IRB ADVISOR

YOUR PRACTICAL GUIDE TO INSTITUTIONAL REVIEW BOARD MANAGEMENT

MAY 2018 Vol. 18, No. 5; p. 49-60

INSIDE

RELIAS
Formerly AHC Media

Preparing for Revised Common Rule? Aim for Efficient, Faster, Better IRB

Shortening IRB review process is one goal

By Melinda Young, Author

With just a couple of months remaining to prepare for the revised Common Rule, the question for human research protection programs (HRPPs) is: What needs to be done to make programs more efficient, faster, better quality, and compliant?

The revised Common Rule's chief focus is on modernizing, strengthening, and making HRPPs more effective through reducing burden, delay, and ambiguity for investigators and by simplifying and modernizing research oversight. *(To view the rule, visit: http://bit.ly/2Gorspk.)*

IRBs have been working toward the same goals for more than a decade, aided by a growing body of research into how to improve IRB operations and make the review process shorter and more efficient.

> THE QUESTION FOR HUMAN RESEARCH PROTECTION PROGRAMS IS: WHAT NEEDS TO BE DONE TO MAKE PROGRAMS MORE EFFICIENT, FASTER, BETTER QUALITY, AND COMPLIANT?

There isn't one path, as IRBs across the country have found. But there are some good examples of best practices. For instance, one HRPP has developed metrics to determine which steps in the IRB review process could be changed to improve review time. Another organization uses a team that identifies areas in need of improvement and oversees changes.

These projects started with questions about their current processes.

Financial Disclosure: Author **Melinda Young**, Medical Writer **Gary Evans**, Editor **Jill Drachenberg**, Editor **Jesse Saffron**, Editorial Group Manager **Terrey L. Hatcher**, Physician Editor **Lindsay McNair**, MD, MPH, MSBioethics, and Nurse Planner **Kay Ball**, PhD, RN, CNOR, CMLSO, FAAN, report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

IRB ADVISOR

IRB Advisor,
ISSN 1535-2064, is published monthly by
AHC Media, a Relias Learning company
111 Corning Road, Suite 250
Cary, NC 27518

Periodicals Postage Paid at Cary, NC, and at additional mailing offices.
GST Registration Number: R128870672.

POSTMASTER: Send address changes to:
IRB Advisor
111 Corning Road, Suite 250
Cary, NC 27518

SUBSCRIBER INFORMATION:
Customer Service: (800) 688-2421.
Customer.Service@AHCMedia.com.
AHCMedia.com

SUBSCRIPTION PRICES:
Subscription rates: U.S.A., Print: 1 year (12 issues) with free AMA Category 1 CreditsTM or Nursing Contact Hours, $419. Add $19.99 for shipping & handling. Online only, single user: 1 year with free AMA Category 1 CreditsTM or Nursing Contact Hours, $377. Outside U.S., add $30 per year, total prepaid in U.S. funds.

MULTIPLE COPIES: Discounts are available for group subscriptions, multiple copies, site licenses, or electronic distribution. For pricing information, please contact our Group Account Managers at Groups@AHCMedia.com or (866) 213-0844.

ACCREDITATION: Relias Learning is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Relias Learning designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits*™. Physicians should claim only credit commensurate with the extent of their participation in the activity.

Relias Learning, LLC, is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Contact hours [1.5] will be awarded to participants who meet the criteria for successful completion. California Board of Registered Nursing, Provider CEP#13791.

This activity is intended for clinical trial research physicians and nurses. It is in effect for 36 months from the date of publication.

Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

AUTHOR: Melinda Young
MEDICAL WRITER: Gary Evans
EDITOR: Jill Drachenberg
EDITOR: Jesse Saffron
EDITORIAL GROUP MANAGER: Terrey L. Hatcher
SENIOR ACCREDITATIONS OFFICER: Lee Landenberger

"One of the most common questions we get from our investigators and study teams is about how long something will take to be reviewed and approved by the IRB," says **Brian Moore**, MS, CIP, IRB director at Wake Forest School of Medicine in Winston-Salem, NC.

"We in the IRB understand there is a significant amount of variability in review time, based on a number of different factors," Moore says. "These factors may depend on the department, whether or not the study is FDA-regulated, who is sponsoring the study, which board is reviewing it, and a whole host of factors."

Based on this question, the organization launched a program to more accurately predict IRB outcomes by using advanced statistics.

"Our goal was to be able to ask some very simple questions of our study teams in order to give them a more accurate estimate of the time it would take to complete the review," Moore says.

Salem State University in Salem, MA, had a different initial question: How could the IRB reduce the number of revisions needed for studies by new researchers?

"We had revision requests for 66% of proposals by students and faculty," says **Megan Williams**, MPA, director of research administration at Salem State University.

The IRB reviews hundreds of proposals a year, including proposals from student investigators, she says.

Since tackling this issue and making changes, the IRB has reduced its revision questions to 25% of proposals, Williams notes.

"There has been a sharp increase in quality of proposals," she adds.

With the revised Common Rule's deadline looming, implementing process improvements is especially important.

"We've had a system of standing committees to look at ongoing needs and new needs as they arise for a long time — more than a decade," says **Lark-Aeryn Speyer**, IRB senior associate regulatory analyst at the University of Michigan in Ann Arbor.

The University of Michigan has a change management process (CMP) that engages various stakeholders in developing educational and other IRB content and process improvements. *(See story on creating a change management process, page 51.)*

"Considering how important the changes are to everyone this particular year, we had to make a more intensive use of our existing processes and flex them somewhat," she says. "We also thought this was a time when more people would be interested in having a good, robust multilevel change management process."

When IRBs seek to change their processes, a good starting point is to collect data. The Wake Forest IRB collected data from 225 studies reviewed by the IRB, starting in July 2016. Metrics included time to approval and days with the IRB and the study team.[1]

Each institution's results are unique because of their different processes and procedures, Moore notes. "In the sense other institutions structure things differently, they could use the same methodology we use, using the same statistical methods, and plug in their own data."

The information was useful in a couple of ways. First, it highlighted potential causes of slowdowns in the IRB review process; secondly, it can be used to give investigators more

accurate predictions about how long their protocol's review might take.

"Our goal is to plug in some basic elements to our prediction equation, and based on the type of sponsor and study design and a couple of other factors, we can say with some confidence it will take X number of days," Moore says. "This gives the investigator the most accurate estimate, so they can plan for when they are ready to start enrollment."

The study and data collection of the review produced the following findings:

- There is variability in how long reviews take, partly due to the particular committee to which it is assigned.
- The institution's eight different IRBs vary in review time between 13 and 16 days.
- Investigators' responsiveness has greater variability.
- When there is no external sponsor and the principal investigator alone receives the IRB's feedback, makes revisions, and resubmits, the review process is faster.
- When other parties are involved and have to approve or sign off on changes, that can extend the timeline.
- The review time was the same regardless of whether a study was regulated by the FDA.
- The number of stipulations the IRB sent back to the study team had a significant correlation and could be used as a surrogate measure of the quality of the submission.

"The first step was to identify where the problems are, and that's what the focus of this project was," Moore says. "Since then, we have done some educational efforts to get our committees as consistent as possible."

Another change was to prioritize communication and feedback to study teams, showing them how to answer IRB questions correctly the first time. This helps reduce lengthy back-and-forth, he adds.

"It allows us to focus on areas that are of concern, and those not of concern that we don't need to spend that much attention on because they had no real impact," Moore says.

One key to collecting study review data is to let all stakeholders know that this process is not punitive. When problems are found, the idea is to come up with solutions — not shame those whose review processes are taking longer, he notes.

"Our first and foremost priority is to review the studies and make sure criteria for approval are met and that participants are safe, protected, and well-informed," Moore explains. "And we do not let our timing data or initiatives get in the way of appropriate participant safety."

The study of review times also acknowledged that some IRBs have more complicated studies to review or might receive poorer-quality submissions, which take longer. Despite some differences, there were ways IRBs and study teams could improve the review process and shorten the time it takes to review a protocol, and that's where the IRB could focus its improvement efforts.

For instance, the IRB used its software to place pop-up windows with links and answers to some questions where there are frequent errors.

"We put a link with instructions and guidance on how to answer those questions with the hope that they're answered correctly and with fewer concerns and stipulations, but we don't have data yet on how it's working," Moore says. ■

REFERENCE

1. Moore B, Wesley D, Rushing J et al. Using advanced statistics to more accurately predict IRB outcomes. Poster presented at the Public Responsibility in Medicine and Research (PRIM&R) Advancing Ethical Research Conference, held Nov. 5-8, 2017, San Antonio. Abstract: 42.

Change Management Process Can Bring All Sides Together for Quality Improvement

One IRB receives process improvement help from a well-designed change management process (CMP) that provides information, implements new procedures, and addresses the revised Common Rule and its effects.

For instance, the IRB held a CMP session to address the core components of the Common Rule regulatory changes, says **Lark-Aeryn Speyer**, IRB senior associate regulatory analyst at the University of Michigan in Ann Arbor.

"In April 2017, when most of us were starting to get our hands into the Common Rule changes, we realized our standing processes were going to serve us pretty well," Speyer says. "But this was such a big, time-sensitive matter, it needed a more intensive plan."

The IRB held the two-day retreat for core members of the Team to

Review E-research Enhancements (TREE). The retreat was held on a Thursday and Friday, from 8 a.m. to 5 p.m.

"We outlined the plan for the following year of the kinds of working groups we would expect to need for the changes and the kinds of deadlines we would expect," Speyer says.

TREE addressed the need to educate the research community and set the tone for the following year of work.

"We planned to approach the Common Rule changes from all directions," Speyer says.

Here are some of the ways TREE and the institution's other committee, the Production Support Team (PST), worked to support education and change:

• **Prioritize changes and effort.** "One of the early steps is prioritizing," Speyer says. "We decide if this is something we should proactively devote a lot of resources to, or should we make a note that people would favor some kind of change when we get around to it."

The working groups, engaged in the Common Rule changes, contained study coordinators, principal investigators, and IRB members. Their work is to take charge of challenges faced by the IRB, viewing the challenges holistically.

"What is the overall outcome we want?" Speyer says.

• **Include IT expertise.** "We take IT's advice on options for using the web-based smart form system for the IRB," she says.

"Information technology support people are part of this," Speyer adds. "They administer the system and are usually very inventive about looking for ways to make it fit any new needs that arise."

For example, a new problem occurred in the protocol application process. The University of Michigan research pharmacy has an ancillary committee that reviews research projects, using the same electronic system as the IRB. They came to the IRB with concerns related to the documentation they need about investigational drugs and processes for storing drugs for a study, Speyer says.

In the last year, there was a new trend in which the protocols were less likely to include specific documents the research pharmacy committee needed. So the committee asked to discuss revisions to their section of the application or to ask for manuals of procedures in a way that would make it easier to obtain the necessary information, she explains.

"They brought this to TREE," Speyer says.

The solution was to make it clear which information was needed and should be uploaded in the system.

"There's a new way these research protocols are being prepared," Speyer says. "We wanted our system to capture information in a way that works for us and for the study teams."

• **Education accompanies any change.** When the IRB makes changes to processes, the change is announced to the research community.

"We had changes we were preparing for the Common Rule, over the course of the last year," Speyer says. "It was an effort involving a huge number of people, and we were trying to spread the word very widely and repeatedly."

Changes that involved the web-based system were communicated by website postings or email.

Some changes were turned into U-Mic presentations, which are short PowerPoints with voiceovers, posted on the IRB website and played for the boards as part of their continuing education, she says.

"For really big changes like the Common Rule efforts, we schedule seminars where we invite the research community to present on the changes," Speyer says.

The information is targeted toward study teams and board members. But when the information is more general in nature, it can be more broadly useful — even outside of the institution, she adds. ■

Committee Helps IRB Prepare for Accreditation and New Common Rule

Accreditation experts say IRBs should not make too many changes when they first seek accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP). It's better to focus on what has to be done and to not do everything.

"We didn't follow that advice," says **Fanny K. Ennever**, PhD, CIP, research compliance officer at Boston Medical Center.

In 2016 and 2017, the Boston Medical Center and Boston University Medical Campus human research protection program (HRPP) tackled both accreditation preparation and a policies and procedures (P&P)

overhaul in anticipation of the revised Common Rule. The 15-month process, including the 800-page accreditation application, required Ennever's full attention, as well as monthly meetings and action by the HRPP advisory committee that consists of IRB chairs, co-chairs, and ex-officio IRB members.

The organization had not sought accreditation previously out of concern that the process would be too resource-intensive, Ennever notes. "But we recognize that in this day and age, you have to be accredited to be a credible IRB."

The IRB's efforts were a success. Boston Medical Center received accreditation from AAHRPP in December 2017.

The purpose of the Common Rule changes is to realign regulations with the goals of human research protection. Changes reduce oversight on low-risk studies and put more scrutiny on higher-risk studies, she says.

"The flexibility coalition has been promoting this for more than a decade," Ennever says.

Years ago, Boston Medical Center unchecked the federalwide assurance box, freeing its research program to have separate policies for federally funded and non-federally funded studies. But the institution never changed its P&Ps until it began preparing for accreditation, she says.

"One of the big questions people had was how difficult it was going to be to have two different kinds of research to specifically keep track of what was funded and what was unfunded," she explains. "We had unchecked the box, but didn't change the policies."

With the Common Rule changes, the sought-after flexibility applies to federally funded research, so the IRB's policy changes reflect that flexibility, Ennever says.

"We made changes almost monthly for a year and a half," Ennever says. "We were making changes, broadly, for the purpose of accreditation, but also so that we could accomplish the things we wanted to — realigning our program to focus on where there was higher risk."

> "THE IDEA BEHIND HAVING AN EXEMPT CATEGORY IS YOU COULD WALK INTO A RECORDS ROOM, PULL A CHART, GET INFORMATION, AND PUT IT RIGHT BACK."

The following is how the organization handled preparation for both accreditation and the revised Common Rule:

• Engage the HRPP committee. The committee and its 12-14 members meet for two hours every month.

The committee discusses changes, considers details, and decides on courses of action. Its motivation for change included the following:

- improve investigator experience;
- use board member time more efficiently;
- follow internal and external mandates;
- meet AAHRPP requirements.[1]

"They discuss flexibility changes, minor changes, and specific changes in policies and procedures," Ennever says.

Ennever made the changes suggested by the committee. She spent more than a year working on the revised, 180-page P&P manual. For each item in the P&Ps, she listed the dates of when the policy first was approved and when its revisions were approved.

• Target inefficient policies and procedures. "The policy change that made people the happiest involved chart reviews," Ennever says.

The chart review policy was revised in February 2018. It reads, "For chart review submissions, additional required information must be provided to determine whether or not the study is eligible for exempt category."

Before the change, researchers could only perform exempt category chart reviews if the reviews were only of existing data. Any new information collected would have triggered an expedited IRB review, she says.

"That made it very difficult to do a chart review," Ennever says. "The idea behind having an exempt category is you could walk into a records room, pull a chart, get information, and put it right back."

But the exempt category did not cover many chart reviews. In the revised Common Rule, there is an additional exempt category for data that exist now and might exist in the future, she adds.

For low-risk chart reviews the expedited review process is burdensome, so the organization changed the policy to reflect the Common Rule changes.

"We took something in a category that required more work, which was expedited review, and moved it into a category that requires less work, which is exempt review," Ennever says.

• Seek institutional approval of

changes. Once the HRPP committee reached consensus about proposed changes in policies and procedures, the change was given to institutional officials — one for Boston Medical Center and one for Boston University Medical Campus — for review. If they approved it, the change was implemented.

"We were fortunate that both institutional officials were engaged in the process," she says.

"I'd write a document explaining what the proposed changes were, the pros and cons, and there'd be discussion at the HRPP committee meeting about it," she adds.

The committee would make suggestions, Ennever would incorporate those changes, and the rewritten policy would go first to the committee and then to the institutional officials for approval.

After a change was approved, it became part of the policies and procedures manual. Then, Ennever communicated the change to the research community through a monthly newsletter.

• **Follow AAHRPP's guidance.** As the IRB prepared for an accreditation submission and visit, Ennever followed AAHRPP's guidance to see where additional changes were needed.

"All the materials provided by AAHRPP were a good guide to the kind of changes we needed and pointed us into the direction of where we had inadequate policies," Ennever says.

IRBs also should look at AAHRPP's reviewer's guide — but only after making changes according to the accreditation organization's materials for sites, she suggests.

"If you look at the reviewer's guide first, you'll feel like there's no way you can have everything done, so first look at their standards and compare those to your own policies and procedures," Ennever says. "Then, prioritize the changes."

Having only one set of P&Ps helped simplify the process. Ennever used Word to add hyperlink cross-references within the text. For instance, when a section listed requirements, each bullet point header had sections with hyperlinks to the pertinent sections.

"It was tedious to set up, but it came in handy for the AAHRPP application," she says.

After nearly one-and-a-half years of making changes, preparing for accreditation, and revising the P&Ps, Ennever says the process was worth the effort.

"The document was unrecognizable after a year-and-a half process," she says. "One of the great accomplishments is that now there's a mindset that changing the policies and procedures is normal, and we developed a very transparent and robust process for making the changes." ■

REFERENCE

1. Ennever F, Feldman J. Case Study: Boston Medical Center and Boston University Medical Campus. Presented at the AAHRPP 2017 Annual Conference, May 9, 2017, Detroit.

Rule Delay, Confusion Cloud SACHRP Meeting

'For what and when do we start preparing?'

A recent meeting of the Secretary's Advisory Committee on Human Research Protections (SACHRP) opened with the standard format of panel members going around the table, introducing themselves for the record. The elephant in the room needed no introduction.

"Interesting times," committee chairman **Stephen Rosenfeld**, MD, MBA, said at the March 13 meeting. "I thought it was probably worth acknowledging things that are not explicitly on the agenda, but are probably in the background — the delay in implementation of the updated Common Rule. As you know, the interim and final rule effective date is now July, until we hear otherwise. There is the possibility that an NPRM [notice of proposed rulemaking] will delay the implementation further. That kind of colors all of the things we will talk about [at this meeting]."

Sitting at his side was **Jerry Menikoff**, MD, JD, director of the Department of Health and Human Services Office for Human Research Protections (HHS OHRP). "Sometimes things don't work out exactly the way you want them to, but it is what it is," he said.

Most of the requirements of the final rule were to become effective Jan. 19, 2018. However, HHS and a host of other federal agencies issued an 11th-hour "interim final rule" that moved the effective date to July 19, 2018. That six-month delay is likely to extend to a full year because the federal agencies "are developing a notice of proposed rulemaking in order to fully engage regulated entities and the public … until Jan. 21, 2019," the federal notice states.[1]

"The interim final rule is out. It spells out what the government is planning to do in terms of a notice of proposed rulemaking," Menikoff said. "As far as where we are, that is still the government's proposed intention. We certainly recognize the need to act expeditiously. It is very desirable that people get as much lead time as possible in order to plan for whatever the end result will be."

With finalization of the revised Common Rule postponed, the conventional wisdom remains that IRBs should continue preparing to comply with the regulation as they await additional clarification and guidance. SACHRP hammered out some of those documents at the meeting, including a "Points for Consideration" document for exemptions to the new requirement to use a single IRB for multisite studies. *(For more information, see related story, page 57.)*

'Incredibly Irresponsible'

Meanwhile, in comments received on the interim final rule, IRB members and others in in the human research protection community were not reticent in expressing opinions. Some saw the delay as a prudent measure that allowed much needed additional time; others as an unpleasant surprise that effectively penalized those that were ready to comply.

"The release of the interim rule in the final hours before implementation was incredibly irresponsible," commented **Megan Roth**, PhD, director of research and sponsored programs and IRB chair at Abilene Christian University in Texas. "Those who had already implemented are now essentially having to undo all of the changes and preparations that were done, as well as retroactively re-review any studies that have been approved under the 2018 rules."

With some skepticism, Roth cited the government's reasoning in announcing the delay, that "allowing the regulation to become effective while further rulemaking for delay is ongoing would create confusion for, and impose unnecessary burdens on, the regulated community."[1]

> "IT IS VERY DESIRABLE THAT PEOPLE GET AS MUCH LEAD TIME AS POSSIBLE IN ORDER TO PLAN FOR WHATEVER THE END RESULT WILL BE."

On the contrary, Roth argued, "the interim rule announcement in the final hours did effectively this because many institutions had already implemented or were in the final stages of implementation."

The federal notice conceded that there may be some costs incurred by the action, and Roth provided details of same.

"There are extensive costs to this," she wrote. "The man hours (and associated costs) that were required to update documents, update websites, reprogram submission portals, conduct training, announce changes to the institutional employees, etc., were effectively wasted."

Further costs must be incurred to "revert websites back to their previous state, reprogram submission portals, [and] communicate to the institution that we are reverting back to the old rules," Roth noted.

The announcement of the interim rule in the "twilight hours" of implementation created a hardship and caused "significant confusion for IRB reviewers and institutional researchers," she concluded.

Conceding that many institutions desired a delay of the compliance date, "and this was supported across the board," Roth said, "the responsible action would have been to uphold the previous language, which allowed institutions to move forward with implementation at any time while ensuring compliance by July."

Retracting that allowance "has caused significant hardship and cost for institutions around the country. It has also caused significant confusion for the researchers affected," Roth said.

Hurry Up and Wait

In some of the comments reviewed, this confusion translated to both demands for expediency and further delay to get everyone on the same page.

"While we understand the six-month delay allows additional time to issue guidance regarding interpretation and implementation of the more ambiguous aspects of the Revised Common Rule, we respectfully request that the effective date not be further delayed," commented **Helene Lake-Bullock**, PhD, JD, director of research compliance subject rights at the University of Kentucky.

Prior to the "last-minute delay," Bullock and colleagues drafted revised policies, programmed a new version of the electronic submission system, and conducted education on the impending regulatory change.

"If the federal agencies determine additional delay is necessary, we

request delay of the compliance date only," Lake-Bullock stated. "A July 2018 effective date allows prepared institutions to move forward with the new regulations while additional guidance is under development."

Actual application of the rule will provide "real-world" experience, which could inform future guidance on the nuances of implementation, she said.

"After our efforts to alert and prepare our research community, postponing implementation again will be confusing for our researchers and damaging to the credibility of human research protections," she commented.

Indeed, expressions of confusion came from such eminent research institutions as Stanford. A comment from the research office and IRB chairs asked, given the level of uncertainty and limited time, if a second interim final rule be issued. The OHRP notice indicates that the NPRM may further delay implementation of the 2018 Common Rule, but there is little information about whether additional changes could be coming, they said.

"Institutions remain in the same limbo experienced during the year leading up to the Jan. 19, 2018, compliance date," Stanford IRB members commented. "The interim final rule has, unfortunately, provided no additional clarity, tools, guidance, templates, or other useful information to our institution in implementing the final rule. While we are not ungrateful for the extra time, the question remains, 'For what and when do we start preparing?'"

Given this conundrum, Stanford IRB chairs proposed "separating the effective date from the compliance date." They proposed an effective date of Jan. 19, 2019, with a compliance date of Jan. 19, 2020, for the revised Common Rule, and Jan. 19, 2022, for the cooperative research provision.

"This would give OHRP time to prepare and disseminate the promised guidance and templates needed to interpret the rule," they said. "Otherwise, there will be negligible time to prepare to make the required changes, and scarce information on which to create policy. The research community must have certainty upon which to revise its compliance programs."

Time and Clarity

Others also argued in favor of time and clarity, with the IRB chair at the University of Tennessee Health Sciences Center arguing that "we believe that a further delay beyond July 19, 2018, in the effective and compliance dates for the revised Common Rule is absolutely necessary."

Terrence F. Ackerman, PhD, and colleagues cited two reasons for this imperative.

"First, there is a series of issues raised by the new rule that require OHRP to develop clarificatory guidance for use by IRBs," he commented. "Second, there must be ample time allotted for IRBs to utilize the guidance to draft necessary materials prior to the effective and compliance dates for the new rule."

Ackerman said, given the number of issues raised and the potential confusion, the effective date should not be made before OHRP issues guidance or before there is ample time for institutions to revise policies and procedures to reflect the guidance. For the latter, they suggested a minimum of six months to a year after guidance is issued.

As it currently stands, IRBs face a dilemma, he emphasized.

"For instance, when a continuation or revision is submitted, is it expected that we re-review the study and consent form according to the revised regulations, including the additional informed consent elements and new key information summary?" he commented. "If so, this would involve a substantial revision of the consent form for the study, thereby creating much additional work for investigators/research coordinators preparing submissions and additional review responsibilities for IRB staff."

Faced with these complexities, IRBs might choose to use the old regulations for studies approved prior to the effective date of the new regulations, and the new regulations for studies approved on or after the effective date, he said.

"In that event, even more substantial administrative burdens will occur," Ackerman said. "The essential problem is that IRBs will need to operate with 'two sets' of all materials relevant to the oversight of studies."

These sets would include standard operating procedures, electronic submission forms, IRB training, policy and procedure guides, consent forms, and checklists.

"This dual system will engender numerous problems …. and will create human mistakes and confusion," he said, recommending that, with some exceptions, the OHRP adopt the position that on the effective date of the new rule all studies must be reviewed according to the new regulations. ■

REFERENCE

1. HHS, et al. Federal Policy for the Protection of Human Subjects: Delay of the Revisions to the Federal Policy for the Protection of Human Subjects. *Fed Reg* 83 FR 2885: Jan. 22, 2018. Available at: http://bit.ly/2C50tbp.

SACHRP Approves Guidance on Exemptions From Single IRB

Three general areas where multiple IRBs may be warranted

A committee recently approved a "points to consider" document that outlines three general areas where exceptions to single IRB oversight can be an option.

The document was approved at the March 13, 2018, meeting of the Secretary's Advisory Committee on Human Research Protections (SACHRP), which has been hammering out guidance documents on the new Common Rule for the Office of Human Research Protections (OHRP).

"We were asked to provide 'guidance' on what might be appropriate exceptions to requirements for single IRB review," said **Michele Russell-Einhorn**, JD, co-chair of the SACHRP subcommittee that worked on the document. "As the discussion progressed, we decided that having a points-to-consider document seemed to make more sense."

The document has culminated in a series of discussions in subcommittees, as panel members tried to parse out the exemption categories.

"We ended up with three exemptions," she said. "One is relating to vulnerable populations. One relates to the number of sites in the study [five or less], and one relates to situations that are politically or otherwise sensitive."

There was a lot of discussion on all of the options, she said, as the panel wrestled with what a single IRB could provide and what is best handled by a small group of multiple IRBs.

"Why is five sites the magic number?" Russell-Einhorn said, giving examples of the questions raised. "Why vulnerable populations or the needs of special populations? Why are these subject to exceptions when the [single] IRB is supposed to have expertise? Why are political or sensitive situations something that a single IRB couldn't deal with?"

One can argue for and against the exemption categories, but ultimately these three groups represented the variety of concerns that could be best served by conducting research under several IRBs rather than designating one oversight board, she explained.

"I don't think any of these three are perfect," she said. "I think the consensus is that these represent three good 'buckets' of situations that would warrant consideration. Remember, this is all about consideration. It isn't that anybody has to do this and has to have exceptions to single IRB review."

The approved document cited the following example of an exemption that illustrates both a small number of IRBs involved and a special research population:

"Research involving surgical placement of a deep brain stimulator in patients with OCD who are treatment refractory, who are drawn from a single site and evaluated by psychiatry at the site for capacity to consent, treatment refractoriness, and follow-up, with surgery conducted at a different location. Given the different research activities at different sites, each site IRB may be best suited to conduct its own review. In addition, with only two sites, the logistics of organizing a single IRB may be inefficient and unnecessary for participant protection. Exception for the single IRB review requirement would be acceptable in this context."

While there is a place for exceptions to the single IRB requirement, it should be remembered that the original idea of streamlining oversight down to a single panel was to improve the review process and better protect research subjects, said **Stephen Rosenfeld**, MD, MBA, chairman of SACHRP.

"It is counterintuitive for many people why a single IRB would be more protective, but it certainly could be," he said. "It's only when those things fail that you should be considering an [exemption] alternative."

There was a lot of back-and-forth in subcommittee discussions, he added.

"There are always two ways to do this," Rosenfeld noted. "You can beef up your single IRB to make sure it's appropriate, or you can go back to individual IRBs. That choice should really be governed by the concerns that drove the single IRB mandate in the first place. Those are efficiencies and protections."

In the discussion before the vote, board member **Sandra H. Berry**, MA, asked who would request the exemption from single board review and, perhaps more important, who would approve or deny it.

"Who would make the decision specifically about whether the [requested] exemption will be honored, or whether in fact it will

just be a single IRB," she said. "How does this work in practice?"

Russell-Einkorn said, "My understanding is that it is the agency that is funding it that makes the decision. That said, with a document like this out for public consumption, an investigator [could argue a study should be exempted]. They would submit their grant and their rationale to a federal agency, and they would decide if they want to go along with that or not."

She added that previous guidance documents had addressed this point in more detail, and the committee approved a motion to amend the document to reference those for more information.

The decision to go to single IRB review for most research has been welcomed by some and condemned by others. In recently submitted comments on the interim final rule, one IRB member found the devil in the lack of details.

"There are fundamental problems with the implementation of single IRBs [in the rule]," wrote **Bruce Larsen**, co-chair of the Department of Human Services IRB in Utah. "It is a rule without actual procedures for implementation; i.e., a rule that lacks the elements of a rule," he wrote in comments.[1] "It is more like a vision statement that states procedures will be worked out within three years."

Perhaps the SACHRP document and other committee guidance will help rectify this situation, but Larsen argues that problems with the approach run deep.

"It seems to require IRBs to work out joint agreements, but lacks an appeal mechanism when an agreement can't be reached," Larsen commented. "There is no recognition that multiple IRBs may be involved. This rule fails to consider the multiplicity of research that may require researchers to approach multiple IRBs, then wait while the IRBs negotiate new single IRB agreements among themselves." ■

REFERENCE

1. HHS, et al. Federal Policy for the Protection of Human Subjects: Delay of the Revisions to the Federal Policy for the Protection of Human Subjects. *Fed Reg* 83 FR 2885: Jan. 22, 2018. Available at: http://bit.ly/2C50tbp.

Should Research Subjects Be Guaranteed Care if Injured?

At a time when social justice movements are coming to the fore, what if research subjects boycotted trials until they were guaranteed medical care if injured? Similar questions have been raised about research subjects involved in testing drugs that they will not be able to afford when they eventually come to market.

Many in the public may assume subjects would be provided medical care as part of agreeing to participate in a trial, but in most cases, it is proceed at your own risk, says **Carl Elliott**, MD, PhD, a professor in the Center for Bioethics at the University of Minnesota.

"At the heart of the United States medical research enterprise is a tremendous injustice," Elliott wrote in a recent commentary.[1] "Unlike virtually every other country in the developed world, the United States does not guarantee payment for the medical care of subjects injured in research studies."

Despite ethical recommendations from various prestigious groups over the years, the status quo holds. "The situation is unlikely to change unless research subjects exercise the only real power they have: boycotting research studies that do not offer paid medical care for subjects who are injured," he wrote. He agreed to field a few questions on this controversial topic in the following interview with *IRB Advisor*.

IRB Advisor: Is your commentary primarily provocative for the purpose of raising awareness, or do you think a research subject boycott could actually be organized to demand action?

Elliott: I would like to think it could happen and it could make a difference, but in the past things have been stacked heavily against this sort of thing. The odds are pretty long. The only events I can think of when there has been a large public backlash against the research establishment are incidents like Tuskegee. It is just very difficult to find a way for research subjects to develop the kind of solidarity with one another that is required for any kind of group action.

IRB Advisor: You cite the case of a patient finding out, to her dismay, in reading a 22-page informed consent form that she would receive no long-term medical care if injured in the trial.

Elliott: You are just told that. Most people are told that. It's like, "This is the deal you are being offered,

and if you don't like it don't enroll in the trial." I think a lot of people like to think that nothing bad is going to happen to them and they skip right over that part.

IRB Advisor: Can an individual IRB decide it would not approve research unless medical coverage was provided?

Elliott: I was on two IRBs in Canada at McGill University. We usually reviewed pharmaceutical research proposals. If they had that provision in them — essentially telling subjects they are responsible for their own medical care if they are injured in the trial — we would strike it out. We told them "Either you get rid of that, or we are not approving the study." That was standard. When I moved to the University of Minnesota, I just assumed that would be the case here as well. I was simply told, "No, of course we don't include that. It's standard." It was shocking. It's really only shocking to the rest of the world. In America, it's the norm.

IRB Advisor: You cite a 2011 presidential commission and other prestigious academic bodies over the years that have recommended that injured research subjects should not have to bear the cost of their medical care. Why has this not happened?

Elliott: It is simply a matter of power. Somebody will have to pay for it, and nobody is interested in that. The only people who have interest in changing the system are research subjects. Institutions that do research are not interested in something that is going to cost them more money.

IRB Advisor: Perhaps your stance will raise awareness and start a conversation about change.

Elliott: I think if there were a high-profile scandal in which subjects were injured and were forced to pay for their own medical expenses, that could raise awareness. But my sense is that, with most of these cases, it becomes a legal issue and nobody talks to the press about what actually happened. The legal settlement is sealed. Finding out about the cases is very difficult. ■

REFERENCE

1. Elliott, C. Power Concedes Nothing without a Demand: The Case for a Patient Boycott of U.S. Clinical Trials. *IRB Ethics Human Research* 2018;40:2:15-18.

FDA Outlines Position on Stem Cell Research

The FDA outlined its stance on the exploding field of regenerative medicine in a new paper,[1] trying to strike a balance in stem cell research oversight to temper risk without blunting reward.

"The potential benefits to human health have spurred major progress in stem-cell biology over the past several decades," the FDA authors wrote. "At the same time, the administration of such stem cells may be associated with serious adverse events. … It is critical to focus on efforts to facilitate the development of such therapies, rather than propagating products with dubious clinical efficacy and possible risks."

The paper was co-authored by FDA Commissioner Scott Gottlieb, MD, and Peter Marks, MD, PhD, director of the FDA Center for Biologics Evaluation and Research.

"Working within the existing regulatory framework, the FDA will make use of all available regulatory pathways and will adopt the use of some new principles that we believe will make the appropriate premarket evaluation of stem cell-based therapies more efficient," the authors noted. "On a large scale, the FDA will be incorporating some new concepts for how small investigators and firms can seek and meet the approval standard for products through efficient, expedited pathways."

For example, the FDA will assist and encourage individuals or small groups of physicians working in regenerative medicine. This could be followed by the approval of a "biologics license" for these physicians or groups.

"How might this work?" the authors asked. "The investigators who manufacture the product will need to agree on and follow a common manufacturing protocol and develop a common clinical trial protocol. Each site will then produce the product to treat the patients who are enrolled in the clinical trial at its own site. Subsequently, the pooled safety and efficacy data from the various sites that are participating in the trial will be submitted as part of a biologics license application for each."

As part of its efforts to facilitate regenerative research, the FDA is encouraging investigators to reach out to the agency early in the process to open a dialogue before more formal discussions are required for an investigational new drug. ■

REFERENCE

1. Marks P, Gottlieb S. Balancing Safety and Innovation for Cell-Based Regenerative Medicine. *N Engl J Med* 2018;378:954-959 DOI:10.1056/NEJMsr1715626.

IRB ADVISOR

CME/CE INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

1. Read and study the activity, using the provided references for further research.
2. Log on to AHCMedia.com, then select My Account to take a post-test.
3. Pass the online test with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the test, a credit letter will be emailed to you instantly.
5. Twice yearly after the test, your browser will be directed to an activity evaluation form, which must be completed to receive your credit letter.

CME/CE QUESTIONS

1. **The IRB at Wake Forest School of Medicine studied its review process, looking for information about review times. Which of the following was not one of its findings?**

   a. There is variability in how long reviews take, partly due to the particular committee to which they are assigned.
   b. The institution's eight different IRBs vary in review time between 13 and 16 days.
   c. The review process is slower when there is no external sponsor and the principal investigator alone receives the IRB's feedback.
   d. Investigators' responsiveness has greater variability.

2. **In preparing for accreditation and the revised Common Rule, which of the following are important steps for an IRB to take?**

   a. Target inefficient policies and procedures; seek institutional approval of changes; follow accrediting organization's guidance.
   b. Focus on the essential elements for informed consent and replace all board members with more than six years of service.
   c. Start new review subcommittees, ask each board member to memorize a portion of the elements for review, and close the IRB office for one week to complete documentation updates.
   d. All of the above

3. **A comment to HHS on the interim final rule from IRB chairs at Stanford University asked which question?**

   a. Given the confusion, will the single IRB requirement be dropped?
   b. Would it be better to revert back to the original Common Rule?
   c. Will a second interim final rule be issued?
   d. Is the HHS waiting until national elections change the political climate?

4. **SACHRP recently approved a "points to consider" document that outlines five general areas where exceptions to single IRB oversight can be an option.**

   a. True
   b. False