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INSIDE

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AHC Media

Top medical journals propose mandating data sharing

Some concerns, but hailed as 'important step in right direction'

By Gary Evans, Senior Staff Writer

The International Committee of Medical Journal Editors (ICMJE) — which counts several prestigious periodicals among its members — is giving authors an offer they can't refuse: Agree to share your clinical trial data with subsequent researchers or your manuscript will not be published. Though transparency has an innate appeal and the stated goal is a noble one —- "to improve the benefit to society from the efforts of patients who volunteer to participate in clinical trials" — there is a little of the devil in the proverbial details.

"Trial participants generously and selflessly volunteer their efforts, and put themselves at risk in clinical trials on the promise that the knowledge gained will be used to help others," says **Darren B. Taichman**, MD, PhD, ICMJE secretary and executive deputy editor of the *Annals of Internal Medicine*. "Making sure that the data generated are made available to ensure the most is learned from them is part of keeping that promise."

> "MAKING SURE THAT THE DATA GENERATED ARE MADE AVAILABLE TO ENSURE THE MOST IS LEARNED FROM THEM IS PART OF KEEPING THAT PROMISE."

The ICMJE proposes that as a condition of consideration for publication of clinical trial studies in its member journals — which also include the *New England Journal of Medicine* and the *Journal of the American Medical Association* — authors would have to agree to share "deidentified individual-patient data (IPD) underlying the results presented in the article (including tables, figures, and appendices or supplementary material)

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no later than 6 months after publication." The ICMJE proposal was outlined in an editorial[1] published on Jan 26, 2016, in the three aforementioned journals and 10 others. "Sharing data should increase confidence and trust in the conclusions drawn from clinical trials, enable independent confirmation of results, and foster the development and testing of new hypotheses," the committee states.

The "results" to be shared are defined as the IPD required to reproduce the article's findings, including necessary metadata. The proposal is open for comments through April 18, 2016, at http://www.icmje.org/.

Those using data collected by others should seek collaboration with those who collected the data. "However, because collaboration will not always be possible, practical, or desired, an alternative means of providing appropriate credit needs to be developed and recognized in the academic community," the ICMJE states. "We welcome ideas about how to provide such credit."

Sponsors of clinical trials are in a position to support and ensure adherence to data sharing obligations, the proposal states. If data sharing agreements are not met, the editors may choose to request additional information; publish an expression of concern; notify the sponsors, funders, or institutions; or in certain cases, to retract the publication, the ICMJE states. "In the rare situation in which compliance with these requirements is impossible, editors may consider authors' requests for exceptions. If an exception is made, the reason(s) must be explained in the publication."

Informed consent for future use

The ICMJE anticipates that the new data-sharing requirement will go into effect for clinical trials that begin to enroll participants beginning one year after the proposed policy is finalized. If adopted as proposed, IRBs would need to determine that when researchers get consent from subjects, they are acknowledging that their data could be used by future researchers.

"Planning to responsibly share clinical trial data must assure the protection of trial participants' rights, an area where the work of IRBs is essential," Taichman says. "For example, IRBs will need to ensure that the consent process for trial enrollment includes appropriate information regarding the plan to and conditions under which data will be shared."

Because informed consent regarding the sharing of de-identified participant-level data is not already in place for many currently ongoing trials, the proposed requirements for data sharing would apply only to those studies that start enrolling patients after the one-year grace period, he emphasized in comments to *IRB Advisor*.

"We do that often now — we ask for permission [for future use]," says **Susan Rose**, PhD, executive director of the Office for the Protection of Research Subjects at the University of Southern California, and member of the *IRB Advisor* editorial board. "It would become a mandatory question, but it shouldn't be a big deal to make that happen."

The ICMJE notes that by taking this action, they "join a growing

consensus, [as] many funders around the world — foundations, government agencies, and industry — now mandate data sharing."

However, details that have to be resolved include standardization of the definition of "clinical trial" among the various entities that oversee the research, Rose says. For example, the National Institutes of Health (NIH) definition of a clinical trial adopted in October 2014 is: "A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes."

In the editorial proposing the new sharing policy, the ICMJE defined a clinical trial as "any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome."

"The NIH definition of clinical trials includes behavioral outcomes and this group says a health-related intervention and a health outcome," Rose says. "So to me that looks like a different definition of clinical trials."

In addition, the ICMJE requires studies to register at ClinicalTrials.gov, but the data fields are not particularly compatible with social and clinical behavioral research, she notes. Thus, a "translator" is needed describe the research in terms acceptable to the NIH website.

"Say [in a study] people are doing exercise to lose weight and to see if that makes them less hungry," Rose says. "They're not taking any drug, using a device or a biologic. If the study [researchers] want to get published in one of these [ICMJE] journals they have to register on ClinicalTrials.gov. But the data fields are not [compatible]. It would be really nice if ClinicalTrials.gov were more user-friendly to social and behavioral studies. These different definitions are a problem because we don't know how to describe a health study with a behavioral come. The definitions have to be the same and they need to be agreed upon."

> "PLANNING TO RESPONSIBLY SHARE CLINICAL TRIAL DATA MUST ASSURE THE PROTECTION OF TRIAL PARTICIPANTS' RIGHTS, AN AREA WHERE THE WORK OF IRBS IS ESSENTIAL."

Though specifics and challenges remain to be worked out, the ICMJE proposal is "an extremely important step in the right direction," says **Robert Klitzman**, MD, professor of psychiatry and director of the Bioethics Master's Program at Columbia University in New York City.

Great promise, a few caveats

"Unfortunately, evidence indicates that pharmaceutical companies have repressed data from trials that do not support their products," Klitzman says.[2] "The number of researchers who have fabricated results, and later had to retract their published papers, is also increasing. Hence, this announcement by ICMJE is very promising. Certainly, several details will have to be worked out — such as when, if ever, exceptions might be made. Moreover, not all journals are members of ICMJE — though most of the world's top-tier journals are. Still, drug companies may decide to publish results in second-tier, non-member journals, and then distribute these articles to physicians who may not know the difference in policies."

Klitzman called for more transparency in clinical trials and IRB oversight in his recently published book, *The Ethics Police?*. He also reported that researchers were frustrated by chronic delays in the approval process at present. *(See the February 2016 issue of* IRB Advisor.*)*

"Critics may argue that publication of results will be delayed [by the ICMJE requirements], but researchers can submit the data six months after publication, and presumably they will already have the data in a usable form," he says. "ICMJE's announcement did not address how to respond to potential arguments about the data being proprietary. This, too, will need to be decided. However, on balance, I think that this effort is vital and well worth considering."

The one-year grace period should address issues that may delay research publication, Taichman says, but concedes that "new undertakings often require extra time" at the onset.

"But we cannot let the extra effort involved stop us from ensuring that we honor the contributions of trial participants by making the most of their data," Taichman says. "And, there are benefits for researchers. Assuring trial participants that the most will be learned from their volunteer efforts should help

encourage others to participate in trials."

The ICMJE proposal would require authors to include a plan for data sharing as a component of clinical trial registration. The plan must include where the researchers will house the data and — if not in a public repository — the mechanism by which they will provide access. The committee references data-sharing plan elements outlined in a 2015 Institute of Medicine Report for additional details.[3] ClinicalTrials.gov has also added a data-sharing component to its registration platform, the editors note.

"We encourage other trial registries to similarly incorporate mechanisms for the registration of data-sharing plans," the ICMJE states. "[Researchers] who want to publish in ICMJE member journals (or nonmember journals that choose to follow these recommendations) should choose a registry that includes a data-sharing plan element as a specified registry item or allows for its entry as a free-text statement in a miscellaneous registry field. Authors may choose to share the deidentified IPD underlying the results presented in the article under less restrictive, but not more restrictive, conditions than were indicated in the registered data sharing plan."

Just as the confidentiality of trial participants must be protected through the deidentification of IPD, the rights of investigators and trial sponsors must also be accommodated. In that regard, the ICMJE proposes the following safeguards:

• ICMJE editors will not consider the deposition of data in a registry to constitute prior publication.

• Authors of secondary analyses using these shared data must attest that their use was in accordance with the terms (if any) agreed to upon their receipt. They must reference the source of the data using a unique identifier of a clinical trial's data set to provide appropriate credit to those who generated it and allow searching for the studies it has supported.

• Authors of secondary analyses must explain completely how theirs differ from previous analyses. In addition, those who generate and then share clinical trial data sets deserve substantial credit for their efforts.

Though signing off on the deal as a member of the ICMJE, the *NEJM* published an editorial that conceded that there are concerns about "research parasites" who had nothing to do with the design and execution of the study but use another group's data for their own ends, "possibly stealing from the research productivity planned by the data gatherers, or even [using] the data to try to disprove what the original investigators had posited."[4]

While noting such concerns, the editorial cites a study[5] in the same issue by investigators who "worked symbiotically, rather than parasitically, with the investigators holding the data, moving the field forward in a way that neither group could have done on its own."

The new authors hypothesized that certain colon cancers might create more aggressive tumors at greater risk of relapse and might be more likely to benefit from adjuvant treatment. Needing a large group of archived patient specimens and tissues, they collaborated with a research consortium funded by the National Cancer Institute. They found that 4% of patients had such tumors, which predicted poorer prognosis and greater benefit from of adjuvant chemotherapy. That generated a new hypothesis that, if proven, means that the vast majority of colon cancer patients can be reassured that "avoiding the unpleasantness of standard adjuvant therapy is unlikely to affect their outcome adversely," the editorial authors noted. "No one expected that."

Using the study as a case in point, the authors outlined the following key criteria for data sharing done right:

• Start with a novel idea, one that is not an obvious extension of the reported work.

• Identify potential collaborators whose collected data may be useful in assessing the hypothesis and propose a collaboration.

• Work together to test the new hypothesis.

• Report the new findings with relevant coauthorship to acknowledge both the group that proposed the new idea and the investigative group that accrued the data that allowed it to be tested.

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A clinical trial disaster in France results in injuries and death

Cause of problem is currently unknown

One man died and five others were seriously injured in January 2016, after they participated in a Phase I clinical trial in France. The trial assessed healthy individuals' responses to an FAAH enzyme inhibitor drug for treating mood and anxiety disorders. The man who died had been pronounced brain dead, according to Bial, the Portugal-based pharmaceutical company conducting the research.

The clinical trial began in June 2015 and through January had enrolled 116 volunteers. Eighty-four volunteers were administered the experimental compound. There were no severe or moderate adverse events reported until Jan. 11, 2016. One of the study volunteers died on Jan. 17, according to a Bial news release.

Bial stopped administering the study drug immediately, and as of late January, one of the six volunteers had returned home. At press time, three others remained hospitalized with physicians predicting full recovery, according to Bial.

Bial is working with French health officials to identify the cause of the problem. The company reports that the pre-clinical studies suggested the drug was safe for humans and that the study was approved by French regulatory authorities and the French Ethics Committee.

This was the second time in a decade in which healthy Phase I volunteers experienced serious reactions to a trial drug: Great Britain also had a Phase I drug trial disaster in March 2006 when an immunomodulatory drug called TGN1412 sent six healthy volunteers into intensive care, where they received organ support. No one died, but one of the sickened volunteers remained hospitalized for six months and had multiple organ failure. *(See story about British trial disaster in the May 2006 issue of* IRB Advisor*.)*

IRB Advisor will look at the investigation of the French clinical trial disaster, as well as how IRBs and the U.S. research community can prevent such clinical trial disasters in the April 2016 issue. ■

Research communities work creatively to improve minority recruitment in CTs

Obstacles are multi-layered

In the three years since Congress passed the Food and Drug Administration (FDA) Safety and Innovation Act of 2012 with its provision encouraging the inclusion of minorities in clinical trials, IRBs and research sites have continued to struggle with the need to diversify study participant pools.

The human research protection community is working harder now than ever to include historically underrepresented populations in clinical trials. Efforts to improve recruitment of minorities and women in clinical trials were boosted by requirements of inclusion spelled out in the National Institutes of Health Revitalization Act of 1993.

But there have been multiple barriers to success, including scars from past research wrongs visited on particular racial and ethnic groups, as well as potential participants' lack of research knowledge and health literacy.

Clinical trial recruitment is time-consuming and costly — especially when research organizations focus on recruiting in underrepresented populations. "We don't have the resources to do this correctly," says **Amelie G. Ramirez**, DrPH, MPH, professor and interim chair of the department of epidemiology and biostatistics, director of the Institute for Health Promotion Research, and associate director for population sciences for the CTRC Cancer Center at the University of Texas Health Sciences Center in San Antonio.

"Reaching out to our minority audiences requires increased information about clinical trials and how they can benefit from them, and it also requires us to be language-specific and to reach members of a population where they are," Ramirez adds.

For instance, Ramirez has found that many people from minority communities are suspicious of clinical trials and are uninformed about how research can improve life for everyone.

"I deal with the Hispanic population," Ramirez says. "And what I hear most from people is, 'I don't want to be treated like a guinea pig.'"

Research programs want people to know how their involvement in clinical trials can help people in the future, but this message needs to be clarified for many people, including those in minority communities, she adds.

Additional obstacles for many Hispanic cancer patients has been that they often come into treatment in later stages of their disease — sometimes too late for inclusion in a clinical trial, or their disease is an orphan cancer, Ramirez says.

"When patients come in so late in the disease [process], it's really difficult and we don't have any options for them," she explains. "Also, we have in the Hispanic population a lot of orphan cancers, and there is no treatment, much less clinical trials."

Recruiting study participants is particularly challenging when the goal is to reach a representative proportion of racial and ethnic minorities, says **S. Azor Hui**, PhD, MSPH, research scientist with Public Health Management Corp. in Philadelphia.

Hui conducts cancer prevention research, including a recent study that looked at a new way to increase participation rates in cancer prevention trials. Because racial and ethnic minorities are underrepresented in cancer prevention trials and novel recruitment strategies are necessary, the study looked at whether at-risk individuals are interested in a new way of identifying higher cancer-risk individuals and recruiting them into cancer clinical prevention trials.[1]

"In my study about the interest and willingness to engage in this new recruitment method, I had to restrict the number of white participants because we wanted to oversample racial and ethnic minority participants," Hui says. *(See story on strategies for recruiting minority trial participants, page 31.)*

Clinical trial work is an extremely important tool that is necessary to advance scientific discovery, but it needs to be as widely available as possible to be effective, says **Sandra E. Brooks**, MD, MBA, chief medical officer of CompleteCare Health Network in Bridgeton, NJ.

"WE NEED TO DEVELOP A LEVEL OF ENGAGEMENT WITH COMMUNITIES THAT MIGHT BE AT RISK FOR A CERTAIN CONDITION, AND DEVELOP TRUST OVERALL FROM A CULTURAL AND HEALTH LITERACY PERSPECTIVE."

In cancer research, there have been some success stories involving minority recruitment, particularly with breast cancer trials that have used targeted strategies to recruit underrepresented minority women, Brooks says.

"They developed a special outreach effort, identifying multiple sites to recruit patients, provided tools for sites to use and staff to help determine eligibility," Brooks explains.

Targeted outreach strategies work, but they take time and resources. In some minority communities, these strategies must be preceded by trust-building efforts, she says.

"We need to develop a level of engagement with communities that might be at risk for a certain condition, and develop trust overall from a cultural and health literacy perspective," Brooks says. "Within that context, we can talk about clinical trial recruitment."

For example, one research organization in Louisiana tested a variety of minority recruitment strategies, including working with community groups, forming a community advisory board, partnering with different churches, and having experts talk with the community about how the disease being studied was affecting their community, she says.

These efforts proved to be successful, Brooks adds.

While these types of minority recruitment efforts can work well, they require funding and require a high level of institutional commitment, she notes.

"Some of our challenges are having the infrastructure to open up enough trials for patients," Brooks adds. "Sites tend to have higher rates of enrollment when they have a higher level of infrastructure or are dedicated to physician and data management support."

In research about enrollment in gynecological cancer trials, Brooks and co-investigators have found that non-white patients and patients of African-American physicians were more likely to enroll in trials.[2]

"Our African-American doctors enrolled patients at very high rates irrespective of the patient's race," Brooks says. "While our study was not designed to explore the reasons for those findings, we determined that the perception of the patient's

interaction with the healthcare team was important."

Trust mattered: "If patients felt that their physician wanted them to go on the trial, then they were more likely to go on the trial," Brooks says. "If they felt pressure to enroll in a trial, they were less likely to go on the trial."

Brooks also was involved in a clinical research paper that concluded that U.S. research organizations will need to engage in specialized training and adopt effective and efficient recruitment strategies to increase minority enrollment and maintain world leadership in cancer care innovation and delivery.[3]

"The goal is to improve participant accrual overall, but specifically to support organizations that that are employing successful strategies in settings with high percentages of minority patients," Brooks says. "We also need a diverse group of physicians who are very dedicated to talking with patients about clinical trials and doing what's required to have a clinical trial program."

The FDA has heightened focus on minority participation in clinical trials in recent years as a result of the 2012 Safety and Innovation Act, says **Jonca Bull**, MD, assistant commissioner for minority health at the FDA.

Section 907 of the 2012 FDA law, required the FDA to develop a report on the extent that subgroups of women and minorities are included in applications for biologics and devices. Section 1138 requires the FDA to ensure adequate information about pharmaceuticals is available for all populations, but especially for underrepresented subpopulations and racial subgroups.

"Based on findings of that report, the FDA developed an action plan addressing whatever gaps or deficiencies are identified," Bull says. "Also, the FDA was asked to look at the existing framework and guidance and their adequacy to helping provide broad, meaningful participation of groups that are critical for a full and complete and thoughtful analysis of medical and safety efficacy."

The FDA's report and resulting action plan identified the following three priority areas:

1. Improve the quality of data submitted to the FDA. "The report found that there was a lot of inconsistency in how commercial sponsors submitted data from populations in the trials," Bull explains. "For example, there might be differences in prevalence of disease in particular subgroups or differences in the course of a disease."

The goal of this priority area is to give clinicians the information they need to make decisions that affect all patients' health, Bull adds.

2. Raise awareness of clinical trials to increase participation. Making changes, including raising awareness of clinical trials, will require a sustained engagement by the research industry in working with patients, she notes.

3. Increase transparency around the data. The FDA publishes a consumer update that provides subgroup information in an accessible format, Bull says.

"Another issue that was deliverable under the law is an agreement from the FDA to convene meetings about patient-focused drug development," Bull says. "The FDA has agreed to do a minimum of 20 of these meetings across diseases."

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Strategies for improving study recruitment of minorities

IRBs have a big role to play

Investigators and IRBs are finding a variety of ways to increase minority representation in studies and clinical trials, including policies mandating such recruitment.

One academic center IRB requires studies to reflect the community of patients they serve, says **Jonca Bull**, MD, assistant commissioner for minority health at the FDA.

"The IRB was firm that studies have a representative population for

that particular community," Bull says.

One way to interpret an IRB's mission to ensure human subject safety and protection is to make certain research studies have enrolled people who represent the groups affected by the condition or disease. Studies must have sufficient information about all of the populations affected by a disease in order to accurately characterize benefits and risk, Bull says.

Another strategy for improving minority recruitment in trials is for research organizations and IRBs to make certain recruitment strategies are outlined in grant and IRB applications, says **Sandra E. Brooks**, MD, MBA, chief medical officer of CompleteCare Health Network in Bridgeton, NJ. Brooks and co-investigators have studied barriers to clinical trial enrollment among minority populations and the general population.

"In our study, clinical trials are available for just 38% of patients," Brooks says. "Physician specialty, ethnicity, practice type — hospital-based or academic — and the presence of data management were associated with availability of trials."

In Brooks' research, investigators found that patients were more likely to enroll if they felt the trial would help them and if they felt their doctor wanted them to go on the trial or if they were concerned they might not receive the best care if they didn't go on the trial.

"They were less likely to enroll if they felt pressure to enroll or if they were providing nonpaid care to someone, which speaks to patients' other commitments," Brooks notes.

In a recent paper, Brooks and other researchers outlined some of the strategies for increasing minority enrollment in clinical trials, including the following[1]:

- Researchers can use novel trial designs that naturally create subgroups from larger disease populations and that include diverse subgroups in the trial design phase.
- Investigators must be culturally sensitive and aware of the effect of appropriate communication and patient trust and be able to encourage clinical trial participation among diverse groups of patients.
- Advertising and research enrollment information should be more widespread and include collaboration with community groups, survivor advocacy groups, churches, and other local institutions.[1]

> "I THINK THE IMPORTANCE OF MINORITY RECRUITMENT IS GAINING MORE VISIBILITY, AND THE NATIONAL CANCER INSTITUTE HAS SUPPORTED THESE EFFORTS FOR SOME TIME, BUT THERE'S STILL A LONG WAY TO GO."

Not all studies are appropriate for focused minority recruitment, but with diseases such as breast cancer that affect subpopulations differently, it's important to have research participants from those subpopulations, Brooks explains.

"As part of the IRB review, there could be a way to address how recruitment of subpopulations is approached," she adds. "I think the importance of minority recruitment is gaining more visibility, and the National Cancer Institute has supported these efforts for some time, but there's still a long way to go."

When researchers make it a priority to improve minority recruitment, they might consider novel strategies instead of relying on traditional advertising and outreach.

For instance, researchers conducting a cancer prevention trial could work with employee wellness programs to reach a demographically representative population of at-risk people, suggests **S. Azor Hui**, PhD, MSPH, research scientist with Public Health Management Corp. in Philadelphia.

"In the past few decades, employee wellness programs have become more and more popular," Hui says.

Such programs typically have online health risk assessment (HRA), including questions about cancer risk. So this information can be used to identify people who could be enrolled in cancer prevention trials, she explains.

"So my proof of concept study proposed using online HRA to link these individuals into cancer prevention trials through an electronic health information transfer system," Hui says. "If someone says they're interested in participating in a cancer prevention trial that might benefit them personally, they can click a link that says, 'I release my health risk assessment responses.'"

The information then goes to an external, secure database where a specialist can view the individual's profile and see whether they could participate in a trial. If there is a trial

that could fit, the specialist could proactively call the at-risk individual to discuss in more detail about what's involved in participating in the trial, Hui adds.

This type of recruitment outreach has the potential reach to a proportionate number of racial and ethnic minorities, as well as a general population. This would be a great improvement over current cancer prevention trial enrollment, which is 80% to 90% white or Asians and vastly underrepresent African-Americans and Latinos, Hui explains.

"Using a workforce population can produce more minorities for studies," she adds.

All strategies for improving minority recruitment in research should begin with better public education about clinical trials, suggests **Amelie G. Ramirez**, DrPH, MPH, professor and interim chair for the department of epidemiology and biostatistics, director of the Institute for Health Promotion Research, and associate director for population sciences for the CTRC Cancer Center at the University of Texas Health Sciences Center in San Antonio.

"When patients come into a clinic and are told they can participate in a clinical trial, it can't be the first time they hear of it," Ramirez says.

"We have found that it helps to use outreach community health workers, particularly for Phase III trials where you're trying to recruit large groups of participants," she adds.

Outreach community health workers explain research to patients and provide information about particular studies.

Education also is needed for physicians, who sometimes will not offer trials to minority populations based on a belief that the studies are too complicated or because the patients might need transportation or have insurance problems that could prevent them from making appointments, Ramirez says.

"We need to help clinicians have an appropriate resource team behind them so that everyone who is eligible is offered to participate," she adds.

Another strategy involves a computer-based program for educating people about clinical trials.

"Right now, we're testing a methodology where we're informing patients before they're offered a clinical trial what it's about," Ramirez says. "We show vignettes of people of different ethnic backgrounds who went through these stages of participation, and at the end the person has a more personalized approach to clinical trials."

Although research is ongoing, preliminary data show the need for additional outreach and educational resources to sustain recruitment of minority populations, Ramirez says.

"We also need trials for some of the orphan cancers that are not as prevalent in other population groups," she adds.

For example, Hispanics have lower rates of breast cancer and prostate cancer than other populations, but Hispanic children have higher rates of leukemia and there are orphan cancers affecting the population. Overall cancer rate for Hispanics is expected to increase by nearly 200% by 2050, she says.

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This IRB "party" gets the job done

It helps to work with fellowship office

There might be a simple solution to IRB workflow issues that stem from graduate student research cycles: A party.

At least, this strategy worked for the Yale University IRB in New Haven, CT, which created "approval parties" to handle the influx of fellowship students' IRB applications each spring.

"We had a lot of fellowship applications come in at the same time and going out at the same time," says **Brandy Lagner**, CIP, senior regulatory analyst, research administration, RESHRP human subjects committee at Yale.

It was challenging for the IRB office to handle these applications while keeping up with the usual workload, so they decided to ask IRB committee members to handle student applications, which mostly resulted in expedited or exempt determinations, she adds.

"The root of the problem was that there are a lot of fellowships awarded in the spring to students, who, mostly, want to do their research immediately, in the summer," says **Stephen Latham**, JD, PhD, chair of the human subjects committee at Yale

University.

Having projects that were time-sensitive, students needed a quick decision from the IRB. This placed considerable pressure on the IRB office and led to workflow bottlenecks, Latham says.

"Everyone on the human subjects committee was aware that we were having problems because of the fellowship study load," Latham adds. "And I had a sense from discussions at committee meetings that most of the committee members would like to help out."

The IRB decided to improve the issue through a two-pronged solution: First, it worked with the university's fellowship office, and, secondly, it asked for committee volunteers to handle some of the expedited/exempt determinations at an "approval party."[1]

The process improvement project also benefited from the committee having a fellowship office representative on the board, Latham notes.

Previously, the fellowship office was unaware of the burden their decision-making timetable placed on the IRB office, he explains.

Once the fellowship office staff learned of how difficult it was for the IRB office to handle all of those additional protocols, they wanted to help out, Latham adds.

"We ended up working closely with the fellowship office, which staggered their review times for rewards," says **Carrie McDaniel**, CIP, senior regulatory analyst, human subjects committee, Yale University.

"Everything in the past was in April, and now they started having fellowship deadlines and awards earlier, from as early as late December and early January through April," McDaniel explains.

The goal was to prevent the springtime bottleneck. Also, the fellowship office's online application form now includes three questions related to human subjects research. A "yes" answer to any of these questions alerts the student that an IRB review is required, and the application links students to the IRB website for submission information.[1]

"We work closely with the fellowship office to find out how many students we can expect," McDaniel says.

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This change reduced the workload to a more manageable level over a four-month period. The second change of asking for IRB members to help with handling the fellowship applications reduced the IRB office's workload even more.

When there are fellowship projects coming in, Latham announces that it is fellowship season and volunteers are needed for reviews.

"It doesn't take many of these to significantly reduce the staff's load," Latham notes. "If we had five people together and each looked at three protocols, that takes away one-third of one month's load from the IRB staff, and it means they can handle the rest."

The approval parties, which might have five attendees and feature breakfast or lunch, serve as an overflow mechanism for the expanded demand, Latham adds.

The parties involve a small group of IRB members sitting around a table, looking at exemption requests and expedited review forms to make sure the right boxes are checked, the right information is gathered, and that principal investigators have answered all questions, Latham explains.

For example, a project might appear to be exempt, but if the investigator did not say that people under age 18 are excluded, then someone would have to call the investigator and ask this question, Latham says.

"When the principal investigator says, 'Right,' we take that box and check it," he explains. "This is easy to do in a group while you're sipping coffee and eating a bagel."

Often, the reviewing committee members will get in touch with student investigators in advance of the meeting, but there have been times when the IRB group has called investigators during the approval party, he adds.

The atmosphere at the approval parties is relaxed, and members find it to be a relaxing and positive experience, Lagner says.

From the student investigators' perspective, it has been a great change. They receive their approvals quickly, enabling them to begin their projects without frustrating delays, McDaniel notes. ■

Should infection control research be IRB exempt?

Groups warn that Common Rule changes could undermine patient safety

The Association for Professionals in Infection Control and Epidemiology (APIC) warns that proposed revisions to the Federal Policy for the Protection of Human Subjects — the "Common Rule" — may have unintended consequences if infection prevention research is not excluded from approval by IRBs.

Commenting on the recently issued Notice of Proposed Rulemaking (NPRM),[1] APIC said infection control research conducted in quality improvement efforts should not require IRB approval.

"Our members have concerns related to activities that would meet the quality improvement (QI) exclusions," APIC stated. "We believe that it is equally and in some cases more important to study the effectiveness (outcome measure) of a practice as it is to increase use of the practice (process measure). It is possible that increasing the use of a process may not provide benefit to a patient population or improve the outcome."

For example, as currently written, evaluation of staff training to improve the use of gloves to prevent transmission of microorganisms would be excluded from the IRB process, but "evaluating the impact of the use of gloves on decreasing transmission of microorganisms would require IRB approval — despite the fact that the use of gloves is a well-established best practice," APIC says in the comment letter. "In order for the intervention to be successful, investigators must know not only how to best educate providers on the process, but also be able to evaluate the outcome of the intervention, in this case the reduction in transmission."

Many infection preventionists participate in state or regional QI collaboratives that measure the outcome of individual or bundled interventions. These QI collaboratives often have a rapid start-up and implementation phase, frequently with timelines mandated by the Centers for Medicare & Medicaid Services, APIC continued.

"Requiring such projects to be subject to IRB approval could act as a disincentive for participation in many organizations due to the added paperwork and burden," APIC warns. "To support the work we perform on a daily basis, our members recommend that both QI processes and outcomes are included in the Common Rule excluded activities."

In addition, APIC expressed concern about the unintended consequences when the regulations are put into place.

"The NPRM notes that public health activities that would not fall under the exemption act include exploratory studies to better understand risk factors," APIC says.

Hospitals and other health settings are required by regulation to report healthcare-associated infections and certain process measures, such as healthcare personnel influenza immunization, to the CDC. The data are examined in efforts to better stratify risks and identify opportunities for improving the health of the population in the future. Furthermore, with new and/or rapidly emerging infectious diseases, the risks may be unknown, APIC stated.

"To require IRB approval before the public health authority can collect data on risk factors will unnecessarily delay detection of those risks," APIC said in the comments. "Not exempting these activities could have a profound unintentional impact not only on public health's ability to perform its duties, but also its ability to halt ongoing transmission of an infectious agent. As pointed out in the NPRM, the line between public health surveillance and epidemiologic research is difficult to establish. We recommend further defining the difference between the two activities, specifically under what purpose or context the activities would be excluded from the Common Rule."

REFERENCE

1. Federal policy for the protection of human subjects; proposed rules. Fed Reg 2015;80(173):53,933-54061. ■

COMING IN FUTURE MONTHS

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CME/CE QUESTIONS

1. An editorial citing key criteria for research data-sharing recommended which of the following?

A. Start with a novel idea
B. Identify potential collaborators
C. Work together to test the new hypothesis
D. All of the above

2. The FDA Safety and Innovation Act of 2012 section 907 requires which of the following?

A. The FDA must require all clinical trial sites to enroll at least 40% racial and ethnic minorities, unless an exception has been approved.
B. The FDA must develop a report on the extent that subgroups of women and minorities are included in applications for biologics and devices.
C. The FDA must monitor clinical trial sites to assess whether their enrollment of minorities is acceptable.
D. All of the above

3. Which of the following is not a strategy for improving clinical trial enrollment for racial and ethnic minorities?

A. Researchers can use novel trial designs that naturally create subgroups from larger disease populations and that include diverse subgroups in the trial design phase.
B. Investigators must be culturally sensitive and aware of the effect of appropriate communication and patient trust and be able to encourage clinical trial participation among diverse groups of patients.
C. IRBs can monitor enrollment and intervene when it appears a clinical trial site is underrepresenting racial and ethnic minorities in recruitment.
D. Advertising and research enrollment information should be more widespread and include collaboration with community groups, survivor advocacy groups, churches, and other local institutions.

4. An infection control group expressed concern about the unintended consequences of the revised Common Rule as proposed, including the ability to halt ongoing transmission of an infectious agent.

A. True
B. False