512.

61. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011).

62. Initial comment deadline was September 26, 2011. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011). HHS and OSTP extended the deadline to October 26, 2011 after multiple requests for extensions. *Advanced Notice of Public Rule Making*, U.S. DEP’T OF HEALTH & HUMAN SERVS., <http://www.hhs.gov/ohrp/humansubjects/index.html> (last visited Apr. 19, 2013).

63. *Information Related to Advanced Notice of Proposed Rulemaking (ANPRM) for Revisions to the Common Rule*, U.S. DEP’T OF HEALTH & HUMAN SERVS., <http://www.hhs.gov/ohrp/humansubjects/anprm2011page.html> (last visited Apr. 19, 2013).

64. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011).

deciding whether to use a central IRB or their own IRB in multi-site studies.<sup>65</sup> The regulations do not suggest guidelines for how to select the IRB of record, but the regulations seemingly give the sponsor unfettered discretion to choose the IRB of record for multi-site studies.<sup>66</sup> Complete sponsor discretion poses a serious concern for research-subjects' interests, since research subjects place trust in an unbiased IRB to protect their welfare. Additionally, while local sites would not be relieved of any obligations under the research-subjects' protection regulations, local internal reviews could be discouraged and would not have regulatory status with the Common Rule under the proposed regulations.<sup>67</sup> Therefore, local IRB review may be limited, if at all necessary, to perspectives of the local community:<sup>68</sup> cultural backgrounds of the research subjects' population, community attitudes about the proposed research, and the capacity of the institution to support the proposed research.<sup>69</sup> However, even this review may be limited as the proposed regulations suggest, in contrast to previous regulations, that "[t]he evaluation of a study's social value, scientific validity, and risks and benefits, and the adequacy of the informed consent document and process generally do not require the unique perspective of a local IRB."<sup>70</sup>

## 2. HHS Support for Proposed Regulations

In addition to HHS and OSTP opinions on the need for central IRB review of multi-site studies, the proposed regulations cited recent academic journal articles in support of the new regulations. These studies highlight concerns with research integrity, site-specific modifications, and variability among local IRB review.<sup>71</sup> Multiple reviews of multi-site studies can affect research integrity when IRB reviews produce different outcomes for identical studies.<sup>72</sup>

65. *Id.*

66. *Id.* at 44,521–22. *See also* Janet M. Lis & Melina G. Murray, *The Ins and Outs of Independent IRBs*, 2 J. HEALTH & LIFE SCI. 73, 79 (2008).

67. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011).

68. *Id.*

69. U.S. DEP'T HEALTH & HUMAN SERVS. ET AL., GUIDANCE FOR INDUSTRY: USING A CENTRALIZED IRB REVIEW PROCESS IN MULTICENTER CLINICAL TRIALS 4–5 (2006) [hereinafter GUIDANCE FOR INDUSTRY].

70. Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011). *Contra* Protection of Human Subjects, 45 C.F.R. § 46.107(a) (2011) (stating the point of local IRBs is to gain the perspective of the community and for researchers to demonstrate the input of local comments on the requirements for a waiver of consent).

71. Kathleen Dziak et al., *Variations Among Institutional Review Board Reviews in a Multisite Health Services Research Study*, 40 HEALTH SERVS. RES. 279, 287 (2005).

72. Human Subjects Research Protection, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011); Dziak et al, *supra* note 71, at 282–83 (examining a study evaluating patient perceptions of care at fifteen primary sites). *See also* Jansen, *supra* note 53, at 7.

Research integrity deals with verifiable methods in research and the adherence to rules, regulations, and guidelines in research.<sup>73</sup> In addition to producing different outcomes, local IRBs sometimes made minor, site-specific modifications during local review of multi-site studies.<sup>74</sup> These site-specific modifications can potentially undermine the scientific validity of a study because they introduce an uncontrolled variance.<sup>75</sup> Another concern is the approval time discrepancy from institution to institution.<sup>76</sup> The variability in the IRB approval process is cited as an “enormous challenge” to human-subjects’ research.<sup>77</sup>

Along with the concerns regarding multiple IRB reviews of a single protocol, HHS supported the central IRB mandate by suggesting that local review is not necessary and does not add protection for subjects.<sup>78</sup> HHS cited to a report that found that there is no data to show that local perspectives are taken into consideration during local IRB review.<sup>79</sup> Additionally, critics of the current system support the notion that a mandatory central IRB review would create a stronger local IRB system,<sup>80</sup> since multiple reviews divert IRB resources from other studies.<sup>81</sup> Along with retaining valuable resources, critics suggest that independent IRBs are less vulnerable to institutional pressures.<sup>82</sup>

However, these challenges pit the interests of scientific research against the interests of human-subjects’ welfare. Although there is no evidence that additional local review helps protect subjects, clearly additional local review does not place subjects at a greater of risk of being injured in research studies. Additionally, these critics fail to address the serious implication that

73. *Research Integrity*, U.S. DEP’T HEALTH & HUMAN SERVS., [http://grants.nih.gov/grants/research\\_integrity/index.htm](http://grants.nih.gov/grants/research_integrity/index.htm) (last visited Apr. 19, 2013).

74. Jansen, *supra* note 53, at 7.

75. *Id.* at 8.

76. Dziak et al., *supra* note 71, at 283. The time it took for the fifteen IRBs to review the study ranged from five to 172 days. *Id.* HHS also cited to a report that indicated that the review time variability concerned study sponsors. Human Subjects Research Protection, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011); NAT’L INST. OF HEALTH ET AL., NATIONAL CONFERENCE ON ALTERNATIVE IRB MODELS: OPTIMIZING HUMAN SUBJECT PROTECTION 6 (2006), available at <https://www.aamc.org/download/75240/data/irbconf06rpt.pdf> [hereinafter NATIONAL CONFERENCE].

77. Dziak et al., *supra* note 71, at 287.

78. Human Subjects Research Protection, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011).

79. Ezekiel J. Emanuel et al., *Oversight of Human Participants Research: Identifying Problems to Evaluate Reform Proposals*, 141 ANN. INTERNAL MED. 282, 283 (2004).

80. *Id.* at 289. Reducing the burden on local IRBs would allow them to “focus on research requiring a local perspective.” *Id.* at 287.

81. Burman & Daum, *supra* note 54, at 330–31 (finding that a multi-site study required a median of thirty staff hours).

82. NATIONAL CONFERENCE, *supra* note 76, at 5.

independent IRBs are more vulnerable to sponsor pressure, since the sponsor is the IRB's customer.<sup>83</sup> While HHS's rationale suggests that the regulations protect important research integrity issues, the proposed regulations were not based on any factual studies showing that a central IRB would improve research-subjects' safety.<sup>84</sup>

C. *Recent Issues with IRBs: Why the Public Should Care About Research Subject Protection Regulations*

IRBs exist in order to protect research-subjects' safety.<sup>85</sup> Improving subject safety should be the top priority for new HHS regulations, especially given the track record of research-subjects' protection.

1. Research Subject Injuries: Effective IRB Regulations are Essential to Protecting Research Volunteers

Research abuses still occur in the United States despite HHS regulations and IRB review of studies.<sup>86</sup> Risks exist for any clinical trial participant, but recent cases of participant injury or death place into question whether financial conflicts of interest put subjects in a greater position of risk.<sup>87</sup> While the more publicized research deaths may have occurred in studies governed by local IRBs,<sup>88</sup> research subjects have been injured in studies governed by for-profit IRBs as well.<sup>89</sup>

Perhaps the most publicized participant injury in recent years was the death of 18-year old Jesse Gelsinger at the University of Pennsylvania in 1999 during a gene-therapy trial.<sup>90</sup> The informed consent form Gelsinger signed failed to mention that several monkeys had died in a prior study<sup>91</sup> and that four research subjects previously suffered severe liver damage.<sup>92</sup> Unfortunately, Gelsinger's death has not been an isolated incident where oversight has failed

83. See *infra* text accompanying notes 221–32.

84. Human Subjects Research Protection, 76 Fed. Reg. 44,512, 44,521–22 (proposed July 26, 2011).

85. Institutional Review Boards, 74 Fed. Reg. 9,578 (proposed March 5, 2009) (to be codified at 45 C.F.R. pt. 46).

86. See *infra* text accompanying notes 91–105.

87. See *infra* text accompanying notes 98–105.

88. Commentators have pointed out that the highly publicized cases of human subjects injuries have been in single-site studies. Burman & Daum, *supra* note 54, at 332.

89. Ezekiel J. Emanuel et al., *Should Society Allow Research Ethics Boards to Be Run as For-Profit Enterprises?*, 3 PLOS MED. 941, 943 (2006).

90. Robin Fretwell Wilson, *Estate of Gelsinger v. Trustees of University of Pennsylvania: Money, Prestige, and Conflicts of Interest in Human Subjects Research*, in HEALTH LAW AND BIOETHICS 229, 229 (Sandra H. Johnson et. al. eds., 2009).

91. *Id.*

92. Sharona Hoffman, *Continued Concern: Human Subject Protection, the Institutional Review Board, and Continuing Review*, 68 TENN. L. REV. 725, 725 (2001).

to protect research subjects. Not long after Gelsinger's death, Ellen Roche, a healthy volunteer, died in an asthma study conducted by Johns Hopkins University.<sup>93</sup> Following Roche's death, the FDA concluded that the study's IRB review was "inadequate"<sup>94</sup> and suspended all federally-funded research at John Hopkins.<sup>95</sup> These are just two cases that demonstrate how things can go wrong at prominent research institutions under local IRB review when the IRB and the researchers lose sight of their priority to protect research subjects.<sup>96</sup>

Although less publicized, independent IRBs and multi-site studies have had recent issues with injured subjects as well. In 2002, Gary Polsgrove died twenty-two days after enrolling in a study at the Fabre Research Clinic in Houston.<sup>97</sup> A Fabre Clinic employee, an employee represented to the FDA as a licensed physician's assistant, with no actual medical training, was responsible for Polsgrove's care during the study.<sup>98</sup> The IRB reviewing the study—the Human Investigation Committee—was run by Fabre, the same man who ran the research clinic.<sup>99</sup> This "IRB held its meetings in restaurants around Houston."<sup>100</sup> Even though the FDA issued a warning to the IRB in 1992 highlighting its conflict of interest, the IRB continued to review studies at the Fabre Clinic, including the study in which Polsgrove was enrolled.<sup>101</sup> In 2004,

93. Hazel Glenn Beh, *The Role of Institutional Review Boards in Protecting Human Subjects: Are We Really Ready to Fix a Broken System?*, 26 LAW & PSYCHOL. REV. 1, 32 (2002). Ellen Roche died on June 3, 2001. *Id.*

94. Jonathan Bor & Tom Pelton, *U.S. Halts Hopkins Research*, THE BALTIMORE SUN (July 20, 2001), <http://www.baltimoresun.com/bal-te.hopkins20jul20,0,5166731.story>.

95. Beh, *supra* note 93, at 32.

96. Daniel L. Icenogle & Whyte H. Dudek, *IRBs, Conflicts and Liability: Will We See IRBs in Court? Or is it When?*, 1 CLINICAL MED. & RES. 63, 64 (2002). Other stories include Kathryn Hamilton's death in a breast cancer study at the renowned Fred Hutchinson Cancer Center and nine-month-old Gage Steven's death in a heartburn study at Pittsburgh Children's Hospital. Duff Wilson & David Heath, *With a Year or Two to Live, Woman Joined Test in Which She was Misled-and Died*, SEATTLE TIMES (Mar. 13, 2001), <http://community.seattletimes.nwsources.com/archive/?date=20010313&slug=hutch13>; Dawn MacKeen, *Kids as Guinea Pigs*, SALON (May 31, 2000), [http://www.salon.com/2000/05/31/drug\\_trials/](http://www.salon.com/2000/05/31/drug_trials/). The shocking part about Hamilton's story is that only *six days* after Hamilton passed, her doctors published a study concluding that the drugs did not work. Wilson & Heath, *supra* note 96.

97. DAVID EVANS ET AL., BLOOMBERG MARKETS, BIG PHARMA'S SHAMEFUL SECRET 4 (2005), available at <http://dcscience.net/pharma-bloomberg.pdf>.

98. *Id.* Astoundingly, a similar situation was uncovered in 2010 when Doctor Kamrava at Napoli LLC conducted a clinical study that was approved by the local IRB at West Coast IVF Clinic, of which Doctor Kamrava and an embryologist were the IRB's only members. Letter from Steven D. Silverman, Dir., Ctr. for Devices and Radiological Health, to Michael M. Kamrava, Chairman, Int'l Review Bd. (Jan. 21, 2011) (on file with the U.S. Dep't of Health & Human Servs.), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2011/ucm240960.htm>.

99. EVANS ET AL., *supra* note 97, at 4.

100. *Id.*

101. *Id.*

Western IRB, the nation's largest for-profit IRB,<sup>102</sup> settled a lawsuit with a research subject for an undisclosed amount after the subject, whose psoriatic arthritis was under control before the study, became so ill during the study that he could barely walk or stand.<sup>103</sup> Other injuries in multi-site studies include the death of a 19-year old University of Rochester student in a Massachusetts Institute of Technology study.<sup>104</sup> In addition to these notorious injuries and deaths, research-subjects' injuries have prompted lawsuits against IRBs.<sup>105</sup>

## 2. IRB Liability: Can IRBs Be Held Liable for Failing to Protect Research Subjects?

Neither the OHRP nor the FDA can require an institution or an IRB to pay damages to an injured research subject.<sup>106</sup> Although injured research subjects have been suing institutions and researchers for a long time, litigation against IRBs has increased in the past decade.<sup>107</sup> Although injured participants have not won a court verdict against an IRB, there are cases where IRBs, including for-profit IRBs, have settled with plaintiffs outside of the courtroom.<sup>108</sup> However, this lack of success in the courtroom has not deterred plaintiffs from adding IRBs and individual IRB members as defendants to lawsuits.<sup>109</sup>

Injured research subjects first opened the door to suing IRB members in *Robertson v. McGee*.<sup>110</sup> *Robertson* arose out of a study at the University of Oklahoma Health Science Center.<sup>111</sup> The plaintiffs alleged that the "IRB members failed to examine the design of the protocol, review the operation of the trial, review proposed amendments to the informed consent forms, review

102. Caroline McNeil, *Debate Over Institutional Review Boards Continues as Alternative Options Emerge*, 99 J. NAT'L CANCER INST. 502, 502 (2007).

103. EVANS ET AL., *supra* note 97, at 6.

104. Dan McGuire, *Rochester Death Halts MIT Funded Study*, THE TECH, April 9, 1996, available at <http://tech.mit.edu/V116/PDF/N17.pdf>.

105. Marjorie Ellen Zettler, *Trials and Tribulations of the IRB Member*, 80 U. TORONTO MED. J. 200, 200–01 (2003).

106. Sharona Hoffman & Jessica Wilen Berg, *The Suitability of IRB Liability*, 67 U. PITT. L. REV. 365, 416 (2005).

107. *See id.* at 382–84; *See Zettler, supra* note 105, at 201.

108. EVANS ET AL., *supra* note 97, at 6 (disclosing that Western IRB settled with Bill Hamlet for an undisclosed amount); Hoffman & Berg, *supra* note 106, at 382; Beh, *supra* note 93, at 29, 31–32 (disclosing the University of Pennsylvania settled with the Gelsinger family after Jesse Gelsinger's death).

109. *See generally, infra* text accompanying notes 114–17; *see also* T.C. *ex rel.* v. A.I. DuPont Hosp. for Children, 368 F. App'x 285, 286–87 (3d Cir. 2010); M.G. *ex rel.* v. A.I. DuPont Hosp. for Children, 393 F. App'x 884, 885–86 (3d Cir. 2010).

110. Hoffman & Berg, *supra* note 106, at 383.

111. *Robertson v. McGee*, No. 01-CV-60-C, 2002, U.S. Dist. LEXIS 4072, at \*5 (D. Okla. Jan. 28, 2002).

amendments to the protocol, and ensure proper reporting.”<sup>112</sup> However, the *Robertson* court did not issue a ruling on the merits because the court concluded that it lacked subject-matter jurisdiction.<sup>113</sup> Similarly, in *Townsend v. University Hospital-University of Colorado*, a research subject’s family members sued the individual members of the University of Colorado IRB after the subject died in the hospital’s care.<sup>114</sup> In this case, the IRB member liability issue was not decided because the court lacked personal jurisdiction.<sup>115</sup> In addition to these decided IRB cases, there are also cases currently pending against IRBs. An injured subject filed a complaint in April 2011 against the individual members of an IRB for failing to use due care in approving a gene therapy protocol.<sup>116</sup> Another recently filed lawsuit against Duke University took a different approach by suing Duke directly for negligence per se for its IRB’s failure to “renew its review of the research as other renowned researchers called the Duke University and/or DUHS Clinical Trials into question.”<sup>117</sup>

Multiple theories have been proposed to hold IRBs liable for research-subject injuries. IRB liability does not fall within typical liability grounds because the IRB does not contract directly with research subjects or make direct representations to them.<sup>118</sup> Furthermore, the Common Rule does not create a private right of action against an IRB.<sup>119</sup> However, IRB members may be found negligent for not taking precautions to ensure that protocols complied with applicable regulations if the plaintiff can demonstrate causation and damages.<sup>120</sup> For example, in *Kus v. Sherman Hospital*, an Illinois Appellate Court held that the IRB could be liable for negligence if it violated a statutory duty imposed by federal regulations.<sup>121</sup>

Others have suggested filing claims against IRBs under the False Claims Act (FCA), although no decisions have been reached on the merits against an

112. Icenogle & Dudek, *supra* note 96, at 65.

113. *Robertson v. McGee*, No. 01-CV-60-C, 2002, U.S. Dist. LEXIS 4072, at \*13 (D. Okla. Jan. 28, 2002).

114. Danielle C. Beasley, *Coupling Responsibility with Liability: Why Institutional Review Board Liability is Good Public Policy*, 36 N. KY. L. REV. 45, 46 (2009).

115. *Id.*

116. Complaint at 32–33, *Zeman v. Williams et al.*, 2011 WL 552700 (D. Mass. 2011) (No. 1:11-CV-10204).

117. Complaint & Demand for Jury Trial at 213, *Aiken v. Duke Univ., et al.*, 2011 WL 4956867 (N.C. Super. 2011) (No. 11 CVS 4721).

118. NATIONAL CONFERENCE, *supra* note 76, at 15.

119. *Id.* at 16.

120. Beasley, *supra* note 114, at 59.

121. David B. Resnik, *Liability for Institutional Review Boards*, 25 J. OF LEGAL MED. 131, 142 (2004). The regulations do not differentiate between local and independent IRBs, so members of independent IRBs could also be held liable for violating their statutory duty. Institutional Review Boards, 21 C.F.R. § 56.107 (2012).

IRB under the FCA.<sup>122</sup> In order to file under the FCA alleging violations of the Common Rule, a plaintiff must meet three conditions: “(1) the government, specifically OHRP, is not aware of the violations; (2) the violations are substantive, material to the government’s decision to fund, and not merely technical; and (3) the IRB knew that the research violated the federal regulations or was reckless in applying them.”<sup>123</sup> Because the plaintiff need not show personal injury, the FCA may be an attractive alternative when proof of causation is challenging.<sup>124</sup> One of the major benefits of the FCA is that society can proactively fix “problem” IRBs instead of having to wait until a research subject is seriously injured or killed in order to file a suit.<sup>125</sup> However, a plaintiff may have difficulty in this type of suit demonstrating that the IRB presented a false claim or caused a false claim to be presented.<sup>126</sup>

Another avenue for recovery would be to consider injured research subjects as third-party beneficiaries to the contract between the federal agency and the research institution.<sup>127</sup> The contract should be looked at as providing the terms under which research protocols must be approved, instead of as a contract to provide potential therapeutic benefits. Therefore, the research subjects would be beneficiaries of this contract.<sup>128</sup> Additionally, fiduciary theory may be an attractive avenue for recovery if the plaintiffs find it challenging to prove the elements of negligence.<sup>129</sup> In this scenario, plaintiffs would have to prove that IRB members are fiduciaries and to identify the IRB members’ defined role.<sup>130</sup>

Not only have IRBs been able to escape liability for research decisions, plaintiffs can also have trouble requesting IRB documents.<sup>131</sup> The laws in some

122. Daniel J. Powell, *Using the False Claims Act as a Basis for Institutional Review Board Liability*, 69 U. CHI. L. REV. 1399, 1400 (2002).

123. *Id.* at 1416.

124. *Id.*

125. *Id.* at 1419.

126. Hoffman & Berg, *supra* note 106, at 401–02.

127. Lori A. Alvino, *Who’s Watching the Watchdogs? Responding to the Erosion of Research Ethics by Enforcing Promises*, 103 COLUM. L. REV. 893, 920–23 (2003).

128. *Id.* at 922.

129. Hoffman & Berg, *supra* note 106, at 394.

130. *Id.*

131. *Dieffenbach v. United States*, 715 F. Supp. 2d 587, 588 (D. Del. 2010). Defendant filed a motion for a protective order covering documents generated through IRB review at the National Lung and Blood Institute and the NIH. *Id.* The court found materials prepared with confidential expectations to be privileged. *Id.* at 598. Any documents made publicly available were not given the same protection. *Id.* Compare *Doe v. Illinois Masonic Medical Center*, 696 N.E.2d 707, 708 (Ill. App. Ct. 1998) (finding Illinois Masonic Medical Center to be protected under the Illinois Medical Studies Act from disclosing IRB files and IRB meeting minutes), with *Konrady v. Oesterling*, 149 F.R.D. 592, 595 (D. Minn. 1993) (holding that an IRB does not fall within the Minnesota evidentiary shield for peer review). In *Konrady*, the court held that an IRB conducts



states, like Illinois, place the priority in protecting IRBs and researchers over protecting research subjects.<sup>132</sup> This misalignment of priorities misses the point of IRBs—IRBs exist to protect research subjects.

The fact that serious issues have occurred both with local IRBs and for-profit IRBs only highlights the issue that HHS's system is not working to protect research subjects. While inadequate ethics review is unacceptable, a company making money off of reviewing its own research is morally repugnant. Regulations should not push more studies toward for-profit companies without safeguards in place to prevent this type of occurrence.

## II. PROPOSED REGULATIONS DO NOT PLACE RESEARCH-SUBJECTS' PROTECTION AS TOP PRIORITY

### A. *Mandating Central IRB Review Effectively Means Overworked Local IRBs Will Defer to Independent IRBs for Multi-Site Studies*

The implications of the proposed regulations on research-subjects' safety are unknown, since no studies exist to show that central IRBs are better for subject protection.<sup>133</sup> However, the few studies on central IRBs that do exist suggest that it would not be feasible for local IRBs to become the central IRB for multi-site studies. With that being said, there is limited data from which to draw these predictions because IRB databases are nonexistent.<sup>134</sup>

IRB operating costs vary substantially from IRB to IRB.<sup>135</sup> Although total IRB costs are debatable, there is consensus that local IRBs are overworked.<sup>136</sup> Overworked local IRBs are not likely to want, nor are they likely to be able to, take on the additional responsibility of overseeing multi-site reviews. Due to

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"process review" rather than "peer review." Dieffenbach, 715 F. Supp. 2d at 596. IRBs protect human subjects by collecting and disseminating information about the studies, even to the public. *Id.* The court in *Illinois Masonic Medical Center* noted that the Illinois statute was broader than the Minnesota statute in *Konrady*. 696 N.E.2d at 710.

132. *Illinois Masonic Medical Center*, 696 N.E.2d at 711 (concluding that the IRB did not have to release meeting notes because the "interests of litigants must yield to other interests, in this case confidentiality, privacy and candid peer review within medical institutions").

133. Human Subjects Research Protection, 76 Fed. Reg. 44,512, 44,522 (proposed July 26, 2011). If this type of study existed, HHS would have used it.

134. Todd H. Wagner et al., *Economies of Scale in Institutional Review Boards*, 42 MED. CARE 817, 818 (2004). In order to improve IRBs, there is a need to develop standards of measurement in order to actually evaluate IRB effectiveness and quality in protecting human subjects, along with cost analysis. Margaret M. Byrne et al., *Variability in the Costs of Institutional Review Board Oversight*, 81 ACAD. MED. 708, 712 (2006).

135. Byrne et al., *supra* note 134, at 711. The study used 2002 survey information to determine the costs of activities. *Id.* at 709. Many institutional IRBs now charge commercial sponsors for review. Emanuel et al., *supra* note 79, at 283.

136. Beh, *supra* note 93, at 35.

limited IRB resources,<sup>137</sup> taking on multi-site studies might steal valuable resources away from institutional research studies. A single multi-site study may capture a large portion of an IRB's budget for multiple years. Additionally, many institutions do not compensate their IRB members for individual efforts,<sup>138</sup> meaning any additional IRB work detracts from members' compensated duties. IRBs that are already struggling with providing adequate continuing review<sup>139</sup> are unlikely to take on studies with significantly more challenging continuing review.

If a local IRB were to be the central IRB for a multi-site study, the time costs of review and continuing review would be a concern. Although initial review would be similar to a regular IRB review, the time cost would be greater since the IRB would have to consider the local context at each site.<sup>140</sup> Under 21 C.F.R. § 56.107(a), IRB members have to "ascertain the acceptability of the proposed research in terms of institutional commitments and regulations, applicable law, and standards or professional conduct and practice."<sup>141</sup> The local IRB would have to become aware of local community concerns at every site in the multi-site study and document these concerns in meeting minutes.<sup>142</sup> Relevant community concerns include local attitudes and local research laws: laws on consent, laws on confidentiality relating to substance abuse, laws on mental healthcare, and laws on HIV/AIDS status.<sup>143</sup> Mechanisms for ensuring adequate local review could include forms, to be filled out by individuals familiar with the local community, that request relevant local information; consultant interviews; or requests for written input from local IRB members at each site.<sup>144</sup> Whichever mechanism is chosen, local community concerns will provide a significant challenge for an unprepared local IRB.

Local IRBs, which are familiar with reviewing studies where they know the researchers,<sup>145</sup> will have to spend time and money on training to learn how to work with unfamiliar institutions, IRB members, and communities. The

137. IRBs have "inadequate resources, unmanageable workloads, and, in some cases, insufficient expertise." Hoffman, *supra* note 92, at 737.

138. Emanuel et al., *supra* note 79, at 283. See also, Jeremy Sugarman et al., *The Cost of Institutional Review Boards in Academic Medical Centers*, 352 NEW ENG. J. MED. 1825, 1825 (2005) (finding 43 percent of institutions do not provide monetary compensation to IRB members in a 2002 survey).

139. Hoffman, *supra* note 92, at 748–49.

140. GUIDANCE FOR INDUSTRY, *supra* note 69, at 2.

141. Institutional Review Boards, 21 C.F.R. § 56.107(a) (2001).

142. Wagner et al., *supra* note 134, at 817; GUIDANCE FOR INDUSTRY, *supra* note 69, at 5 (citing 21 C.F.R. § 56.115(a)).

143. Lis & Murray, *supra* note 66, at 98–102.

144. GUIDANCE FOR INDUSTRY, *supra* note 69, at 5.

145. Wagner et al., *supra* note 134, at 817.

institutions may have conflicting policies and procedures, which would have to be considered in order to preserve the ethical beliefs of each institution.<sup>146</sup> For example, Catholic institutions will have different rules than non-denominational institutions.<sup>147</sup> In addition, there would be an added time cost to familiarize IRB members with other states' applicable laws.<sup>148</sup> State laws play an important role in research conduct,<sup>149</sup> as federal regulations do not override state laws, which provide additional protection for research subjects.<sup>150</sup> Since many IRBs do not have budgets, re-training staff members to deal with off-site studies may be cost-prohibitive, time-prohibitive, and undesirable.<sup>151</sup>

Continuing review will also be a major concern for local IRBs, and the importance of continuing review cannot be overlooked.<sup>152</sup> Separating the reviewers from the research study site makes the IRB's job in monitoring research even more difficult.<sup>153</sup> Since staff and board time costs are the majority of IRB costs, the amount of staff and board hours to cover continuing review of far-away institutions would significantly increase IRB costs.<sup>154</sup> Local IRBs may not have the resources to adequately review different sites.<sup>155</sup> Not only would travel time increase, but technology costs—faxes, phones, web pages, databases—would likely increase as well for an IRB to sufficiently review off-site locations.<sup>156</sup> Since IRBs are already struggling with providing

146. NATIONAL CONFERENCE, *supra* note 76, at 4.

147. See CORNELL UNIVERSITY OFFICE OF RESEARCH INTEGRITY AND ASSURANCE HUMAN RESEARCH PARTICIPANT PROTECTION PROGRAM, SOP 10: INFORMED CONSENT OPTIONS, PROCESSES, AND DOCUMENTATION 1 (2010) (demonstrating an IRB can have final authority regarding their own various policies).

148. Wagner et al., *supra* note 134, at 822.

149. COLEMAN ET AL., *supra* note 35, at 163. For example, California law requires identification of the research sponsor, the funding source, or the name of the manufacturer. *Id.* at 166. Maryland law requires all human subjects research adhere to federal regulations. Emanuel et al., *supra* note 79, at 283.

150. Protection of Human Research Subjects, 45 C.F.R. § 46.101(f) (2011).

151. Wagner et al., *supra* note 134, at 818. The cost of training each staff member averaged \$1,155. *Id.*

152. A thorough continuing review in the *Gelsinger* case might have focused on the serious treatment side effects of other participants, possibly resulting in the IRB suspending the clinical trial before his death. Hoffman, *supra* note 92, at 726. See also *Kus v. Sherman Hosp.*, 644 N.E.2d 1214, 1218 (Ill. App. Ct. 1995) (stating, in a lawsuit against a hospital and not the IRB, that continuing review of the study by the IRB in this case would have discovered modified consent forms).

153. Lemmens & Freedman, *supra* note 51, at 573.

154. Byrne et al., *supra* note 134, at 711.

155. Wagner et al., *supra* note 134, at 820 (finding current continuing reviews to take up 12 percent of an IRB's review time). This percentage of IRB time would increase significantly when many more sites are added for continuing review.

156. *Id.* at 821–22.

adequate continuing review,<sup>157</sup> the daunting task of following-up at every research site may be enough in itself to deter local IRBs from becoming central IRBs for multi-site studies. Consequently, local IRBs may not desire to become a central IRB for multi-site studies.

In addition to the burdens on the local IRB, there is no evidence that sponsors would choose to work with local IRBs when turnaround time at independent IRBs is significantly faster.<sup>158</sup> In a recent study, initial review at the National Cancer Institute (NCI) Central IRB averaged 7.9 hours, compared to the mean time of 14 hours at local IRB sites.<sup>159</sup> In addition to IRB staff time, there was also a difference in the number of days it took to get the study passed.<sup>160</sup> At the central IRB site, the entire approval process took, on average, 28.3 days, while the approval process averaged 62.3 days at the local sites.<sup>161</sup> Since sponsors value faster and more predictable reviews, they are willing to pay to use independent IRBs.<sup>162</sup> Because there are few nonprofit, independent IRBs, the majority of the independent IRBs used by sponsors are for-profit companies.<sup>163</sup> While these for-profit IRBs may be more efficient for sponsors, relying solely on independent IRBs for multi-site studies raises concerns regarding the welfare of research subjects.

157. Seven out of nine IRBs sent FDA warning letters in 2011 were cited for failures relating to continuing review. *Inspections, Compliance, Enforcement, and Criminal Investigations*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2011/default.htm> (last visited Apr. 19, 2013). In fact, one IRB was cited in both 2010 and 2011 for failing to conduct continuing review. Letter from Leslie K. Ball, Dir., Food & Drug Admin., to Alice M. Gerard, President & Chief Exec. Officer, Bay Regional Medical Center (Sept. 9, 2010) (on file with the U.S. Dep't of Health & Human Servs.), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2010/ucm225596.htm>; Letter from Leslie K. Ball, Dir. Food & Drug Admin., to Philip Incarnati, President & Chief Exec. Officer, McLaren Health Care (Dec. 2, 2011) (on file with the U.S. Dep't of Health & Human Servs.), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2011/ucm284969.htm>. See also 1998 Office of Inspector General statement criticizing IRBs for failing to provide adequate continuing review of studies. Wagner et al., *supra* note 134, at 822.

158. One study found the average decision time for independent IRBs to be eleven days compared with thirty-seven days for academic IRBs. Lis & Murray, *supra* note 66, at 87. See also Todd H. Wagner et al., *Costs and Benefits of the National Cancer Institute Central Institutional Review Board*, 28 J. OF CLINICAL ONCOLOGY 662, 664 (2010), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2816001/pdf/zlj662.pdf>.

159. Wagner et al., *supra* note 158, at 664.

160. *Id.*

161. *Id.*

162. *Id.* at 665.

163. Compare Macklin, *supra* note 23, at 19 (stating that there are some not-for-profit independent IRBs, but that information on them is scarce), with *Commercial Institutional Review Boards*, *supra* note 23 (listing forty-six active commercial IRBs).

*B. Independent IRBs are not in the Research-Subjects' Best Interests*

1. Broken Independent IRBs

Although IRB subject safety issues are not isolated to independent IRBs,<sup>164</sup> local IRB issues do not make for-profit IRB problems go away.<sup>165</sup> The two recent sting operations involving Coast IRB and Essex IRB illustrate major concerns with mandating the use of central IRBs without any changes in research-subjects' protection or without requiring any additional oversight of for-profit IRBs. As shocking as the Coast IRB incident was, the Essex IRB incident was unnerving. HHS has not done anything in the past two years to remedy the "rubber-stamping" highlighted in the Coast IRB sting operation.

In late 2008, the Government Accountability Office (GAO) created a fake protocol, based on a study for a product that the FDA had removed from the market after patient deaths, and submitted the protocol to three IRBs to determine whether IRBs were "rubberstamping" research studies.<sup>166</sup> Coast IRB approved this protocol unanimously, 7-0.<sup>167</sup> The other two IRBs, who rejected the study protocol, commented that the study was "the most complicated thing that I have ever seen" and was "a terrible risk for the patient."<sup>168</sup> They both questioned patient safety in the protocol.<sup>169</sup> Whereas, Coast IRB's primary reviewing doctor told the board members that the protocol "looks fine" and that it was "probably very safe."<sup>170</sup> Furthermore, Coast IRB was only given information on 2.5 percent of the product, and the board never asked what made up the other 97.5 percent of the product that was to be placed in the subject's body.<sup>171</sup> Coast IRB discovered the fraud only after being contacted by congressional investigators *five months* after approval.<sup>172</sup> Therefore, experimentation with this deadly product could have been occurring on research subjects for five months.<sup>173</sup>

164. *IRB Seals Fate by Approving Fake Protocol in Federal Sting*, IRB ADVISOR, July 1, 2009 (statement of Marjorie Speers, Executive Director, AAHRPP).

165. Emanuel et al., *supra* note 89, at 944.

166. *Hearing on IRBs*, *supra* note 1, at 4 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

167. *Id.* at 5.

168. *Id.* One of the IRBs unanimously *rejected* the protocol. *Id.*

169. *Id.*

170. *Id.*

171. *Hearing on IRBs*, *supra* note 1, at 42.

172. *Id.* at 5 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

173. *Id.* at 27 (statement of Gregory Kutz, Managing Director, Government Accountability Office) (declaring that since federal money was not involved, Coast IRB approval was the only step necessary before experimentation).

Coast IRB had reviewed thousands of clinical trials before the sting operation,<sup>174</sup> and it had overseen 300 studies in the month prior to the investigation.<sup>175</sup> Its lax “review” of this product raises questions regarding the quality of review it gave all of the other studies it had overseen in the past. In fact, Coast IRB approved all 356 protocols it reviewed in the previous five years, with only a single dissenting vote.<sup>176</sup> That means that only *one out of* 2,492 votes over five years was a vote to disapprove a study.<sup>177</sup> In the meantime, Coast IRB’s revenue more than doubled from 2004 to 2008 to \$9.3 million.<sup>178</sup>

Moreover, Coast IRB had other conflicts with the FDA prior to this sting operation. On March 11, 2008, Coast IRB received a warning letter from the FDA regarding regulatory violations.<sup>179</sup> Coast IRB allowed an inexperienced IRB member, an employee with only a high school education,<sup>180</sup> to conduct an expedited review of a study, which did not qualify for expedited review.<sup>181</sup> Coast IRB directed the member to conduct the review despite the full board’s disapproval of the study’s recruitment advertisement.<sup>182</sup> The FDA also cited Coast IRB for not following its own standard operating procedures.<sup>183</sup> As a result, the FDA suspended Coast IRB’s ability to use expedited review procedures.<sup>184</sup> Just a year later, the FDA issued its death-inducing warning letter to Coast IRB relating to the sting operation.<sup>185</sup> The FDA cited Coast IRB for multiple failures in not obtaining sufficient information to identify any reasonably foreseeable risks to subjects.<sup>186</sup> As a result, on April 14, 2009,

174. *Id.* at 15.

175. Barry Meier, *Medical Review Firm, After Federal Sting, Goes out of Business*, N.Y. TIMES (Apr. 23, 2009), <http://www.nytimes.com/2009/04/23/business/23coast.html>.

176. *Hearing on IRBs*, *supra* note 1, at 46 (statement of Rep. Edward J. Markey).

177. *Id.* In contrast, one of the other IRBs contacted by the GAO in this sting operation had seven votes of disapproval in this study alone. *Id.* (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

178. Meier, *supra* note 175.

179. Letter from Leslie K. Ball, Dir., Food & Drug Admin., to Darren McDaniel, Chief Exec. Officer, Coast Institutional Review Board (Mar. 11, 2008) (on file with U.S. Dep’t of Health & Human Servs.), *available at* <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048374.htm> [hereinafter Coast Letter 2008].

180. *Hearing on IRBs*, *supra* note 1, at 33 (statement of Rep. Donna M. Christensen).

181. Coast Letter 2008, *supra* note 179.

182. *Id.*

183. *Id.*

184. *Id.*

185. Letter from Deborah M. Autor, Dir., Ctr. for Drug Evaluation & Res., to Daniel Dueber, Chief Exec. Officer, Coast Institutional Review Board (Apr. 14, 2009) (on file with U.S. Dep’t of Health & Human Servs.), *available at* <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm136673.htm>.

186. *Id.* Failure to determine risks to subjects were minimized under 21 C.F.R. 56.111(a); failure to determine that risks to subjects were reasonable in relation to anticipated benefits under

Coast IRB voluntarily agreed to review no new studies as well as not to add subjects to ongoing studies.<sup>187</sup> Only a few days later, Coast IRB closed shop for good.<sup>188</sup>

In response to the sting operation, Coast IRB's Chief Executive Officer (CEO) lashed out at the government, telling congressional investigators that they "wasted five weeks of my valuable time" and that it was "unconscionable" for his government to do this to him.<sup>189</sup> Additionally, Coast IRB did not fire any employees after the incident, not even the IRB chairman who admitted to not reading the protocol.<sup>190</sup> The fact that Coast IRB's CEO was more concerned about his company's reputation than he was about potential safety breaches in his company makes one wonder where Coast IRB placed its priorities.<sup>191</sup>

Fast-forward two years. The same day that HHS released these proposed regulations, the FDA issued a warning letter to Essex IRB for approving a fake study<sup>192</sup> based on a drug that was withdrawn from the market in 2004 after an increased risk of heart attacks and strokes.<sup>193</sup> Essex IRB approved a trial from the *same* made-up sponsor and clinical investigator that was used in the Coast IRB sting.<sup>194</sup> In addition, Essex IRB took a known adverse event *out* of the informed consent form without documenting its rationale for the removal.<sup>195</sup> Essex IRB could not produce meeting minutes that documented actions taken by the IRB, and it failed to follow its standard operating procedure.<sup>196</sup> As a

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21 C.F.R. 56.111(a)(2); failure to make a risk determination; and failure to ensure basic elements of informed consent in consent form. *Id.*

187. *Id.*

188. *Coast IRB Folds After FDA Warning, GAO Sting*, BIOWORLD TODAY 1, 8 (Apr. 24, 2009).

189. *Hearing on IRBs*, *supra* note 1, at 76–77 (statement of Daniel Dueber, CEO, Coast IRB, LLC).

190. *Id.* at 81.

191. *Id.* at 78.

192. *Who Watches the Watchmen?* 476 NATURE 125 (Aug. 11, 2011). This sting operation was run by journalists. *Id.* Essex IRB was considered a major for-profit IRB in 2006. Emanuel et al., *supra* note 89, at 943.

193. U.S. DEP'T OF HEALTH & HUMAN SERVS., MAR. 14–21 INSPECTION OF ESSEX INSTITUTIONAL REVIEW BOARD, INC. (Mar. 21, 2011), *available at* [http://www.circare.org/fda/wls/essexirb\\_fdafoia\\_2011-6068.pdf](http://www.circare.org/fda/wls/essexirb_fdafoia_2011-6068.pdf). Essex IRB failed to warn for the potential cardiovascular risk in the informed consent form. *Id.*

194. *Id.*

195. *Id.*

196. *Id.* Essex only discovered the fictitious study after the FDA posted an alert regarding a phony research application. Mari Serebrov, *SEC Files Fraud Charges Against Biotech Executives*, 22 BIOWORLD TODAY 1, 5 (Aug. 4, 2011).

result, the FDA required Essex IRB to make changes and to submit audits of ongoing pediatric studies.<sup>197</sup>

Essex IRB, like Coast IRB, had run into trouble with the FDA in the past. In 1998, Essex IRB failed to consider local conditions and standards in initial review and continuing review of studies.<sup>198</sup> In response to these citations, the FDA stopped Essex IRB from approving new studies until the office had assurance that corrections were made.<sup>199</sup> In 2000, Essex IRB failed to conduct adequate continuing review and failed to fulfill requirements for expedited review.<sup>200</sup> Again, Essex IRB failed to prepare adequate IRB documents.<sup>201</sup> The FDA concluded that Essex IRB's procedures were inadequate to protect the rights of research subjects.<sup>202</sup>

Essex IRB's response to the latest citations raises questions about its business's priorities as well. Essex IRB responded in a letter to the FDA in a similar manner that Coast IRB's CEO responded in the congressional hearings.<sup>203</sup> Essex IRB expressed that its IRB was designed to review clinical research and not to detect fabricated submissions.<sup>204</sup>

Although an incident as flagrant as making up a company and a drug has not occurred, research scientists have been convicted or accused of fraudulent activity, making it important for IRBs to be able to isolate these issues. A lawsuit filed in September 2011 accused a Duke University researcher of falsifying medical research.<sup>205</sup> In addition, in 2011, two researchers at the Lee

197. Letter from Leslie K. Ball, Dir., Food & Drug Admin., to Nancy Waggoner, Chief Exec. Officer, Essex Institutional Review Board, Inc. (July 26, 2011) (on file with U.S. Dep't of Health & Human Servs.), *available at* <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2011/ucm266114.htm>.

198. Letter from David A. Lepay, Dir., Ctr. for Drug Evaluation & Res., to William C. Waggoner, President & Chairman, Essex Institutional Review Board, Inc. (Aug. 27, 1998) (on file with U.S. Dep't of Health & Human Servs.), *available at* <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/1998/UCM066739.pdf>.

199. *Id.*

200. Letter from Steven A. Masiello, Dir., Ctr. for Biologics Evaluation & Res., to Glenn P. Lambert, Chairman, Essex Institutional Review Board, Inc. (Mar. 01, 2000) (on file with U.S. Dep't of Health & Human Servs.), *available at* <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/2000/UCM068175.pdf>.

201. *Id.* Essex IRB also failed to record the attendance and voting of IRB members. *Id.*

202. *Id.*

203. Letter from Glenn P. Lambert, Chairman, Essex Institutional Review Board, Inc., to Douglas I. Ellsworth, District Dir., Food & Drug Admin. (Apr. 11, 2011) (on file with author), *available at* [http://www.circare.org/fdawls/essexirb\\_fdafoia\\_2011-6068.pdf](http://www.circare.org/fdawls/essexirb_fdafoia_2011-6068.pdf).

204. *Id.*

205. Duke University was sued for negligence per se for the IRB's failure. Complaint at 1, *Aiken v. Duke Univ.*, No. 11 CVS 4721 (N.C. Super. Ct. Sept. 7, 2011) (alleging that plaintiffs were exposed to improper and unnecessary chemotherapy due to falsified medical research). Researcher at the University of Texas MD Anderson Cancer Center issued warnings that the research was faulty to the researchers and to Duke University from 2006-07. *Id.* at 10. *Nature*



Research Institute in Lenexa, Kansas were charged with falsifying study data in a clinical drug trial.<sup>206</sup> Along with the 2011 incidents, 2010 saw multiple papers retracted from journals after scientific misconduct or data falsification.<sup>207</sup> Doctors have also strayed in research, which has impacted patient care and the medical market.<sup>208</sup> For example, a Massachusetts anesthesiologist was convicted of health care fraud after falsifying clinical research about pain management producing six false articles over six years.<sup>209</sup> Unfortunately, issues of fraud need to be considered at every step for research-subjects' protection. Since IRBs' primary responsibility is to ensure protection of subjects, IRB review processes must be robust enough to detect fraudulent activity.

## 2. Safety Issues for Research Subjects under Central IRB Mandate

There is not any published evidence that demonstrates how well a central IRB would work to protect research subjects in all multi-site studies.<sup>210</sup> Although there is some IRB efficiency data, IRB efficiency metrics do not consider IRB quality.<sup>211</sup> The NCI is currently working on a pilot study where the local IRBs at twenty-five sites are responsible for reviewing local context and the central IRB does not consider local context.<sup>212</sup> Why propose

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Medicine published in a November 2007 issue the MD Anderson researcher's notice letter pointing out errors in the study. *Id.* at 14. A University of Michigan researcher highlighted the same issues. *Id.* at 17.

206. Indictment at 1, *United States v. Sharp*, No. 5:11-cr-40042-RDR (D. Kan. June 1, 2011). The researchers allegedly knowingly accepted two subjects that were not qualified for a study due to age and employment. *Id.* at 6.

207. On September 24, 2010, more papers, making a total of six papers, were retracted after scientists were accused of scientific misconduct; in December 2010, the International Anesthesia Research Society retracted a paper after finding falsified data. Praveen K. Neema, *Medical Research: Is Everything Alright?*, 27 J. ANAESTHESIOLOGY CLINICAL PHARMACOLOGY 155, 159–61 (2011).

208. Sentencing Memorandum at 8, *United States v. Reuben*, No. 10-CR-30002-MAP (D. Mass. June 22, 2010);

Brendan Borrell, *A Medical Madoff: Anesthesiologist Faked Data in 21 Studies*, SCI. AM. (Mar. 10, 2009), <http://www.scientificamerican.com/article.cfm?id=a-medical-madoff-anesthesiologist-faked-data>. Studies resulted in "the sale of billions of dollars of the potentially dangerous drugs . . . Celebrex and Vioxx." *Id.*

209. *Reuben*, No. 10-CR-30002-MAP at 3–4. Reuben received a six-month sentence for the fraud. Neema, *supra* note 207, at 159.

210. The NCI Central IRB model does not scale well. Memorandum from National Heart, Lung, and Blood Institute Working Group, Facilitating NHLBI Clinical Trials Through Optimization of the IRB Process: Are Central IRBs the Solution (June 28–29, 2011) (on file with author). Without evidence demonstrating appropriate parallels between the NCI and other central IRBs, studies using the NCI Central IRB are not effective in showing central IRB efficacy.

211. *Id.*

212. *Id.* Pilot will be evaluated in late 2012. *Id.*

regulations to force multi-site studies to use a central IRB for local review before finding out the results of this study? The NCI needs to develop metrics to assess the quality of IRB review before removing additional eyes of protection.<sup>213</sup> There is just not any information out there that shows how often issues arise related to local context.<sup>214</sup> Additionally, current NCI data should not be used as a model for a mandatory central IRB because NCI parameters vary from the proposed central IRB regulations in vital aspects. For example, with the NCI, a majority of institutions still use their own local review for NCI studies,<sup>215</sup> which would be discouraged under the proposed regulations. Moreover, the NCI central IRB is required to have the expertise to adequately assess the protocol.<sup>216</sup> The proposed regulations have no such requirement for the central IRB in multi-site studies.<sup>217</sup> A central IRB will not function to protect subjects if it does not have the expertise to adequately assess the protocol. Therefore, additional studies are necessary from sources that model the proposed regulations in order to accurately determine that a central IRB would adequately protect research subjects.

Although there is limited information on the effectiveness of a mandatory central IRB, it is well known that independent IRBs inherently have conflicts of interests. The Institute of Medicine defines a conflict of interest as a circumstance that creates a risk that a primary interest—the promotion of and protection of research integrity and research-subjects' welfare—will be “unduly influenced by a secondary interest,” such as financial interests, pursuit of professional advancement, and the desire to do favors for others.<sup>218</sup> Conflicts of interest place scientific integrity into question, and they jeopardize public trust in research.<sup>219</sup>

Independent IRBs have a conflict of interest regardless of whether they are actually influenced by the secondary interest.<sup>220</sup> For-profit IRBs have an

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213. *Id.*

214. Nancy N. Dubler, National Heart, Lung, and Blood Institute Working Group, Central IRB Considerations: Issues of Ethics and Liability (June 28–29, 2011) (on file with author).

215. *Emanuel Proposes U.S. Move to Regional IRB System*, 12 GUIDE TO GOOD CLINICAL PRAC. NEWSL. 12 (2005). See also Winifred A. Meeker-O'Connell, *Institutional Review Boards: Current Compliance Trends and Emerging Models*, 9 J. OF HEALTH CARE COMPLIANCE 5, 8–9 (2009) (stating that as of May 2005, only about a quarter of participating sites accepted the CIRB review).

216. *IRB Models: Institutions Consider Central IRB Variations*, 12 GUIDE TO GOOD CLINICAL PRAC. NEWSL. 18 (2004). Oncologists and other health care practitioners are on the NCI's Central IRB Board. Meeker-O'Connell, *supra* note 215, at 8.

217. Human Subjects Research Protections, 76 Fed. Reg. 44,512 (proposed July 26, 2011) (to be codified at 21 C.F.R. pt. 50, 56).

218. INSTITUTE OF MEDICINE, CONFLICTS OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE 6 (2009).

219. *Id.* at 2.

220. See *id.* at 47.

incentive to approve clinical trials: if the IRB does not approve the trial, the applicants may use a different IRB for the succeeding study.<sup>221</sup> Employees are well aware that rejecting protocols is not good for the company's bottom line.<sup>222</sup> This long-term relationship between independent IRBs and sponsors increases the risk that the sponsors influence independent IRB behavior.<sup>223</sup> Many question whether for-profit IRBs can "impartially assess industry-sponsored research when their revenue comes from the very firms funding the studies."<sup>224</sup> Although funding for administrative review at an institution may seem similar to funding a for-profit IRB, the IRB members at the institution are not paid directly by the sponsors nor does the institution make a profit from the funding, in contrast to for-profit IRBs.<sup>225</sup> Even though local IRBs may have ulterior motives, such as prestige, to approve trials, money is the "most powerful incentive to cut corners."<sup>226</sup>

In comparison, judges who have financial conflicts of interest are disqualified from review when there is "clear potential for personal loss" and when "the financial interest is not too remote."<sup>227</sup> Additionally, physician interaction with pharmaceutical companies is highly regulated.<sup>228</sup> Scrutinizing financial conflicts of interests is appropriate for IRB review, especially when the research takes place within a commercial context.<sup>229</sup> Uninfluenced IRB

221. *Who Watches the Watchmen?*, *supra* note 192.

222. Lemmens & Freedman, *supra* note 51, at 567.

223. See INSTITUTE OF MEDICINE, *supra* note 218, at 54.

224. Meeker-O'Connell, *supra* note 215, at 7.

225. *See id.*

226. *Who Watches the Watchmen?*, *supra* note 192. The cutting of corners could be subconscious, but there is data that money and bias go hand-in-hand in research. *See generally* Katherine Harmon, *Industry-Sponsored Drug Trials More Likely to Report Positive Results*, SCI. AM., <http://blogs.scientificamerican.com/observations/2010/08/02/industry-sponsored-drug-trials-more-likely-to-report-positive-results/> (last visited Apr. 19, 2013) (finding that 85 percent of industry-funded studies reported positive outcomes compared to just 50 percent of government-funded studies).

227. Lemmens & Freedman, *supra* note 51, at 560.

228. *See Interactions with Pharmaceutical Industry Representatives*, AM. MED. ASS'N, <http://www.ama-assn.org/ama/pub/physician-resources/legal-topics/business-management-topics/interactions-pharmaceutical-industry-representatives.page> (last visited Apr. 19, 2013). For example, the 2008 Pharmaceutical Research and Manufacturers of American do not allow pharmaceutical companies to give doctors non-educational items, such as pens. INSTITUTE OF MEDICINE, *supra* note 218, at 79. The regulations were created in order to enforce the AMA's policy to place the physician-patient relationship ahead of economic self-interest. *Ethical Guidelines for Gifts to Physicians from Industry*, AM. MED. ASS'N, <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/about-ethics-group/ethics-resource-center/education-al-resources/guidelines-gifts-physicians.page> (last visited Apr. 19, 2013).

229. *See* Macklin, *supra* note 23, at 15.

review improves the likelihood that the IRB is best performing its role in evaluating risks and potential benefits for research subjects.<sup>230</sup>

Relationships can also create a separate conflict of interest, in addition to the financial conflict of interest, for independent IRBs. For example, the Human Investigation Committee IRB that policed the Fabre Research Clinic was founded by the same doctor who ran the clinic.<sup>231</sup> In 1992, the FDA issued a warning letter to the Human Investigation Committee IRB, stating that it had a conflict of interest in reviewing studies at the Fabre clinic.<sup>232</sup> This same IRB, with the same conflict of interest, was overseeing studies at the Fabre clinic when a volunteer died in 2002.<sup>233</sup> In fact, the FDA had inspected the clinic just six days before the volunteer joined the study.<sup>234</sup> It was not until nearly thirteen years after the FDA first got wind of the conflict of interest issue and after human protection failures were found in six inspections<sup>235</sup> that the FDA finally shut down the Fabre clinic.<sup>236</sup> In addition, Miami-based Southern IRB has overseen testing at facilities where the husband of the owner of Southern IRB is a vice president.<sup>237</sup> Most recently, on January 21, 2011, the FDA sent Napoli LLC a warning letter because its study investigator, Doctor Kamrava, also sat on the IRB that approved his studies.<sup>238</sup> These conflicts of interest are unlikely to go away because a tremendous amount of money is spent on research and development.<sup>239</sup>

Both HHS and FDA regulations prohibit an IRB member with a conflict of interest from participating in the IRB's review of the study,<sup>240</sup> although what constitutes a conflict of interest is undefined.<sup>241</sup> However, the regulations are

230. *Id.*

231. EVANS ET AL., *supra* note 97, at 14.

232. *Id.* at 4.

233. *Id.*

234. *Id.*

235. *Id.*

236. *Id.* The Human Investigation Committee currently is not registered as an active IRB with OHRP. *Office for Human Research Protections (OHRP) Database for Registered IORGs & IRBs, Approved FWAs, and Documents Received in the Last 60 Days*, U.S. DEP'T OF HEALTH AND HUMAN SERVS., <http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc> (last visited Apr. 19, 2013).

237. EVANS ET AL., *supra* note 97, at 2.

238. Letter from Steven D. Silverman, Dir., Ctr. for Devices and Radiological Health, to Michael M. Kamrava, Chairman, Napoli LLC (Jan. 21, 2011) (on file with the U.S. Dep't of Health and Human Servs.), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2011/ucm240960.htm>.

239. Ken Gatter, *Fixing Cracks: A Discourse Norm to Repair the Crumbling Regulatory Structure Supporting Clinical Research and Protecting Human Subjects*, 73 U. MO. KANSAS CITY L. REV. 581, 584 (2005).

240. IRB membership, 45 C.F.R. § 46.107(e) (2011); IRB membership, 21 C.F.R. § 56.107(e) (2011).

241. Icenogle & Dudek, *supra* note 96, at 65.

silent as to conflicts of interest the IRB has as an entity. Simple reliance upon IRB member integrity is not sufficient to address for-profit IRBs' conflicts of interest.<sup>242</sup>

In addition to the conflict of interest issues with independent IRBs, a 2011 study indicates that local IRB members are not fond of central IRBs and that the majority of medical school IRB members see no reason to use a central IRB.<sup>243</sup> IRB members were concerned that moving review away from the site of the research study compromises research subjects' safety because distant IRBs may not be able to make informed decisions that local IRBs can make.<sup>244</sup> After the actual protocol review, the second most important element is that the reviewers know the researcher's integrity; local reviewers can have the "personal understanding, feel, and flavor that's needed for a heightened level of review."<sup>245</sup> Local review members are committed to the local community, and local IRB members do not see for-profit IRBs as having this same commitment.<sup>246</sup> Additionally, these IRB members were concerned that the quality of central IRB reviews can range considerably.<sup>247</sup> It is these concerns for central IRB quality that create a need for stronger independent IRB standards.

### 3. OHRP Regulation of IRBs is Insufficient for Research-Subjects' Protection

"Anyone who can bring together five people, including a community representative, a physician, a lawyer, and an ethicist, can set up shop [as an IRB] and start competing for business."<sup>248</sup> Although IRB registration is required, the federal government does not endorse with registration that the registered IRB meets any standards.<sup>249</sup> HHS receives three hundred applications each month to register IRB boards, a fact which congressmen have suggested indicates that there should be concern about people seeing

242. Lemmens & Freedman, *supra* note 51, at 558.

243. Robert Klitzman, *How Local IRBs View Central IRBs in the U.S.*, 12 BMC MED. ETHICS 1, 2, 4 (2011). Klitzman conducted two-hour phone interviews with forty-six IRB chairs, directors, administrators, and members. *Id.* at 3.

244. *Id.* at 4, 6. "The farther away you get from the actual group of subjects, the harder it is for a committee to judge the risk and benefits . . . . An IRB in another state could not make as informed a decision." *Id.* at 6.

245. *Id.* at 6 (emphasis removed).

246. *See id.* at 7.

247. Klitzman, *supra* note 243, at 9, 11.

248. Emanuel et al., *supra* note 89, at 942.

249. *Hearing on IRBs*, *supra* note 1, at 59 (statement of Jerry Menikoff, Dir., Office for Human Research Protections, Health and Human Services).

IRBs as a “quick way to get rich.”<sup>250</sup> A group of five people could also create an IRB in order to easily approve its own studies, instead of being forced to submit protocols to unaffiliated IRBs.

The same GAO sting operation that caught Coast IRB “rubber-stamping” approvals also registered a fake IRB online with HHS and solicited research protocols on its website.<sup>251</sup> The GAO’s fake IRB’s CEO was Truper Dawg,<sup>252</sup> and the IRB was located in the town of Cheatsville, Arizona.<sup>253</sup> HHS registered this IRB with no questions asked.<sup>254</sup> Additionally, the bogus IRB received research protocols from one company because the research coordinator liked the IRB’s low price and quick turnaround time.<sup>255</sup> This demonstrates that for-profit IRBs are already enticing researchers to select review based on price and time instead of quality of review. Forcing institutions to use an IRB chosen by the sponsor, based on price and speed, for review of studies occurring at its premises places both research subjects and the quality of research at that institution at risk.

Even with these known risks that for-profit IRBs place on subjects, OHRP rarely investigates IRBs.<sup>256</sup> In fact, in the past, the FDA has inspected just 1 percent of study sites.<sup>257</sup> The FDA measures compliance by reviewing records and consent forms because there currently is no standard to measure the quality of IRB decisions.<sup>258</sup> IRBs are not required to visit or inspect test centers at any time,<sup>259</sup> so central IRBs may be clueless as to the ins and outs of the institutions with which they are working. Additionally, there are no well-defined standards for continuing review.<sup>260</sup> In fact, one IRB member admitted that his continuing review process was complete after he verified that there

250. *Id.*; *Id.* at 1–2 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce). Some of the 300 applications are amendments or renewals. *Id.* at 59 (statement of Jerry Menikoff, Dir., Office for Human Research Protections, Health and Human Services).

251. *Id.* at 5 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

252. Roy M. Poses, *Sham Studies and the Commercial IRBs that Approve Them, and Sham IRBs and the Government Department that Registers Them*, HEALTH CARE RENEWAL (Mar. 31, 2009, 3:07 PM), <http://hcrenewal.blogspot.com/2009/03/sham-studies-and-commercial-irbs-that.html>.

253. *Hearing on IRBs*, *supra* note 1, at 9 (statement of Rep. Greg Walden).

254. *Id.* at 5 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

255. *Id.*

256. Powell, *supra* note 122, at 1418.

257. Paul Gelsinger & Adil E. Shamoo, *Eight Years After Jesse’s Death, Are Human Research Subjects Any Safer?*, 38 HASTINGS CENTER REP. 25, 25 (2008).

258. See Scott Burris & Jen Welsh, *Regulatory Paradox: A Review of Enforcement Letters Issued by the Office of Human Research Protection*, 101 NW. U. L. REV. 643, 644 (2007).

259. EVANS ET AL., *supra* note 97, at 17.

260. See Richard S. Saver, *Medical Research Oversight from the Corporate Governance Perspective: Comparing Institutional Review Boards and Corporate Boards*, 46 WM. & MARY L. REV. 619, 669 (2004).

were no deaths in the study.<sup>261</sup> The current status of IRB regulations are in trouble and the proposed regulations do nothing to remedy these issues.

The recent sting operations indicate that independent IRBs may threaten the safety of research subjects by “rubber-stamping” protocol approval. Without a doubt, however, independent IRBs have a conflict of interest that increases the risk of harm to research subjects. The current and the proposed regulations regarding independent IRBs are insufficient to ensure research-subjects’ safety. Above all, there is no evidence that shows research subjects will be better protected, or even afforded the same protection given under the current regulations, by these proposed regulations. Therefore, the proposed regulations should be amended to place an emphasis on research-subjects’ protection.

### III. SUGGESTIONS FOR REGULATIONS IN ORDER TO PRIORITIZE RESEARCH-SUBJECTS’ PROTECTION

If forty-four IRBs could not catch a major problem with a study,<sup>262</sup> then fundamental IRB issues need to be addressed before mandating review be moved to a single IRB. It does not make practical sense to take away additional eyes of oversight for research-subjects’ protection when IRBs are not functioning as they ought to function.<sup>263</sup> The IRB system needs help because IRBs appear to have a short-term memory when it comes to adverse incidents<sup>264</sup>—IRBs have forgotten incidents, such as Jesse Gelsinger’s death, all too quickly.<sup>265</sup> Fundamental change is necessary in order to give IRBs the capabilities to adequately monitor multi-site research.<sup>266</sup> Suggestions for change include improving the method by which a sponsor chooses an IRB, increasing IRB transparency, enforcing IRB turnaround time restrictions, creating standards for measuring and tracking IRB quality, and developing avenues of redress for injured research subjects.

261. David Heath & Duff Wilson, *System’s Serious Flaws Have Led Many to Call for Regulatory Reform*, SEATTLE TIMES, Mar. 15, 2001, at A11.

262. *ARDSNET Case Reverberates with Ethics, Oversight Questions*, 11 No.5 GUIDE TO GOOD CLINICAL PRAC. NEWSL. 1 (2004). The Acute Respiratory Distress Syndrome Network (ARDSNet) trial was suspended because it exposed patients to inappropriate risks when it randomized ventilation treatment for critically ill patients. *Id.* The study was reviewed by forty-four IRBs at the participating research sites. *Id.*

263. *IRB Seals Fate by Approving Fake Protocol in Federal Sting*, IRB ADVISOR, July 1, 2009 (Executive Director of AAHRPP states that a number of IRBs are not functioning at the level at which they ought to be).

264. See *KD ex rel. Dieffenbach v. United States*, 715 F. Supp. 2d 587, 598 (D. Del. 2010).

265. In a recent complaint, plaintiffs allege that a gene therapy study failed to mention in an informed consent form that Gelsinger died in a prior gene therapy experiment. Amended Complaint at 8, *Zeman v. Williams*, No. 11-10204-MLW (D. Mass. Apr. 20, 2011).

266. Burris & Welsh, *supra* note 258, at 682.

A drastic option would be to follow the precedent of other countries and either ban for-profit IRBs from reviewing studies or have the government designate the IRB to review each multi-site study. For example, Switzerland banned commercial IRBs in response to an incident similar to the Fabre incident in the United States.<sup>267</sup> Swiss officials created new regulations requiring regulatory approval of IRBs, which resulted in no commercial IRBs being approved.<sup>268</sup> Similarly, a policy in Alberta, Canada requires all research to be reviewed by designated IRBs,<sup>269</sup> which takes the power away from the sponsor to be able to pick the fastest and cheapest IRB review. Eliminating for-profit IRBs or changing how sponsors could choose an IRB would help reduce the risk to research subjects by ensuring that sponsors cannot pay their way into research studies. While banning independent IRBs may not be a popular option in the United States, there is support for creating non-profit IRBs to review studies.<sup>270</sup> If required to use a central IRB, prominent research universities and major research sites could band together to place pressure on sponsors to select non-profit IRBs for multi-site studies.<sup>271</sup> Another option would be to have a national board select the IRB to review each study, similar to the Canadian policy. The national board could consider IRB expertise and quality metrics to select the most appropriate IRB for the respective multi-site study. Although both banning for-profit IRBs and requiring that a national board select the IRB for each study would require significant changes to the current regulations, these suggestions would promote the primary purpose of IRBs in protecting research-subjects' welfare.

A less radical option would be to propose regulations that increase the transparency in the IRB process. Regulations need to control who can create a for-profit IRB, and they need to explicitly discuss conflicts of interest and interactions with sponsors. The regulations should be written so as to minimize the circumstances where reasonable individuals would have reason to question whether professional judgment has been improperly influenced, even if it has not actually been influenced.<sup>272</sup> The regulations should provide research subjects more information about the IRB process, since the public interest is best served by encouraging transparency and integrity in research.<sup>273</sup>

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267. Emanuel et al., *supra* note 89, at 943.

268. *Id.* The Swiss Supreme Court upheld the new regulations. *Id.*

269. David Forster, *Independent Institutional Review Boards*, 32 SETON HALL L. REV. 513, 519 (2002).

270. Macklin, *supra* note 23, at 19.

271. *Id.* Research universities and research sites have a vested interest in quality IRB review, since their reputations are on the line for all research that occurs at their premises. This interest may be strong enough to initiate action.

272. See INSTITUTE OF MEDICINE., *supra* 218, at 49. However, disclosure alone does not eliminate conflicts of interest. *Id.* at 29.

273. Konrad v. Oesterling, 149 F.R.D. 592, 597 (D. Minn. 1993).



Transparency would be improved if the consent form disclosed to research subjects the IRB name, the IRB's profit or non-profit status, and the changes, if any, that the IRB made to the protocol before approval. Research subjects, as well as the research sites, will be better able to assess the risk of undue influence on the IRB's judgment if they are given sufficient information regarding the nature, scope, duration, and monetary value of the IRB's relationship with the study sponsor.<sup>274</sup>

This transparency will help improve volunteer trust in medical research.<sup>275</sup> Research subjects currently have no assurances that an IRB places their welfare as its highest priority, since these for-profit companies can hide behind the walls of secrecy.<sup>276</sup> All states should enact a law, following Maryland's lead, requiring IRBs to make all meeting minutes available to the public. This disclosure and improved transparency could provide incentives for sponsors to choose reputable IRBs.

Regulations should also set review time minimums so that independent IRBs can no longer advertise or compete on the speed of review. Since recent IRB failures have been linked to IRB time constraints,<sup>277</sup> time-pressured reviews should be avoided whenever possible. The regulations need to set minimum turnaround times for IRB review, which would help ensure that independent IRBs are not squeezing the reviews into short turnaround times in order to compete for business.<sup>278</sup> Forty-eight hour guarantees, like the one the Essex IRB promises on its website,<sup>279</sup> should not be allowed. Reducing the ability for independent IRBs to compete on review time will improve research-subjects' protection.

In addition, HHS should create standards by which to evaluate IRB quality, and then the agencies should rely on this quality data before creating new regulations. Simply relying on public comment does not provide the same kind of support as factual data, especially when considering that the lives and well-being of research subjects are at stake. The agencies could require independent

274. See INSTITUTE OF MEDICINE, *supra* 218, at 67. Although some studies have found that research participants' decisions to participate in studies are not affected by the investigator's financial relationships, these studies did not fully explain the risks of conflicts of interests to the research subjects. *Id.* at 78. In addition, research subjects may feel differently about the IRB being financially supported by the study sponsors than they do about investigators, given the IRB's primary purpose is to protect research subjects.

275. See Lemmens & Freedman, *supra* note 51, at 577.

276. See *supra* text accompanying note 132.

277. Saver, *supra* note 260, at 660. IRBs may spend two to eight minutes on average on a given protocol. *Id.* at 659.

278. The president of one of America's largest independent IRBs says that it advertises speed and efficiency to research sponsors. Lemmens & Freedman, *supra* note 51, at 551.

279. Sponsors will be notified of action within forty-eight hours of Board review. *Full Board Review*, ESSEX INSTITUTIONAL REVIEW BOARD, INC., <http://www.essexirb.com/submissions/fullboard.htm> (last visited Apr. 19, 2013).

IRBs to be accredited through institutions like the Association for the Accreditation of Human Research Protections Programs (AAHRPP).<sup>280</sup> However, since none of the accreditation standards are revolutionary, it is unknown whether accreditation will solve the issues with IRBs.<sup>281</sup> Before mandating a central IRB, HHS should review data from the NCI and other recent recommendations. For example, in September 2011, President Obama ordered the Presidential Commission for the Study of Bioethical issues to review research-subjects' protection.<sup>282</sup> Additionally, the Secretary's Advisory Committee on Human Research Protections recommended that a single federal agency review all research, regardless of whether it involves federal funding or is an FDA-regulated product, and that uniform standards for managing conflicts of interests be created.<sup>283</sup> Research subjects will be better protected with a research protocol overhaul rather than the quick-fix "protections" these proposed regulations provide.

Regulations focusing on improving IRBs are vital to the protection of research subjects; however, legal remedies for injured research subjects should also be addressed in the new regulations. The current regulations provide no legal remedies or redress for research-subjects' injuries.<sup>284</sup> While institutions or IRBs may be able to require study sponsors to indemnify them for negligence in research studies,<sup>285</sup> research subjects do not have a similar redress for their injuries. Research subjects, as a practical matter, are unable to contract with the study sponsors for help when something goes awry in a study.<sup>286</sup> IRBs should be held legally responsible when they play a role in a

280. See ASSOCIATION FOR THE ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS, INC., <http://www.aahrpp.org/> (last visited Apr. 19, 2013). The other accrediting company, the Partnership For Human Research Protection (PHRP) dissolved in 2005. *PHRP Accreditation Group Dissolves*, THOMPSON (Sept. 8, 2005), <http://www.thompson.com/public/printpage.jsp?id=1122&pageid=newsbrief>. Essex IRB was accredited by PHRP. *Partnership for Human Research Protection (PHRP) Accreditation*, ESSEX INSTITUTIONAL REVIEW BOARD, INC., <http://www.essexirb.com/about/phrp.htm> (last visited Apr. 19, 2013).

281. Icenogle & Dudek, *supra* note 96, at 67. Critics argue that accreditation adds another layer of regulation "to an already heavily regulated environment." Beasley, *supra* note 114, at 61.

282. *SACHRP Urges Simplified Federal Trial Oversight*, 18 No.12 GUIDE TO GOOD CLINICAL PRAC. NEWSL. 15 (2011).

283. *Id.*

284. See Human Subjects Research Protections, 76 Fed. Reg. 44,512, 44,512–31 (proposed July 26, 2011) (to be codified at 21 C.F.R. pt. 50, 56).

285. See Lis & Murray, *supra* note 66, at 118–20. Essex IRB requires sponsors to sign an indemnification agreement to release Essex IRB from ordinary negligence. Indemnification Agreement, ESSEX INSTITUTIONAL REVIEW BOARD, available at <http://www.essexirb.com/forms/indemnification.htm> (last visited Apr. 19, 2013).

286. Michelle M. Mello & Steven Joffe, *Compact versus Contract – Industry Sponsors' Obligations to Their Research Subjects*, 356 NEW ENG. J. MED. 2737, 2739–40 (2007).

subject's injury.<sup>287</sup> The public health is not served when IRBs, especially for-profit IRBs, can escape the consequences of misconduct.<sup>288</sup> Research studies advance public health by improving options for treatment of diseases, but there can be no scientific progress in clinical trials without volunteer subjects. The public health benefits when volunteers trust the research system. However, volunteer subjects will lose confidence in the system if for-profit IRBs cannot be held liable for decisions that cause injuries. A benefit of turning to the legal system is that it adds no bureaucracy to the regulated environment.<sup>289</sup> If HHS wants to outsource ethical reviews to for-profit companies, research subjects should be provided an easier way to be compensated from the IRBs that fail to protect them.

Proposed regulations simply cannot rely on just the goodwill of IRB members—research subjects require more than goodwill to be protected from the risks of clinical trials.<sup>290</sup> Quality IRB reviews depend on an effective protocol process review,<sup>291</sup> and new proposed regulations are necessary in order to effectively protect research subjects.

#### CONCLUSION

HHS designed IRBs for the primary purpose of protecting human subjects volunteering in research studies.<sup>292</sup> These volunteers put their lives at risk in clinical trials, which may be of no benefit to them.<sup>293</sup> At a minimum, the public owes these volunteers the dignity of having someone look out for their best interests. Regulations that will push more research review into the hands of for-profit IRBs without any additional oversight does not give these research subjects the protection they deserve. Central IRBs might be the solution for multi-site trials, but only with additional regulations that adequately protect research subjects, not with the present regulations that serve research integrity interests rather than individual safety interests.

When one out of three IRBs tested in a sting operation was found to have “rubber-stamped” a protocol's approval,<sup>294</sup> it raises concerns about all other IRBs. Catching Essex IRB in a similar sting two years later demands action from HHS. IRB reform is necessary to improve the protection of research subjects. If HHS wants to mandate the use of central IRBs, at a minimum the

287. Hoffman & Berg, *supra* note 106, at 411.

288. *See id.* at 406–11.

289. Beasley, *supra* note 114, at 61.

290. Lemmens & Freedman, *supra* note 51, at 575.

291. Carl H. Coleman, *Rationalizing Risk Assessment in Human Subject Research*, 46 ARIZ. L. REV. 1, 13 (2004).

292. *See supra* text accompanying note 9.

293. Hoffman, *supra* note 92, at 738.

294. *Hearing on IRBs*, *supra* note 1, at 2 (statement of Rep. Bart Stupak, Chairman, Comm. on Energy and Commerce).

regulations should provide standards for measuring IRB quality, increased transparency, stronger regulation of independent IRBs, and an avenue of redress for injured subjects. There is injustice in leaving research subjects without redress when the companies profiting from their protocol review fail to protect them.

Protecting research subjects does not require that research efforts take a backseat to the research-subjects' interests, it simply requires that the research subjects' safety be placed ahead of financial interests.<sup>295</sup>

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295. Robert Gatter, *Walking the Talk of Trust in Human Subjects Research: The Challenge of Regulating Financial Conflicts of Interest*, 52 EMORY L.J. 327, 360 (2003).

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