In recent years there has been growing frustration on the part of some researchers, research ethics experts, and others that the policies and practices of institutional review boards (IRBs) often create unnecessary barriers for the human research enterprise. Commentaries with provocative titles such as “The Dysregulation of Human Subjects Research,”1 “Pruning the Regulatory Tree,”2 and “Breaking the Camel’s Back: Multicenter Clinical Trials and Local Institutional Review Boards”3 reflect the dissatisfaction of some investigators. Indeed, Fost and Levine have asserted that “the national system for the protection of human research participants is indeed a system in jeopardy” and that “the major source of the threat to its proper functioning is the increasing pressure [on IRBs] to perform tasks that either do not require doing, could be done better by others, or could be done more efficiently using expedited review procedures.”4

Given the growing concern about the negative impact IRB policies and procedures may have on the research enterprise, the American College of Neuropsychopharmacology (ACNP) conducted a survey of its members to learn about their experiences with IRBs. The ACNP is a professional society that promotes brain, behavior, and psychopharmacology research. Individuals who conduct high quality research are elected to be members.5 We report here on the survey and the findings of the study.

Study Methods

The survey developed by Ness6 to explore the impact of the HIPAA Privacy Rule on clinical research was used with permission as a model for constructing the ACNP survey.7 The title for the ACNP survey, “Solutions for Common IRB Issues in Neuropsychiatry,” was purposefully selected to emphasize the constructive intent. Content areas were derived from a literature review and input from members of the ACNP’s Human Research Committee. A draft survey was pilot tested with 10 members of the Human Research Committee for clarity and technological adequacy.

The ACNP membership was invited to complete the anonymous survey in September 2009, with a two-month window for reply. Surveys were distributed to 887 members via e-mail, including three e-mail reminders. A total of 143 members accessed the survey; 18 were excluded from the sample because they did not perform clinical research that yielded a response sample of 125. The response rate of 35% (125/353) is comparable to that identified in a meta-analysis of response rates for Internet or Web-based surveys of 39.6% (±19.6%).8

Several mechanisms were used to acquire information via the survey. First, questions with forced-choice responses (rather than open-ended ones) were posed. Second, ACNP members were asked to rate their perceptions about certain issues—such as the amount of time the IRB approval process added to delays in protocol initiation—on five-point Likert scales. Space for additional detailed comments was provided for most queries. Third, respondents were asked open-ended questions such as: “Tell us about your IRB experiences. This will help us to understand the circumstances in which the IRB has affected your research.” The 29-item survey covered several topics: 1) characteristics of respondents; 2) effect of IRB review of human subjects research on public trust; 3) impact of IRBs on scientific inquiry; 4) impact of single IRBs and of multiple or centralized IRBs on protocol review; and 5) potential solutions to problems arising from the IRB review of research protocols. The time frame for responses was

restricted to the past three years. Simple descriptive statistics that retained each content response category were used to analyze the survey data.

Characteristics of the respondents are displayed in Table 1. The majority (75%) obtained their final professional degree between 1970 and 1994, consistent with the acceptance of senior scientists into the ACNP. The respondents were primarily academic physicians who conducted federally funded randomized clinical trials. They were highly experienced in IRB procedures, with 62% serving on and 16% chairing a review panel within an IRB. Over the three-year period prior to the survey, the majority (70%) submitted more than five protocols to an IRB.

**IRBs, Participant Protection, and Public Trust**

IRB review of research represents one of the mechanisms that allows the public to be confident that research with human subjects is ethically conducted. Nearly two-thirds (66%) of respondents believed that IRBs strengthened public trust in research. They noted that no better alternative mechanism has been identified to protect research participants. Seventy-five percent of respondents said that IRB review of research enhanced the protection of human subjects. Respondent comments about the IRB’s role in protecting research participants included statements that IRBs provide guidance in simplifying the wording of consent forms; that they help establish “more explicit ethical boundaries” for human subjects research; and that “it can be difficult for a researcher to focus on human subjects issues and to consider them as fully as they are considered by an IRB.” The latter comment emphasized the importance of the “second opinion” that IRB review of protocols provides. However, several respondents noted that the public is more likely to be aware of negative publicity related to egregious ethical or other violations than of the day-to-day work of the IRB involving appropriately conducted studies, which constitute the vast majority of research with humans.

There were also comments critical of IRBs that focused on actions that do not contribute to the protection of research participants. In the words of one respondent,

IRB reviews today are reactive, and basically an over-reaction to a small number of researchers who violated rules of conduct in studies with human subjects. IRBs should develop a triage system where competitive renewals with no issues should be rubber-stamped; low-risk research should be given less scrutiny; and at-

<table>
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<th>Table 1. Characteristics of ACNP Survey Respondents</th>
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<tr>
<td><strong>Year obtained final professional degree</strong></td>
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<td>Before 1970</td>
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| **Degree**                                       |
| MD                                              | 95 (77) |
| PhD                                             | 47 (38) |
| MS                                              | 18 (15) |
| MPH                                             | 2 (2)   |
| Other                                           | 1 (1)   |

| **Employment site**                             |
| Academia                                        | 100 (81) |
| Government                                      | 15 (12)  |
| Industry                                        | 4 (3)    |
| Other                                           | 5 (4)    |

| **Research funding source**                     |
| Federal                                         | 111 (91) |
| Industry                                        | 59 (48)  |
| Foundation                                      | 60 (49)  |
| Other                                           | 11 (9)   |

| **Area of research**                            |
| Randomized clinical trials                      | 51 (41)  |
| Clinical observational studies                  | 30 (24)  |
| Basic science                                   | 11 (9)   |
| Other (genetics, brain imaging, drug development, translational) | 32 (26) |

| **Protocols submitted in last three years**     |
| 0–5                                             | 38 (30)  |
| 5–10                                            | 45 (35)  |
| 10–20                                           | 29 (23)  |
| More than 20                                    | 16 (12)  |

1 Total over 100% due to nonexclusive categories.
tention should be spent more on protocols that involve real risk to human beings.

Impact of IRBs on Scientific Inquiry

Complaints about IRBs include the claim that investigators do not pursue some research because of the perception that the IRB will not approve their study. Slightly more than a quarter (26.4%) of the respondents acknowledged that they had abandoned potential research due to this concern. The types of scientific investigations they did not pursue involved 1) studies with a vulnerable subject population (based upon age or underlying medical or psychological status), 2) challenge studies in which a psychoactive substance is used to provoke symptoms to assess the disorder or the response to treatment interventions, 3) projects that raised additional regulatory requirements (such as a Food and Drug Administration Investigational New Drug or Device approval), and 4) studies with procedures to obtain biological samples (such as cerebrospinal fluid). Several respondents gave examples of how “unpredictable” IRBs could be about whether they would approve a study. For example, one respondent said that the IRB approved “protocols for serial spinal taps . . . but would not approve a study . . . which involved handing out a survey to patients in the waiting room in a psychiatric ER.” Another respondent described a different situation:

In the last three years, essentially every innovative protocol we have developed has either had to be modified to the point of making the science of questionable value, and/or been processed so slowly that by the time it was approved, our competitors at another university presented the results of the same kind of study. We had submitted our protocols the same month based on a preclinical paper that had come out. . . . In several cases, procedures which have been used successfully and safely in many published studies were deemed unacceptable, or generated so much anxiety that an additional round of review was carried out with ad hoc experts.

Impact of Multiple IRBs

Multiple IRBs within the same organization or at different institutions reviewing the same protocol for a multisite study increased the complexity of obtaining approval. Over a third (35.7%) of respondents worked with multiple IRBs, which included collaborative programs between agencies that maintained separate reviews (such as the Veterans Administration and state government programs), as well as multiple panels of IRBs within the same university. The major problem investigators experienced was delay in the IRB’s review of their protocols. They reported that separate IRBs did not consistently apply the same standards for reviewing protocols. The most extreme examples were from two investigators, each with five IRBs reviewing the same studies. According to one respondent:

Each [IRB] requires changes, even if very minor things, to show they have been diligent . . . and then every other IRB has to approve the changes made by everyone else, so it becomes an endless battle to make sure all IRBs have approved everything (who gets the final word on revision, etc.) and that all have the most recent updated copy in their files, etc. Also, some IRBs will require format changes that are not acceptable to other IRBs and each has their own idiosyncratic language for consent forms. Ultimately after the committees had [agreed] on the consent form . . . I had a 27-page document which was so long that a new concern was raised: it was too lengthy for the patients to comprehend it all and we should also have a synopsis one-page form.

It is increasingly the norm for investigators to perform studies that bridge institutions to consolidate expertise and increase access to research participants. Nearly 80% of respondents had studies that required IRB reviews from more than one institution, and over 80% reported approval delays directly related to requirements at each institution involved in a multisite trial. Respondents specifically pointed out that IRBs reviewing protocols for multisite trials did not harmonize their requirements for approval. Thus, investigators answered to IRBs that differed in their assessments of research-related risk, in what constitutes acceptable informed consent, and in consent form language. Several respondents said they were not able to compete for multisite studies because of these complexities. Respondents also reported that participants in multisite trials were asked to sign separate consent forms, often containing conflicting language regarding the same study. The difficulties increased with multinational studies, where the format, length, and language of
consent forms increased the time required to produce a document acceptable to all parties.

A centralized IRB system might resolve some of the dilemmas related to multisite studies. Although a third of respondents (32.8%) had access to a central IRB, many were not able to use central IRBs as sole sources of approval for studies, which underscores the current minimal but potentially substantial impact on the review process that central IRBs offer. Very few of the respondents reported using a central IRB, and when they did so, their local IRB insisted that it also had to approve the protocol. However, only 6.5% of respondents involved in multisite studies said they were unable to obtain approvals from both the central IRB and their local IRB.

**Additional Issues**

Of note, the majority of respondents (65%) indicated that the IRB review process improved their protocols. Nonetheless, they also pointed out that IRBs often raised concerns about studies involving certain populations of participants—for example, individuals with severe mental illness (particularly psychosis and/or substance abuse); children under 18; individuals with psychiatric conditions and comorbid medical conditions; and elderly, demented, or suicidal patients. The well-intentioned concern about conducting research with vulnerable populations raises the issue of protecting such participants to the extent that they are excluded from research studies, which results in little data to use to structure interventions. The majority (84%) of respondents made protocol changes to satisfy the IRB about including participants from vulnerable populations. More than half (56%) reported that these changes had minimal impact on how many subjects were recruited for studies. However, 28% of respondents reported that the required changes substantially reduced the number of participants from vulnerable populations in their study, prevented any recruitment of those individuals, or rendered the consent form too lengthy or complex to use. One respondent described problems with the IRB involving a placebo-controlled trial with participants who had postpartum depression:

The justification of the use of a placebo control added nine months to the review process. The study was a randomized trial already funded by the National Institute for Mental Health for postpartum depression. The IRB insisted the placebo was unethical and asked for this cell to be removed from the study.

Other respondents pointed out problems when the studies involved adolescents. One respondent wrote:

The IRB requires that we have two research assistants for each child under [sleep] study and at least one parent must also stay in the lab overnight. Most parents are not willing to do this and by having two research assistants simultaneously, we lost half of the available nights for research studies.

Difficulty obtaining enough participants for trials was also attributed to several other factors: delays in IRB reviews that resulted in discordance with National Institutes of Health (NIH) budget calendars when funding was from that source; the need for additional, no-cost extensions from the NIH; and failing to meet recruitment targets. Paradoxically, 15% of respondents reported that the impact of IRB policies often resulted in an increase in the number of participants enrolled in studies because researchers went to other countries to recruit participants.

Another issue is whether IRB procedures should differ for research funded by industry compared to projects supported by the NIH or a nonprofit foundation. Most respondents (81%) said that procedures should be identical. An interesting observation was that local IRBs slowed the pace of approval for industry-sponsored studies, which made academic investigators noncompetitive. Several respondents indicated that they believe NIH studies should be fast-tracked by IRBs since they have received peer review at the funder level and will also be monitored by the NIH Office of Human Subjects Research.

A question of major relevance to neuropsychiatry research is whether IRBs view such studies through a different lens than they do other types of research. The survey included the question, “Do you believe that studies in neuropsychiatry are at a disadvantage compared with other studies in medicine; that is, do IRBs view psychiatric trials differently than other medical studies?” Sixty-five percent of respondents answered in the affirmative. Some respondents raised concerns that some IRB members might view such studies through the same lens of stigma as the general public. Wrote one respondent, “The nonpsychiatrically trained members of IRBs are affected by the same stigma that impacts the public. Many are also misinformed, and it is crucial to have representatives from psychiatry on committees.” According to another respondent,

IRB members often see themselves in a ‘parens patriae’ role to protect people with mental illnesses and apply very different standards to psychiatrically ill patients relative to persons with other medical conditions. They
exhibit serious prejudice against people with mental illnesses, often requiring substituted judgment in situations where that is inappropriate. Many members seem to want to have someone else other than the patient making decisions about their lives. I believe that it is stigmatizing and demeaning to patients.

Another respondent raised the concern that some IRB members may not have an accurate understanding about the cognitive capacity of individuals with psychiatric disorders to consent to research: “It does not seem that our IRB understands the populations we use (drug dependent and psychiatric patients). For example, it took a while to convince our Chair that patients could even give informed consent.” This view was echoed in the comments of another respondent:

There is a not-so-subtle bias against patients with schizophrenia and other serious mental illnesses that they lack the capacity to give informed consent unless proven otherwise. This is not true with most other psy-

Respondents repeatedly noted that IRB members should be made aware that many persons with a mental illness have the capacity to give informed consent for research.

psychiatric disorders. The consenting process and capacity assessments have become very burdensome, at least with academic IRBs.

These comments suggest that the protection of vulnerable mentally ill subjects may overlap with the impact of stigma. The respondents repeatedly suggested that IRB members should be made aware that many persons with a mental illness have the capacity to give informed consent for research. Educating IRB members may reduce undue protectionism and the potential for stigmatizing such individuals with a mental illness. It may also ensure that the mentally ill are included in studies when appropriate and necessary. One respondent noted that “stigma against the mentally ill remains common, and therefore, these studies are reviewed at a more critical level. The correct response, though, is not to weaken review of psychiatric studies, but to bring other areas of medicine up to the same more rigorous standards.”

Although ACNP members clearly had some concerns about IRB review of neuropsychiatry studies, 67% described exemplary interactions with their IRBs. Positive experiences were attributed to effective communication to facilitate timely approvals and having a helpful contact on the IRB. As discussed by Carline,9 effective communication leads to trust and greater probability of successful IRB approval due to integration of differing viewpoints. Respondents reported that their own participation as an IRB member was educational and increased the confidence of fellow IRB members when

### Table 2. Respondent Recommendations for Improving IRB Review of Neuropsychiatry Studies

- Develop universal standards—for example, a standard for minimum-risk studies of children, adolescents, or adults for brain imaging, standardized “boilerplates,” etc.
- Include mental health experts on IRB committees.
- Use IRBs devoted specifically to mental health review, which could lead to greater stability and predictability in reviews. When a distinct mental health IRB is not available, a departmental review can be instituted before the institution’s review to reduce delays.
- Improve the continuity and stability of their membership by increasing the proportion of scientists who remain on the IRBs for longer (i.e., five-year) terms.
- Educate members about capacity to consent for mentally ill and cognitively impaired patients.
- Construct standards for appropriate management plans for studies that include assessments of suicidality.
- Develop understandable standard formats to present the adverse effects of psychotropic drugs, rather than a long list of adverse events that compromise the intent of the consent document.
- Develop an appeals process for reviews with procedures for appeal; for example, a mental health oversight committee of highly experienced reviewers (perhaps former IRB chairs) could be called on to perform a second level of debate and resolution for proposals that are without resolution from the first level of review.
- Facilitate communication with IRB members, arrange for investigators to meet the IRB members and/or the IRB chair directly, use negotiation skills to give attention to both “sides” of a debate, and provide a chance to run “thorny” issues by the IRB before formal submission.
- Assess the impact of stigma and protectionism of the mentally ill on the IRB review process and outcome.
- Pursue a “case log” approach, which would develop local and central IRB reference materials to improve finding resolutions by learning from others’ experiences in addressing concerns in neuropsychiatry research.
their research protocols were being reviewed. Appreci-
ating the process from both vantages (as a reviewer and
an applicant) improved communication and trust.

Discussion

O
erall, respondent members of the ACNP had
positive views about the impact of IRBs on
human subjects protections and public trust in the
research enterprise. Yet respondents’ experiences with
IRBs varied, and they identified tension between satis-
fying IRB requirements and resource allocation. One
particular resource that was lacking was time, which
resulted in delays in reviewing research protocols. The
costs of developing IRB applications, liaison time (i.e.,
working with the IRB collaboratively to solve prob-
lems), and modifications resulting from discussion are
borne by academic institutions, the government, and
ultimately society. Delays in IRB approval increased dif-
ficulty complying with recruitment targets and budget
time frames. An ongoing debate is whether increased
human subjects protections justify increased costs.

Some respondents reported that they have not pur-
sued research questions based upon the likelihood that
their IRB would not approve their study due to con-
cerns about novel aspects of the study or specific ethical
disputes. The impact of not bringing proposals to the
IRB means that some novel, cutting-edge research may
never get conducted.

Table 2 summarizes respondents’ recommendations
for improving IRB review of neuropsychiatry studies.
Two novel recommendations were made. The first was
for an IRB “case log” of common concerns related to
neuropsychiatry studies, conceptualized as similar to
precedent case law. These cases and the changes to the
protocols that allowed them to move forward would
be captured and recorded for reference. Such a case
log would provide precedent cases to which both IRB
members and investigators could refer. The second
novel recommendation was to evaluate the degree to
which protectionism and stigma impact the IRB review
process in neuropsychiatry protocols.

The recommendation to develop a “case log” would
provide a method for capturing debate and resolu-
tion about common IRB concerns in neuropsychiatry
within and across institutions. A case log might also
decrease the variability in decisions about similar
studies, improve continuity for grant protocol reviews
when IRB membership changes, and serve as a resource
to investigators who must substantiate their protocol
design choices. It is also possible that a case log could
decrease the turnaround time for review of protocols
because precedent cases would be available for inves-
tigators to review while they are developing their proto-
col and for IRB members to review before convened
meetings. This concept was recently described by Bean
and colleagues,10 who developed and are implementing
a decision bank to promote a transition from ad-hoc
decision-making to an issue-based, operational IRB
model.

A striking observation by ACNP members was the
interplay of stigma related to mental illness and pro-
tectionism of vulnerable populations in the IRB review
process. Mental disorders are common in the United
States. One in four (26.2%) Americans 18 years and
older have a diagnosable mental disorder.11 Despite
increasing public awareness of the neurobiological basis
of mental illness, no decrease in stigma has occurred
over the period from 1996 to 2006, and levels remain
high.12 An approach to reducing stigma is to focus on
the abilities, competencies, and community integration
of persons with mental illness.13 This theme is reflected
in respondents’ comments about the need to educate
IRB members, particularly with respect to the decision-
making capacities of people with mental disorders, in
order to reduce IRBs’ inappropriate protectionism.

The strengths of this study are that respondents had
extensive experience with IRBs reviewing their re-
search, and 62% had experience being an IRB mem-
ber. However, we note several limitations. The sample
population was restricted to members of a specialized
professional organization, the response rate was low,
and confidential Web-based surveys do not allow the
number of individuals invited to participate to be de-
rived from an accurate denominator.

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