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IDSA
Infectious Diseases Society of America

July 19, 2011

By electronic submission

U.S. Department of Health and Human Services
Office for Civil Rights
Attention: HIPAA Privacy Rule Accounting of Disclosures
Hubert H. Humphrey Building, Room 509F
200 Independence Avenue, SW
Washington, DC 20201

RE: HIPAA Privacy Rule Accounting of Disclosures under the Health Information Technology for Economic and Clinical Health Act (RIN 0991-AB62)

Dear Sir/Madam:

The Infectious Diseases Society of America (IDSA) is pleased to have this opportunity to comment on the notice of proposed rulemaking cited above. IDSA represents more than 9,300 infectious diseases physicians and scientists devoted to patient care, prevention, public health, education, and research in the area of infectious diseases. IDSA strongly supports protecting the privacy of our patients and enabling health research that ultimately impacts patient care and public health. The U.S. Department of Health and Human Services (HHS) can act to ensure that both goals are achieved.

IDSA appreciates that HHS is considering exempting research from one of the requirements—the Accounting of Disclosures (AOD)—of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. The Society has been concerned about the increasing regulatory oversight of health research and its lasting impact on advances in research, patient care and training of future researchers. We previously highlighted many of the unintended consequences of the HIPAA Privacy Rule in the enclosed 2009 publication, "Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts".[1]

Accounting of Disclosures

IDSA urges HHS to exempt research activities from the AOD requirement, as the Department is currently considering. The AOD requirement is representative of the primary limitation of the Privacy Rule, which is that it provides inadequate privacy protection for individuals while negatively impacting the conduct of

[1] Infectious Diseases Society of America, "Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts," Clinical Infectious Diseases 49 (2009).

health research. Compliance with the AOD requirement provides little value for individuals while placing undue administrative burden on research institutions. It is evident that there is little demand from individuals for AOD reports. A December 2009 survey of American Health Information Management Association (AHIMA) members revealed that 60% of their organizations had never received an AOD request for any purpose, and only 7% had received 11 or more since the Privacy Rule's 2003 compliance date.[2] HHS' request for information (RFI) in May 2010 appeared to generate comparable responses, with 30 respondents having received no AOD requests, and 90 having received less than 20 requests since 2003. It is reasonable to presume that AOD requests that were motivated by research inquiries are only a fraction of these. The clear lack of requests demonstrates that AOD reports provide little utility to individuals.

Despite the limited potential benefit to individuals, research institutions are required to track disclosure information, posing significant challenges to institutions, including administrators and investigators. According to the AHIMA respondents, "tracking disclosures is a frustrating challenge and a near impossibility. Most report that the way their organizations disclose information—from multiple departments through disparate IT systems—makes it difficult to compile a complete and accurate accounting."[3] It is challenging to capture all the information required for a standard accounting—including description of protected health information (PHI), name and address of entity receiving the PHI and purpose of disclosure[4]—a fact that HHS has implicitly acknowledged by introducing the concept of an access report in this rulemaking. Even the allowed alternative accounting for research protocols of 50 or more subjects is challenging, as it requires the institution to provide an account of all research protocols for which the individual's PHI may have been disclosed, and to include the following information:

- the name of the protocol or research activity;
- a plain-language description of the research protocol or activity, purpose of the research, and criteria for selecting particular records;
- a description of the type of PHI disclosed;
- the date or period of time during which the disclosure(s) occurred or may have occurred, including the date of the last disclosure during the accounting period;
- the name, address, and telephone number of the entity that sponsored the research and of the researcher who received the PHI;
- a statement that the individual's PHI may or may not have been disclosed for a particular protocol or research activity.[5]

Thus, even the simplified accounting requirement creates significant administrative burden, and provides little useful information for the individual, as a large institution could have hundreds of protocols for which an individual's PHI "may or may not have been disclosed". IDSA agrees

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[2] American Health Information Management Association, "Few Requests for Today's Accountings," Journal of AHIMA 81(2010): 33-34.
[3] AHIMA 2010.
[4] See 45 C.F.R. §164.528(b)(2)
[5] See 45 C.F.R. §164.528(b)(4)

with the recommendations of the Institute of Medicine (IOM) and the HHS Secretary's Advisory Committee on Human Research Protections that the accounting of disclosures requirement should not apply to research activities.

Although this would be a positive first step for HHS to take, there are many more significant concerns with the Privacy Rule. Further actions are needed to ensure that the conduct of research critical to improving the nation's health is not unduly impacted and that patients' privacy is safeguarded.

Additional Recommendations

IDSA supports the conclusions of the IOM in 2009 that the HIPAA Privacy Rule impedes critical health research while not adequately protecting patient privacy.[6] We concur with the IOM that the ideal solution is to exempt research from the HIPAA Privacy Rule and replace it with a new rules-based framework that is better able to provide authentic privacy protection and enable the conduct of vital research. Until that is accomplished, HHS can take intermediate steps that will mitigate the negative impact of the HIPAA Privacy Rule on health research. In addition to exempting research from the AOD requirement as proposed in this rulemaking, HHS should reduce the list of data elements that are considered PHI in the research context because de-identification often results in a dataset with little analytical utility. Finally, HHS should provide guidance that clearly defines quality improvement efforts as separate from research, as the unclear distinction is unnecessarily overburdening the institutional review board (IRB) process with non-research activities.

The Need to Amend HIPAA in the Research Context

The HIPAA Privacy Rule does not adequately protect patient privacy, but instead hinders critical research that would benefit patients and society as a whole. One of the underlying arguments of the Privacy Rule is that an individual has the right to decide how their health information is used. But choice and notification do not actually provide protection of the individual's health information, and rather shift the burden of guarding health information from the institution to the individual. As the IOM report explained:

> However, consent (authorization) itself cannot achieve the separate aim of privacy protection. The Privacy Rule, as currently defined and operationalized in practice, does not provide effective privacy safeguards for information based research because of an over-reliance on informed consent, rather than comprehensive privacy protections.[7]

Individuals often do not read or do not understand notice forms before deciding on authorization, in healthcare and in other contexts.[8] Bioethicist Arthur Caplan and colleagues

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[6] Institute of Medicine, Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health through Research (Washington, DC: National Academy of Sciences, 2009).
[7] IOM, Beyond the HIPAA Privacy Rule, 250.
[8] Fred Cate, "Protecting Privacy in Health Research: The Limits of Individual Choice," California Law Review 98 (2011).

have argued that requiring an individual to be contacted each time their health information may be used in a study could be considered intrusive and counter to privacy concerns.[9] When individual authorization cannot easily be sought, investigators can turn to an IRB or privacy board to grant a waiver of authorization, based on whether a study produces "minimal risk" to individual privacy. Most institutions utilize the IRBs that were constituted to review the medical risk of interventional research to review privacy risk, which they usually do not have the expertise or the processes to accurately review. Thus, instead of providing authentic privacy protections, the HIPAA Privacy Rule has placed the onus on uninformed individuals or ill-suited IRBs to evaluate privacy risk. The IOM proposed a general rules-based framework for using health information in research that would establish privacy protection guidelines for data use, with specific details to be later developed by privacy experts and researchers. IDSA supports this general framework and the efforts of groups that are working to think through the details of such a framework, such as Indiana University's National Institutes of Health (NIH)-funded project on "Protecting Privacy in Health Research" (http://cacr.iu.edu/pphr).

Beyond not providing adequate privacy protection, the Privacy Rule has created significant unintended impediments to the conduct of critical health research. Several publications, including *Beyond the HIPAA Privacy Rule* and "Grinding to a Halt" detail the Privacy Rule's impact on research more comprehensively. Notably, the IOM panel examined HIPAA's impact on several aspects of health research by reviewing several surveys of researchers and administrators, and by commissioning its own studies.[10] Here we highlight a few of the critical effects.

Studies involving information-based methods such as epidemiological and health systems research are the most significantly impacted. By prompting full IRB review for studies that often did not require IRB review or could undergo expedited review, the Privacy Rule has increased the workload of already overburdened IRBs, leading to long delays in reviews of studies. IRB members and review processes were not established to evaluate privacy, and the end result of HIPAA implementation is that IRBs are not able to adequately review privacy protections or human subject research protections. Addition of months or years to a research timeline can be catastrophic to grant-funded timelines or for trainees who have limited time to gain research experience. Investigators have even abandoned studies rather than contemplate protracted IRB review. The Privacy Rule has had a negative impact on the conduct of research involving medical record review, which is often an entry point for medical students and other trainee clinical researchers. At a time when the numbers of physician scientists are already low and decreasing, the clinical research enterprise cannot afford to lose more promising young investigators.

Addition of HIPAA authorization requests to patients has decreased patient enrollment and introduced selection bias into these studies. These developments threaten to affect the general

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[9] David J. Casarett, "Bioethical Issues in Pharmacoepidemiological Research," in *Pharmacoepidemiology*, 4th ed., edited by B. L. Strom (West Sussex, England: John Wiley & Sons, Ltd.)

[10] IOM, Beyond the HIPAA Privacy Rule, 199-243.

applicability of study findings, and thus have a broader impact on patient care. Research costs have increased, as research groups and institutions have had to devote more staff time and other resources to compliance with regulatory requirements. The lengthening of IRB review time and time for patient accrual has also added to study costs. The ultimate price, however, is the slowing of the pace of discovery and ultimate effect on patient care. A comprehensive overhaul of the HIPAA Privacy Rule, as it relates to research, is urgently needed.

Deidentification of Protected Health Information

IDSA recommends that HHS reduce the number of identifiers that are considered PHI in the research context. Under the Privacy Rule, a dataset can be deidentified by removing a list of 18 data elements that are considered unique identifiers. Although deidentification eliminates the need for authorization or a waiver, it often results in loss of critical information for study purposes. The current list of 18 identifiers is needlessly broad and includes elements that an informed, reasonable individual would not consider identifying information. For example, the list includes any date variable such as the date of hospital admission, any age over 89 years, and any geographic location below the level of a state. Reducing the list of PHI to those elements that are more reasonably considered identifying (e.g. name, address, Social Security number), would provide the same level of privacy without unnecessarily impeding research. HHS may have tried to address this issue by creating a "limited dataset" that can also be used without authorization, but this is not much of an improvement, as it requires removal of 16 of the 18 identifiers. Reducing the number of identifiers would also bring the provisions of the Privacy Rule more in harmony with the Common Rule, the set of federal regulations that protects human research subjects.[11]

Distinction between Research and Quality Improvement

IDSA also urges HHS to provide guidance to institutions that clearly delineates quality improvement activities from research. IRB waiver of HIPAA authorization is increasingly sought for data-gathering activities, many of which were not intended to be covered by the Privacy Rule. A prime example is quality improvement, which is often required of health care institutions by accrediting agencies. HIPAA classifies "quality assessment and improvement efforts" as healthcare operations, not research.[12] Unfortunately, there has been a lack of consensus among investigators, hospital administrators, IRBs and even the HHS Office of Human Research Protections (OHRP) about the distinction between research and quality improvement activities. Because of the confusion, institutions act conservatively and refer increasing numbers of studies for full IRB review. The Hastings Center convened stakeholders to discuss quality improvement and established some characteristics of quality improvement, research and the overlap.[13] IDSA recommends that HHS utilize these or similar criteria in a guidance document on quality improvement.

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[11] See 45 C.F.R. 46

[12] See 45 C.F.R. §164.501

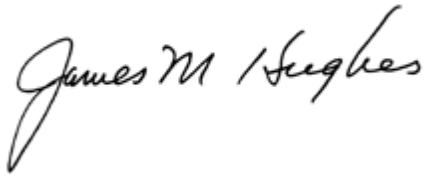
[13] Joanne Lynn et. al., "The Ethics of Using Quality Improvement Methods in Health Care," Annals of Internal Medicine 146 (2007): 666–674.

Conclusions

IDSA appreciates this opportunity to express our concern about the impact of the HIPAA Privacy Rule on health research. Unless HHS acts to address the accounting of disclosures and the other concerns we have highlighted, vital health research will continue to be impeded. IDSA, like IOM and others, supports the exemption of research from the current HIPAA requirements and the adoption of a new research-specific privacy protection framework that provides individuals with more authentic privacy protection while facilitating in an efficient and effective manner the conduct of essential health research. Until that is accomplished, HHS can take intermediate actions to mitigate the negative impact of the Privacy Rule. IDSA recommends that HHS: 1) exempt research activities from the accounting of disclosures requirement as it is currently considering, 2) redefine protected health information in the context of research, and 3) provide guidance clearly delineating quality improvement efforts from research activities.

Should you have any questions or comments, please do not hesitate to contact Audrey Jackson, PhD, IDSA's Program Officer for Science and Research at ajackson@idsociety.org or 703-299-1216.

Sincerely,



James M. Hughes, MD, FIDSA
President

Enclosure: "Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts," *Clinical Infectious Diseases* 49 (2009).

Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts

Infectious Diseases Society of America[a]
Infectious Diseases Society of America, Arlington, Virginia

The Infectious Diseases Society of America is concerned that excessive regulatory oversight is seriously affecting translational research and quality improvement efforts. Careful studies on the subject of research oversight have documented the adverse effects of regulatory burden on clinical, epidemiological, and health systems research. We identified 5 problem areas. First, the application of the Health Insurance Portability and Accountability Act to research has overburdened institutional review boards (IRBs), confused prospective research participants, and slowed research and increased its cost. Second, local review of multicenter studies delays research and does not improve protocols or consent forms. Third, reporting of off-site adverse events to local IRBs is wasteful of the resources of sponsors, investigators, and local IRBs and does not add to participant safety. Fourth, uncertainties about key terms in the regulations governing pediatric research lead to marked differences in the ways that local IRBs review research involving children. Fifth, the lack of consensus on when IRB review is required for quality improvement efforts is slowing progress in this critical area. Relatively simple steps, which do not require legislation or a change in the Common Rule, could improve regulatory oversight in these problem areas.

Epidemiological and clinical research is important in every field of medicine, particularly for infectious diseases. Interactions between humankind and the microbial world are remarkably dynamic; new infections are discovered, and previously-described pathogens spread to new areas and develop enhanced virulence and antimicrobial resistance. There have been tremendous successes in research on infectious diseases. Within 3 years of the first clinical description of AIDS, the pathogen had been identified, and soon thereafter, therapy was developed that has saved hundreds of thousands of lives. Such progress requires a flexible research infrastructure that can assimilate new ideas and respond quickly to urgent research questions.

Six years ago, Califf and Muhlbaier [1] warned that "the system of research could become increasingly paralyzed as most of the transaction costs for research may be exhausted in response to regulations that have no useful purpose" (p. 917). Evidence gathered in the subsequent years has heightened concerns about excessive regulatory burden on translational research and quality improvement efforts. The Infectious Diseases Society of America (IDSA) is concerned that the research infrastructure in the United States is slowly grinding to a halt under this increasing burden of ineffective regulatory oversight (and similar problems have been noted in other countries) [2–5].

Institutional review boards (IRBs) are overwhelmed by the application of the Health Insurance Portability and Accountability Act (HIPAA) to research. Federally sponsored studies are being delayed and becoming

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[a] This article (written by William Burman and Robert Daum) was developed for the Infectious Diseases Society of America (IDSA) Research Committee: Edward Janoff (chair), Paul Bohjanen, Helen Boucher, William Burman, Richard D'Aquila, Barry Eisenstein, Carol Kauffman, Clifford Lane, David Margolis, Gary Marshall, Debra Poutsiaka, Adam Ratner, Barth Reller, Louis Rice, Edward Ryan, Paul Spearman, Chloe Thio, and Padma Natarajan (Research Committee staff). It was approved by the IDSA Board of Directors on 4 February 2009.

Reprints or correspondence: Dr. William Burman, 605 Bannock St., Denver, CO 80204 (bburman@dhha.org).

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more expensive as a result of regulatory burden [6–8]. Industry-sponsored clinical trials have largely left academic medical centers and are now moving out of the United States [9]. Quality improvement efforts are held up by uncertainties about when and how IRB review should be done. Finally, increasing regulatory burden is a major disincentive to trainees who are considering a career in research [10–12].

We are concerned about the current oversight system, but we are in complete agreement about the need for independent review of research involving humans. The unfortunate history of abuse of vulnerable subjects in research must not be repeated. To agree on the need for independent oversight, however, is not to defend the redundancies and inefficiencies that consume resources and delay research but do not contribute to the safety and privacy of research participants. The subject of research oversight has itself become the subject of careful quantitative research. We used this literature to identify 5 areas in which pragmatic steps can be taken to improve research oversight (Table 1)—steps that would not require new legislation or a change in the Common Rule [13].

THE EXAMPLE OF HIPAA

HIPAA legislation was enacted to facilitate electronic billing, improve privacy protections, and promote continuity of health insurance coverage [14]. Notably, an advisory committee for the Department of Health and Human Services (DHHS) "identified no instances of breaches of confidentiality resulting from researcher use of records" [15] and noted the confidentiality protections that have long been a part of research oversight. Despite the lack of evidence of a problem and over the strong objections of the research community [16, 17], DHHS included research in HIPAA regulations [18]. As a result, many more forms of investigation and quality improvement require review, and an "authorization form" was added to the consent process [19].

The negative repercussions of HIPAA have echoed throughout the system. The workload of IRBs increased [20] at a time when they were already overloaded [21–23]. HIPAA authorization forms average 2 pages and use complex, legalistic language [19, 24, 25] unlikely to be understood by study participants [26]. In 2 controlled trials, prospective participants randomized to receive a HIPAA authorization form were less likely to enroll in a study than were participants who received only the informed consent document [27, 28].

A wide variety of research has been adversely affected by HIPAA [6, 29, 30], and the cost of doing multicenter studies has increased [7, 31]. Enrollment in epidemiological cohort studies and some clinical trials decreased markedly [7, 31–33],

Table 1. Problems with the Human Subjects Protection System and Suggested Remedies That Do Not Require Legislation or Changes in the Common Rule

Problem	Possible remedy
Negative effects of HIPAA on a wide variety of research	Remove research from the list of activities covered by HIPAA regulations
Duplicative review of multicenter studies by the local IRBs of all participating sites	Expand the availability of central review panels for federally funded research Provide incentives for the use of central review
Redundant review of individual adverse event reports by the IRBs of all participating study sites	Harmonize guidance documents on adverse event review from FDA and OHRP Complete the development of a single electronic adverse event reporting form that would fulfill reporting requirements to all involved federal agencies Refocus the efforts of local IRBs on the evaluation of adverse event reports from single-site studies
Uncertainties about the appropriate level of review for some studies among children	Provide updated guidance for key terms, such as "minimal risk" and "minor increase over minimal risk" Make the national review of selected pediatric studies (the "407 process") much more efficient Make the results of previous national reviews readily available through a searchable Web site
Uncertainties about the role of IRBs in the review of quality improvement efforts	Provide clear guidance of the criteria for IRB review of quality improvement activities
Barriers to medical record research that are a disincentive to research by trainees	Remove research from the list of activities covered by HIPAA regulations
Lack of resources at OHRP to provide timely guidance and review of human subjects protection issues	Increase funding for OHRP Provide OHRP a clear mandate to produce timely updates in guidance and review

NOTE. FDA, US Food and Drug Administration; HIPAA, Health Insurance Portability and Accountability Act; IRB, institutional review board; OHRP; Office for Human Research Protection.

Table 2. Proposed Benefits of Local Review of Multicenter Protocols and the Evidence Regarding Those Benefits

Aspect of the research oversight system	Proposed benefit	Evidence base	
		For	Against
HIPAA	Improve protection of patient confidentiality	None	Authorization forms have inappropriately complex wording [24–26] Requirement for an authorization form decreases participation in research [27, 28] Decreased enrollment in epidemiological studies in the post-HIPAA era [31–33, 38] Biased enrollment into epidemiological studies in the post-HIPAA era [32, 33] Increased delays in study implementation [7, 20, 35] Increased costs for research [31, 35, 38]
Local review of multicenter studies	Assure appropriateness of the protocol and consent form for the local population	None	Increased workload for local investigators [5, 34, 39] Increased costs of multicenter studies [40, 41] Marked differences in the type of review done at local sites [34, 42–50] Changes in consent forms that make them longer and more difficult to read [39, 51] Errors in locally approved versions of consent forms [39, 42] Substantial delays in the implementation of multicenter research [2, 8, 39, 45, 47, 52]
Adverse event review by the local IRB	Protect the safety of research participants	None	Substantial effort by the local investigator and IRB [53]
Pediatric-specific regulations for research oversight	Provide enhanced oversight for children, as a vulnerable population	None	Marked interinstitutional differences in the review of pediatric research [43, 44, 54] Delays in resolution of pediatric studies requiring national review (the "407 process") [55]

NOTE. HIPAA, Health Insurance Portability and Accountability Act; IRB, institutional review board.

and selection biases were introduced [32, 33]. Health systems research has been particularly compromised [20, 30, 34, 35]. Although HIPAA regulations allow research on de-identified data without patient consent, the removal of HIPAA-defined identifiers from medical records resulted in a 31% reduction in data, including information of vital importance for research and quality improvement [36].

We are particularly concerned about HIPAA's effects on medical record reviews, because such studies are often the initial exposure of trainees to research. Medical record review introduces patient-oriented research, and its retrospective nature often allows completion of a project in the limited time available during training. In the post-HIPAA era, nearly all record reviews are judged to require IRB approval, and an increasing percentage are sent for full-committee review [20]. Even expedited review often requires 1–3 months [37]—a delay that may preclude completion of a project.

The application of HIPAA to research is a lesson in unintended consequences. HIPAA legislation was not directed toward research, and there was no need to augment the existing confidentiality protections. Six years later, prospective participants are confused by authorization forms, IRBs are even more overburdened, research takes longer and costs more, and investigators are discouraged by the resulting "thicket of regulatory ambiguity" [6]. The Secretary of DHHS should remove research from the purview of HIPAA, as part of a "new framework for ensuring privacy" [30].

REDUNDANT REVIEW OF MULTICENTER STUDIES

Many clinical trials and epidemiological studies require multiple sites to accrue participants and produce generalizable results. Traditionally, each study site submits the protocol and informed consent document to its own local IRB. Local review is said to be important to assure that unique aspects of the local study population are dealt with appropriately (Table 2). Thus, a multicenter study may be reviewed by hundreds of IRBs.

Local review of multicenter studies requires substantial effort and expense. Sites in a tuberculosis study estimated that submission required a median of 30 h of staff time [39]. Local IRB review of a multicenter observational study required 15,000 pages of documents and consumed 16.8% of the entire budget

[40]. Local review also delays study implementation; the median times to approval for multicenter protocols ranged from 1.5 to 15 months [2, 8, 34, 39, 45, 52, 56].

The outcomes of local review of multicenter studies have not been reported in detail for a large number of studies, but the available data are quite consistent. Study protocols are seldom changed, but local IRBs often have markedly different interpretations about review of multicenter studies of a wide variety of types: pediatric [43, 44, 54], epidemiological [45, 57], health services [3, 34, 46, 47, 58], and minimal risk research [48, 49].

Changes in consent forms are usually required during local review [39, 42, 45]. In studies that have carefully evaluated these changes, consent forms became longer [51] and more complex [39]. Indeed, local IRBs often require complex language to be used in consent forms [59]. Finally, errors in the study description or in the description of possible adverse effects have been made and approved during local review [39, 42].

In summary, local review of multicenter protocols delays study implementation and consumes valuable resources of local IRBs and investigators. That neither protocols nor consent forms are improved in the process (Table 2) strongly suggests that local review of multicenter studies is another unnecessarily redundant part of the system.

STEPS TO INCREASE USE OF CENTRAL REVIEW

Federal regulations allow one IRB to rely on the review of another IRB [60], allowing central or cooperative review of multicenter studies. Since being introduced by the National Cancer Institute (NCI) [61], the idea of central IRB review has slowly gained ground. The 2 NCI central IRBs have now been accepted by 600 local IRBs [62], and other federal agencies have begun to use the model [63, 64]. We recommend that all major institutes and centers at the National Institutes of Health (NIH) develop a central IRB for multicenter studies.

Despite encouragement from the Office for Human Research Protection (OHRP) and the US Food and Drug Administration (FDA), cooperative review is underused [65]. Local institutions continue to have concerns or lack of familiarity with central review [66, 67]. NIH and other federal agencies that fund research should develop incentives for central IRB review; applicants who use a central IRB could receive points toward the peer-reviewed score of a grant application.

ADVERSE EVENT REPORTING

Careful monitoring of adverse events is critical in interventional studies; despite extensive preclinical testing, there may be serious unanticipated side effects from new treatments [68, 69]. Data centers for multicenter trials have sophisticated systems for reporting and analysis of adverse events. Reports are completed over the internet and analyzed using software packages and professional review. The data center can review real-time data, by assigned treatment arm. If concerns are identified, they can be reviewed with the Data Monitoring Committee, an independent committee of subject experts and biostatisticians. This 21st century system is the way that human subjects are and should be protected in interventional biomedical research.

Despite this robust method for monitoring patient safety in multicenter trials, there is a parallel system of adverse event reporting (Figure 1). Reports of serious adverse events (often as paper documents) are sent to all other investigators using the same study medication or device. Investigators review these reports and forward copies to their IRB. The local IRB reviews and stores these reports, consuming 9% of its resources in the process [53]. Importantly, neither the investigator nor the IRB have access to data elements—study assignment and denominators—that would make adverse event reports meaningful. OHRP and FDA agreed that this parallel system is not required by the Common Rule [70] and that it has the effect of "in-

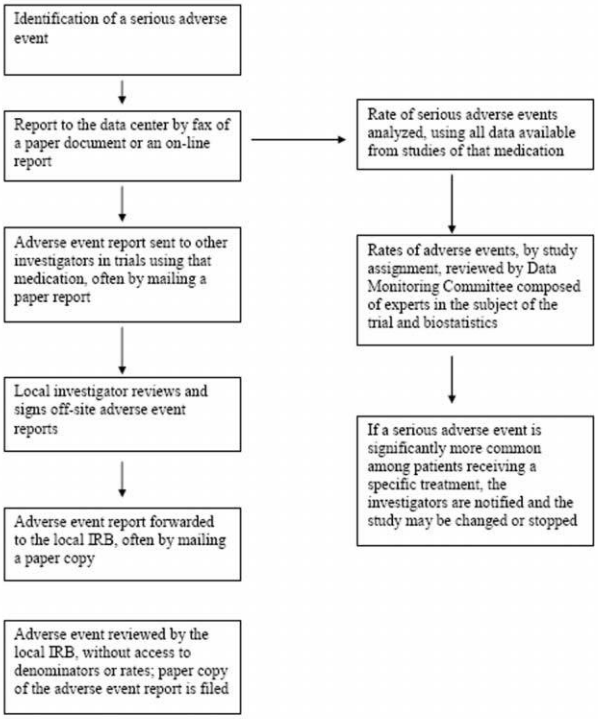

Figure 1. Data flow in the current system for reporting and analyzing serious adverse event reports.

hibiting rather than enhancing IRBs' ability to adequately protect human subjects" [71]

Thus, there is general agreement that the system of adverse event reporting includes a redundant and expensive process that does nothing to improve patient safety. OHRP and FDA have responded to this situation with updated guidance documents [70, 72]. Unfortunately, these 2 documents differ in several important ways, leading to continued uncertainties about adverse event review.

The responsibility for adverse event analysis from multicenter studies lies with data centers and data monitoring committees; IRBs and site investigators should have no role, other than responding to a finding by a data monitoring committee. OHRP and FDA should develop consensus guidance on adverse event reporting. It is notable that most highly publicized cases of serious injury to research subjects have been in single-site studies [73, 74]. Freed of the wasteful effort of reviewing adverse events from multicenter studies, local IRBs can focus on reviewing reports from single-site studies.

BARRIERS TO THE INVOLVEMENT OF CHILDREN IN RESEARCH

Children are unable to provide fully informed consent for participation in research and, therefore, have an enhanced level of regulatory protection. However, children have frequently been excluded from research. In the absence of data on pediatric-specific side effects or pharmacokinetics, new treatments have been used off-label for children [75]. Thus, an overzealous effort to protect children can have the paradoxical effect of harming children when lack of inclusion in research leads to use of inappropriate medications or inappropriate doses in children [76].

The Common Rule contains sections on oversight of pediatric research [77]. However, uncertainties about the interpretation of regulatory terms used to classify pediatric research ("minimal risk") and institutional risk aversion has led to markedly different decisions about pediatric trials by local IRBs [54]. The Common Rule allows national-level review by a panel of pediatricians and bioethicists to provide guidance on studies which raise concerns at the local level (the "407 process"). Although well-intentioned, the "407 process" has been so slow as to be a major impediment to research, requiring a median of 27 months for decisions about proposed pediatric trials [55].

We recommend that OHRP work with pediatric researchers, the IRB community and bioethicists to provide clarity about key definitions for pediatric research. Furthermore, OHRP should continue its efforts to streamline the "407 process."

REVIEW OF QUALITY IMPROVEMENT PROJECTS

In recent years, quality improvement projects have been emphasized and required as a means of improving the health care system. At the same time, IRBs have become increasingly involved in review of quality improvement efforts. However, the lack of consensus [78] regarding when and how IRBs should review quality improvement activities was highlighted by a recent high-profile case. The Michigan Hospital Association evaluated the effect of a simple checklist on catheter-related bacteremia. The project was reviewed by the IRB of one of the consulting quality improvement experts and was judged to not be research, because all items on the checklist were part of national standards. The project was strikingly successful in decreasing rates of catheter-related bacteremia [79], and plans were made to disseminate it to other hospitals. OHRP reviewed the project after its publication and determined that the project was research and had not been adequately reviewed [80]. In the ensuing outcry from hospital administrators and quality improvement officers [81], OHRP eventually reversed its decision [82], but the chilling effects of OHRP's handling of this case are likely to affect review of quality improvement activities for some time.

HIPAA regulations led to the perception that review of patient records by someone other than a direct care provider requires IRB review, particularly if there is intent to publish. However, a recent multidisciplinary panel of bioethicists, quality improvement officers, and regulatory officials reached very different conclusions [50]. The panel noted that both patients and providers have an ethical obligation to participate in quality improvement efforts, a fundamental distinction from research. The panel proposed that most quality improvement efforts should *not* be reviewed by an IRB, even when there is an intention to publish the outcomes. The panel's deliberations provide a fresh perspective that is needed to move the field beyond post-HIPAA hyper-expansiveness.

FUND OHRP AT A LEVEL CONSISTENT WITH ITS BROAD MISSION

Several of the recommendations above call for actions from OHRP, but this agency remains critically underfunded. Despite being responsible for a broad range of policy issues and oversight of thousands of IRBs, OHRP is a small agency, with a budget that has not kept pace with inflation (2008 budget of $4.7 million) [83]. Congress should increase funding for OHRP, coupled with a mandate to provide policy guidance on the subjects outlined above.

SUMMARY: RESTORING THE BALANCE IN RESEARCH OVERSIGHT

As an organization devoted to the prevention and care of infectious diseases, the IDSA reiterates its commitment to responsible research oversight. Both for the protection of research participants and to foster public trust in the process, research oversight is critical. However, time and resources are finite, and there are urgent needs for research on many illnesses. The evidence from careful studies provides compelling evidence that the current system includes practices that delay research and increase its costs while failing to contribute to the safety or privacy of research participants.

It will be critical that the much-needed public discourse on appropriate regulatory oversight for research and quality improvement be framed in a broader context than has been true in recent years, a perspective that acknowledges the rare and reprehensible instances of investigator fraud or inattention to participant safety, but one that also provides data on how inefficiencies and redundancies in the current system unduly delay vital research. Patients and disease advocacy groups, as well as researchers and regulators, need to be a part of this discussion. The need for research and the need for oversight are not competing agendas; they are 2 pillars that support the research enterprise. It is time to restore the balance.

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