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IN THIS ISSUE

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Balancing act: Reducing regulatory burdens without increasing risks

"Unchecking the box" works for one site

It might seem too daring to make changes to human subjects oversight programs by easing ethics review procedures. But several research organizations have found that some measured changes can help reduce investigators' regulatory burden without increasing risk to subjects.

For instance, one program has expanded the number of studies that qualify for exemptions and is working on a project to give principal investigators (PIs) more flexibility in making minor modifications to projects without seeking IRB approval.

Another has reduced its IRB review application form from 25 pages to four. And still another institution has tackled the issue of IRB "mission creep."

That's not to say the changes were made easily. In each case, research officials worked carefully to identify areas that could be changed without impacting the protection of human subjects.

They started with goals of reducing regulatory burden through practical changes and greater efficiency.

For example, the Ann Arbor, MI-based University of Michigan's research office began this project with the goal of developing projects that will reduce regulatory burden while requiring minimal policy changes, says **Judith Birk**, JD, regulatory affairs associate in the office of the vice president for research at the University of Michigan.

The institution has included in policies and procedures its process for making changes. These involve demonstration projects of nonfederally-funded studies and exclude research regulated by the Food & Drug Administration (FDA).

"We put this in our standard operating procedures (SOPs)," Birk says. "We have a page of guidance on each project, and then we have a separate workflow diagram and top level policies that are specific to our institution."

An audit of the demonstration projects showed that PIs and the IRB stayed within the parameters of the project, she adds.

Currently federal regulations require annual review even when these

do not provide additional protection to human subjects.

"We developed two projects," Birk says. "One was to move some annual reviews into an exemption category, and the other was to move to a two-year continuing research approval, depending on study characteristics."

For example, there are projects that had full oversight at the beginning and have now gone through their life cycles, and the only remaining activity is analysis of identifiable data, Birk explains.

"We can move those projects into the exemption category, and they don't have to come back to the IRB for an annual review," Birk says.

Define boundaries, ensure transparency

At the University of Texas Health Science Center in Houston, TX, the goal to make changes was prompted by concern over IRB mission creep, says **Peter Davies**, MD, PhD, executive vice president for research at the University of Texas Health Science Center. The University of Texas, which includes more than a dozen academic and health-related campuses, has a task force reviewing the missions and situations with IRBs.

"We were also interested in obtaining cooperation among our campuses, coming from our involvement in the clinical and translational science awards (CTSA) movement, Davies says.

"CTSAs have an emphasis on lowering barriers to research, and one barrier involves IRB issues," he adds. "Overall, our concern is on the expanding pressures on all the participants and investigators to meet increasingly complex regulatory requirements."

The task force was charged with a broad mandate to review the situation and identify areas in which there were opportunities to fix problems and make recommendations.

The result was an effort to define research boundaries, ensure transparency, provide pre-review to address scientific issues, and take practical measures like eliminating redundancy in IRB reviews, and build a culture of trust in research ethics.

"It took over a year and a series of meetings with representatives from many campuses," Davies says. "We heard from experts in the field of human subjects research; we did teleconferences and met with consultants."

After hearing what other universities were doing about this issue and hearing the university's own problems described by campus representatives, the task force reached several conclusions.

"The bottom line is we first of all felt that a great deal of effort was being expended by institutions to provide appropriate levels of protection to participants of research," Davies says. "The system was working well, but was under a

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lot of strain."

The task force came up with eight different classes of recommendations. **(See story about University of Texas' solutions, p. 28.)**

The goal at one small institution was more modest, but equally important to its human subjects research program. The Southern College of Optometry in Memphis, TN, expected faculty members to participate in research, but very little actually was taking place.

"Not a lot of research had been done in the last couple of years," says **Patricia M. Cisarik**, OD, PhD, associate professor and IRB chair.

One reason for this was that the IRB review process seemed too daunting to many of the professors, she notes.

For instance, although many of the studies qualify for expedited review, the IRB review application was 25 pages long.

"I couldn't see our people being thrilled about filling out a 25-page document so I streamlined it to four pages," Cisarik says. "Most research we do here does not require full IRB review and doesn't have great morbidity and mortality associated with it."

Rather than make researchers wade through pages of questions regarding special populations who rarely, if ever, are seen by the college's clinicians, Cisarik removed these pages, leaving them accessible through an online link.

So if an investigator does have study participants who would qualify, he or she can easily obtain the extra pages to complete. **(See story about other changes to make research reviews simpler, p. 29.)**

The University of Michigan's research office has also made it possible for some investigators of non-federally-funded projects involving identifiable datasets to obtain an initial review exemption, Birk says.

Previously, the exemption was made only for dataset studies involving non-identifiable data, say Birk and **Jan Hewett**, BSN, JD, director of the University of Michigan Medical School IRB.

"The medical school side has not initiated this exemption yet because we have to worry about privacy board review," Hewett adds. "The privacy board sees all of the studies, whether or not they're federally-funded, so this exemption mostly was done on the behavioral health science side."

The University of Michigan also changed the continuing review cycle for some research projects. The university's social-behavioral IRB sees many projects that are of minimal risk, and yearly reviews provide no further protection to human subjects, Birk says. These have been extended to reviews every two years, she adds.

These changes to increase the number of exempt studies and to move to a two-year continuing review cycle have affected 38% of projects seen by the social and behavioral IRB and 20% of new projects submitted to the health sciences IRB, Birk says.

Flexibility for minor changes

Principal investigators also are burdened by the requirement to seek IRB approval each time their project is modified in any way. So the university addresses this with a new proposal, Birk says.

"We're looking for a unit to pilot this with," she explains. "This is a project where we give flexibility to principal investigators to make minor modifications to projects without seeking advance IRB approval."

For example, suppose a PI is working on a study in the field, somewhere off-campus either in the United States or overseas, Birk says.

"Suddenly the study interviewer stumbles on a situation that requires him to make changes to study parameters, adding a few minor questions to the survey instrument," she explains. "This proposal would allow PIs to make those changes without having to seek IRB approval."

They could make the changes under a broader study approval, and, theoretically, this could decrease risk to subjects, she adds.

"We think this will reduce noncompliance because they won't have to seek IRB approval to make the change," Birk says. "And, again, this would involve nonfederally-funded studies with no more than minimal risk."

The criteria for studies to be given this type of flexibility would be whether or not they hold a National Institutes of Health (NIH)-issued certificate of confidentiality, Birk says.

"Those certificates disallow any modifications to procedures," she explains. "Similarly, some research contracts might disallow modifications."

Some nonfederally-funded studies still can have the NIH-issued certificate.

Before making these types of changes, research institutions need to "uncheck the box" on their Federal-Wide Assurance (FWA), Birk and Hewett say.

An institution's research policies and procedures should include information about how the institution will handle demonstration projects.

"That's the document we can point to and say, 'Here we are engaged in doing demonstration pro-

jects,'" Hewett says.

"We talked with OHRP [Office for Human Research Protection] about how the institution was setting up its demonstration projects, Birk says. "OHRP felt it was an appropriate model." ■

Ebbing the tide: PIs fight "mission creep"

Action plan has 8 recommendations

Review board mission creep: nearly every research organization experiences it, and most clinical trial sites resent it.

Still, in these days of more focused public attention on research and human subjects protection, mission creep among ethics review boards is inevitable.

Some institutions are making concerted efforts to improve definitions, policies and procedures to reduce mission creep whenever possible. One major institution, the University of Texas Health Science Center in Houston, TX, has devoted considerable time and resources to reducing regulatory burden and mission creep.

One of their chief strategies was to come up with eight regulatory and fundamental recommendations. Here's their action plan:

1. Define boundaries of regulating human subjects research. "In discussing the issue of mission creep, we felt a lot could be gained in terms of facilitating the process by having our university system define much more clearly the boundaries of regulatory human subjects research," says **Peter Davies**, MD, PhD, executive vice president for research at the University of Texas Health Science Center.

"We charged our university system with helping to put together a roster of areas and issues," Davies says. "We made a point that this would be a living document, and over time different issues would arise that would be considered under that process."

The goal is to create guidelines for research campuses to use when determining whether or not studies are appropriate for IRB review, Davies adds.

2. Encourage IRBs to be flexible.

"We received a lot of advice and had internal discussion about the idea of encouraging our IRBs to utilize the flexibility that already exists in current regulations and to promote ways to facilitate IRBs in utilizing this flexibility much more effectively," Davies says.

3. Reconsider applicability of Federal Wide Assurance (FWA).

"The choice is making informed decisions about whether to apply the common rule only to federally-sponsored research or to all research," Davies explains.

"There are arguments on both sides that need to be considered in terms of filing a limited FWA," he adds.

With a limited FWA, the institution would commit to apply the common rule only to federally-funded research, he says.

"The vast majority of UT campuses applied the FWA to all human subjects research on campuses, but there is increasing interest in limiting it to only federally-sponsored research," Davies says.

The idea of limiting the FWA is that there can be appropriate levels of protection for subjects without sites necessarily following all the elements of the common rule.

4. Adopt measures ensuring adequate scientific review.

"Institutions in our UT system were encouraged to adopt measures that would ensure adequate scientific and scholarly pre-review of human subjects research," Davies says.

Rather than relying on IRBs to provide all of the necessary review, research sites should have mechanisms for pre-review to address some of the scientific and literature questions about research projects, he adds.

5. Promote efficiency and reduce regulatory burden.

"The idea is to look carefully at applying the appropriate level of IRB review," Davies says. "Sometimes IRBs tend to be cautious and go beyond what is necessary."

There are mechanisms that can help IRBs and IRB staff more clearly decide what is appropriate for a particular type of study, he says.

"We have over a dozen different campuses, and some are major medical centers with very sophisticated IRBs," Davies explains. "Others are small, academic campuses in regions of the state that are not heavily populated."

What the campuses need are mechanisms coordinated at a central location for providing advice and consultation about which level of review is necessary, he adds.

6. Reduce number of IRB reviews per protocol.

Often there are several IRBs reviewing a single protocol, and that's a redundancy problem, Davies says.

"So we're creating a memorandum of under-

standing at a system-wide level that allows for reciprocity within our IRBs," Davies says. "This is becoming much easier as we go through more and more institutions receiving accreditation."

IRBs can defer to one another rather than duplicating the whole review process, he adds.

"This is something particularly important with the clinical and translational science award (CTSA) projects, where there is a lot of interest in creating multi-site trials across CTSAs," Davies says. "The UT system is creating templates for use as we streamline the process."

7. Reward IRB members and staff.

Research institutions need to do a better job of recruiting, retaining, and rewarding IRB members and staff, Davies says.

"We need to ensure people have access to appropriate levels of training and professional development," he says. "They need to be excellent at what they do."

UT has a point person overseeing this process and implementing activities to enhance recruitment, rewarding and retaining IRB staff and members.

8. Build culture of trust.

"This last one is the one we spent the most time on, and in some ways it's the most important," Davies says. "We need to build a culture of trust, building processes and conscience to create a foundation for ethical human subjects research."

This is the cornerstone of all the systems created to reduce mission creep and regulatory burden, and each research campus needs to be aware of and committed to the process, he adds.

This also suggests a policy of transparency in areas of conflicts of interest and providing leadership at every level of a university, Davies says.

"CTSAs have been remarkably important in setting up community engagement processes," he says. "In a variety of different ways, the research establishment and communities have facilitated open dialogues, and the research agenda is set by communities themselves." ■

Small research institution has some big tips

Cut paperwork; encourage research

Research sites can improve the way they handle regulatory requirements and encourage more investigators to conduct research by making simple changes, an expert says.

The clinical research policies and procedures at The Southern College of Optometry in Memphis, TN, discouraged researchers even as the college's overall aim was to promote investigation.

"This is a small, private institution with a specific mission of training professionals," says **Patricia M. Cisarik**, OD, PhD, an associate professor and IRB chair in the eye center administration of the college.

"Research is not a big part of the institution, but it's expected that faculty members will participate in some research as part of their ongoing education and promotion," Cisarik says.

However, potential researchers often were discouraged by the paperwork and regulatory burden of conducting research. So only a handful of investigators would initiate all the studies.

The college under Cisarik's leadership sought to encourage more researchers by making some specific changes to how protocols are approved and handled. As a result of the changes, the number of people engaging in research has doubled, Cisarik says.

"We had one person submit a study who had been here for 20 years, but who hasn't done a study in 10 years," Cisarik says.

Also, a summer research program for students had six-to-seven participants who each did a short research project, she adds.

"There's at least one who has an abstract waiting to be accepted," Cisarik says. "And we've actually participated in an FDA drug study, and they had not done one here in a very long time."

The drug sponsor was pleased with how efficiently and quickly the IRB approval process went, Cisarik notes.

"We had everything ready to go in a month's time," she adds.

Here are some of the ways the institution improved its regulatory process:

• **IRB information was posted online:** "Like most institutions we have an Intranet, but nothing was put on there regarding the IRB process other than an application," Cisarik says.

"No procedures or protocols or procedures were posted," she adds. "There were 'Follow under various circumstances' rules."

Cisarik took advantage of SharePoint and MS Word software by posting information online and creating interactive documents with links between various protocol statements and procedures to Internet sites where regulations could be read.

"We made two different documents, one for exempt procedures and one for full procedures, and we put those online," Cisarik says. "As a person is filling out the documents, he or she could link to our Intranet Web sites."

• **Make it possible for protocol attachments:** "Other institutions would have boxes for different parts of the protocol," Cisarik says. "And investigators say, 'If we need to make a change it's hard for me to go back in and make a change in the box itself.'"

So now they can attach a change to the protocol, using select headings.

"That makes it easier for the principal investigator," Cisarik says. "If they need to go back and make an edit on a protocol because of something we require, they don't have to go back in and refill the application."

• **Improve the IRB process:** "We've increased the number of times the IRB meets," Cisarik says.

As IRB chair, Cisarik keeps everyone updated on IRB business, and she's facilitated the process of making the college's research more visible to the community.

"Most research we see are expedited procedures, so I've been very conscientious about getting their applications within three days," Cisarik says. "The university gives me four hours a week to work on IRB work."

From one-third to half the IRB submissions fall into an exempt category because they involve surveys or data already collected, she says.

Investigators of exempt research do not have to meet with the IRB, but the college still requires them to complete an IRB application so that there is some kind of oversight, Cisarik says.

"It helps the institution keep track of what research is going on here, and also from a public relations and marketing standpoint it's easier for them to figure out who is doing what," she adds.

Despite the fact that most research projects were exempt, investigators shied away.

"We'd have individuals who want to do this kind of research but wouldn't take the initiative," Cisarik adds. "I let them know that once they go through the IRB application process and answer the questions about study subjects and procedures that they have half the things they need when they write a paper on the results."

So completing an IRB application helps push their project forward.

The goal is to encourage investigators to start projects without worrying about a difficult and time-consuming IRB submission process, she notes.

"It's not as big a deal to get through the IRB process as they had the impression it was," she adds.

• **Educate and address HIPAA:** "We did a one-hour presentation that required attendance of all faculty members," Cisarik says.

Also, the college established a hybrid entity status, showing which part of research falls under HIPAA regulations and which doesn't, she says.

"Now I have a document where I can look at it with the principal investigator to see why you do or don't have to fill out HIPAA documentation," she adds.

The hybrid entity document specifies an institution's status and outlines exactly which types of projects are impacted.

"If you're going to test a medication on a patient in your clinic, and you're trying a new medication to slow down progression of cataracts, then you have to follow HIPAA regulations because these involve patient care," Cisarik explains.

Another study might recruit 100 students or college employees to collect data on contact lens use, and this would not fall under HIPAA regulations because the study wouldn't be dealing with patient records, Cisarik adds.

The focus on reducing research regulatory burden has been so successful for the institution that college leaders have considered holding an annual research seminar to showcase the work of research students.

"It would provide a little padding for their resumes, and it gives us marketing and publicity opportunities," Cisarik says. "We're hoping to organize that for May." ■

Compliance Corner

Checklists, tools, help site manage QA/QI reviews

Forms help with trial oversight

Increasing numbers of research institutions have opened offices to provide oversight of investigator-initiated clinical trials, but they often lack the basic tools needed for this process.

"You need a checklist of what to look for when reviewing consent form documents," says **Cindy Kern**, RN, CCRC, CIP, education and compliance

coordinator and assistant director for the office of investigator-sponsored IND/IDE support at the University of Pittsburgh in Pittsburgh, PA.

The University of Pittsburgh has developed a series of checklists and tools, including a signature, training, and delegated responsibility log, to assist with trial oversight.

"Our office reviews any research that is not funded by industry because no one else would be monitoring that research," Kern says. "It's unlikely they'd have CRO monitoring, and it wouldn't be an efficient use of our time to look at studies already monitored by industry."

The reviews are called RISE for Research Investigator Start-up Education, and they've helped prevent problems, especially for less experienced investigators because they're typically held very early in a study.

Since the review process was enhanced and improved with checklist tools, the office has not found as many significant issues in ongoing research, Kern notes.

"That's ended up increasing the morale in our office because we're not dealing with as many negative issues," she says.

Also, RISE reviews are shorter since they take place before a study has enrolled subjects. This change resulted in the institution increasing its investigations from meetings with 43 investigators in the first 10 months of 2005 to meeting with 48 investigators in the same period in 2006 and 72 investigators in the first 10 months of 2007, Kern says.

"That's a 33% increase," she adds.

This increase in reviews occurred despite a period when the support office worked with fewer staff due to budget cuts.

"So even though we had less staff, we could still make an impact on conduct of research at the university," Kern says. **(See story on review procedures, p. 32.)**

Here's how the tools are used:

• **Use simple MS Word worksheets:** "Our worksheets are merely tables in a Word document," Kern says. "We address all eligibility criteria, and then we go through the study procedures."

This process can take eight to 15 hours, depending on the complexity of the protocol, she says.

"For each meeting with the study team we have two members of our office who attend," she explains. "One of us takes primary responsibility for that meeting, and that's the person who develops the worksheets."

The worksheets are developed from the protocols and consent documents.

"We use that information to pull out all points that need to be addressed during documentation," Kern explains. "It's really what they write in their protocol, and we reinforce with them that they indicated it in the protocol."

The support office also recommends that investigators keep a running tab on all adverse events in a study, Kern says.

"We provide them with some documents to keep track of adverse events, and we do an assessment of that," she says.

• **Use checklists during reviews:** The checklists for good clinical practice (GCP) include protocol adherence, safety monitoring, institutional review board processes, regulatory documents, subjects records, drug or device accountability and handling, and investigator involvement.

Compliance coordinators use checklists when meeting with investigators.

"What we like to do is ask them how they plan to implement their study," Kern says. "So I say to them, 'Tell me what you're going to do with the certificates from the time subjects come in to the time they're finished with study participation.'"

Compliance coordinators review the protocol and consent document for study procedures and eligibility criteria, and then they make a checklist based on these.

"Once we have those worksheets in place then we take them with us and hand them to the study team and discuss how they'll document all of those things," Kern explains. "We have templates that we make specific to each study."

The office also sends an electronic version of the templates to the investigator so they can alter and use them as needed. **(See sample informed consent template, p. 33.)**

"Most of the time they find those very helpful in documenting everything they need to have documented," Kern says.

Each checklist has space for simple answers of "yes," "no," and "N/A."

"Each page has space for notes about findings or other things that need to be addressed," Kern says. "There might be comments that necessitate an investigator responding to a report."

• **Stress importance of documentation:** "One of the things we try to reinforce with investigators is that if it wasn't documented then it wasn't done," Kern says. "'Let's look at your records and see how complete a story you can tell with your

documentation,' so things have improved a lot."

For example, the GCP checklist for regulatory documents lists these areas of focus:

- FDA 1572 current, signed, dated, complete, correct;
- Required CVs on file;
- Financial disclosure forms completed by all listed investigators and sub-investigators;
- Protocol and accompanying instruction manual;
- Current clinical laboratory certification and normal ranges;
- Current investigator brochure;
- Documentation of all regulatory submissions (IRB, scientific review, FDA, CTRC, Radiation Safety);
- IND annual reports.

And the drug or device accountability and handling checklist includes these items:

- Records of receipt;
- Records of subject dispensing and returns;
- Records of disposition;
- Documentation of transfers;
- Storage conditions/monitoring methods per protocol;
- Drug supply agreement in place;
- Secured storage area.

"We emphasize to study teams that everything has to be documented," Kern says. "Once they grasp that process their documentation is much better." ■

Institution's reviews proactive, educational, and boost compliance

Catch PIs before they make mistakes

The University of Pittsburgh in Pittsburgh, PA, has developed a thorough, review process that serves as an educational opportunity, as well as a way to prevent clinical research problems.

Here's how it works:

• **Schedule initial visit:** The initial visit often occurs before the trial site has enrolled subjects, although some occur later in the study cycle, says **Cindy Kern**, RN, CCRC, CIP, education and compliance coordinator and assistant director for the office of investigator-sponsored IND/IDE support at the University of Pittsburgh.

"If there are subjects enrolled we may be at the site for six to eight hours, depending on the nature of the study," Kern says. "If there are no subjects, we're generally out in two hours."

• **Time reviews to enhance teaching moments:** "In the past we would go out after a study had been ongoing for a couple of years," Kern says. "Now we try to meet with them soon after the IRB approval, if possible, and prior to subject enrollment."

Called RISE for Research Investigator Start-up Education, this process is proactive, preventing problems, and it's educational for clinical research investigators and coordinators.

Reviewers help investigators assess whether they have all necessary data in place. Also, it makes it less crucial to conduct a post-enrollment review.

"We may go back six months, eight months, maybe a year later to see if they've put everything in place," Kern says. "But most times we don't go back unless an issue arises."

In the four years since starting RISE, the organization has seen positive outcomes: "The investigators we've gone back to assess have actually implemented a lot of things we've suggested, and their records are in very good shape," Kern says.

The support office surveys researchers anonymously four times a year, and about 75% have returned positive comments, she adds.

• **Assess trial site compliance:** "Generally, we can tell by the tone with which we're received when we have an interview," Kern says.

"I can honestly say that almost all the folks with whom we've met have been very receptive and appreciative of the tools we've provided," she adds. "A few won't feel they need any assistance, but that's generally the exception."

What to leave in, what to leave out

One area that has shown improvement involves inclusion/exclusion criteria.

"We try to stress with folks that not only do they need to address the presence of inclusion criteria, but the absence of exclusion criteria," Kern explains.

"An example is a person with poor kidney function," she says. "We need to see documentation that the kidney function was assessed, and the subject does indeed have appropriate kidney function to participate in the study."

In another example, if a study participant has to use an approved method of birth control,

reviewers want to see what kind of birth control is being used and whether the participant is willing to use that method of birth control throughout the trial."

"We tell them they need to show the details and not just check a box saying they're using birth control," Kern says. "We're seeing improvement in that area."

• **Review safety assessment plan:** "When we go in to meet with investigators we want to assess how they are making sure they're following the protocol with a minimal amount of risk for subjects," Kern says. "We want to know who is doing this assessment and how they are assessing safety on an ongoing basis."

For instance, is a site following a data safety and monitoring (DSM) plan?

Some investigators will write in their protocols that they plan to follow a DSM plan, but then they do not follow through with actually creating one, she notes.

"We say, 'We want you to describe what you're willing to do to assess ongoing patient safety, and be realistic,'" Kern says. "Once we have them thinking about this process we might find they have a good approach, but have to give it more thought and document it when they're done."

• **Suggest study modifications when needed:** Sometimes a study needs to be modified because of issues that arise, and the support office will make this recommendation as needed.

For example, there might be a study in which adverse events are occurring at a greater-than-expected frequency, Kern says.

The support office will suggest the investigator assess all factors that might influence adverse events. If the assessment reveals the study is not causing too many problems other than occurring at a greater frequency than anticipated, then the investigator will need to inform subjects and modify the informed consent document, Kern says.

"So the investigator would have to change the protocol and consent document to reflect the greater occurrence," she adds. "Then we also tell them they will have to come up with a modified consent to provide to participants who already are enrolled in the study, reflecting the new finding." ■

An informed consent process checklist

Below are sample questions from the "Documentation of the Informed Consent Process" checklist developed by the University of Pittsburgh in Pittsburgh, PA:

• List the persons present during the informed consent discussion.

• Who explained the details of study participation? Note approximate length of time of discussion.

• Were all risks and benefits of study participation presented to the subject (and family)?

• Were all questions answered to the subject's (and family's) satisfaction?

• Does the subject appear to understand all terms of participation and agree to enrollment? How is comprehension assessed?

• Was the consent document signed by all parties prior to the performance of any study-related procedures?

• Was a copy of the consent document provided to the subject?

The checklist also includes space to list the IRB number, principal investigator's name and subject ID. It is signed and dated with time recorded by the investigator.

Oncology survey finds optimism, cost concerns

Personalized medicine is hot trend

Oncologists and medical directors say that 38% of their patients could benefit from participation in clinical trials, but only about 5% actually enroll in an oncology study per month, according to a recent survey.

The low trial participation is due to perceived cost barriers, the survey found.

"Oncologists understand science and the potential benefits these [investigational] drugs provide," says **Scott Bazemore**, director of clinical research development at U.S. Oncology Research of U.S. Oncology in The Woodlands, TX.

The problem is a matter of navigating red tape and bureaucracy, Bazemore says.

U.S. Oncology sponsored the survey, which was conducted by KJT Group. The survey included 299 oncologists, hematologists, and clinical trial professionals. Interviews were conducted in the summer of 2009.

U.S. Oncology is affiliated with 1,310 physicians in 493 locations, including 98 radiation oncology facilities in 39 states.

The study also found acceptance and optimism

among oncologists for clinical trials that involve personalized medicine.

Overall, 57.5% of respondents said they are optimistic about the future of clinical trials in the United States, while 17.1% expressed pessimism, and 21.1% said they were ambivalent.

More than half of the oncologists and medical directors surveyed believe it would be easier to recruit patients to clinical trials for targeted therapies than to large-scale, randomized trials of more traditional cytotoxic therapies.

The rise of personalized medicine

Personalized medicine is a growing trend in oncology, Bazemore notes.

"The last five years have been exponential in the era of personalized medicine," he says. "It's been out there for a while, but the biggest jump into this was the perception a couple of years ago where they looked at targeting a specific marker in breast cancer patients and targeting that specifically."

The idea is to stop throwing a lot of chemicals at patients but instead targeting specific proteins, he adds.

"We're quickly heading toward an era where no one really cares about the location of the tumor, whether in the breast, prostate, or lung, but we'll look at that specific tumor and target treatment for it," Bazemore says.

This approach preserves more of the healthy tissue.

Some call it precision medicine because the treatment looks at the precise way to exploit the genetic signature of a tumor by battling it with a drug that attacks the biomarkers on that cancer cell, sparing the normal tissue, Bazemore explains.

"The better the technology gets in identifying markers and new pathways, the faster we have new targets to exploit," he adds. "As the science gets better it dictates what happens downstream in the clinic."

This means there need to be more personalized medicine clinical trials conducted by physician scientists, he says.

"There is a high level of acceptance of precision or personalized medicine in community-based medical systems," Bazemore says. "The biggest barrier is insurance coverage."

Sponsors will pay for the investigational drug, and insurers pay for standard care, but the gray area involves the expensive process of identifying the target area for precision medicine, he explains.

"The new genetic signature and protein expression level is a very new test, and it's not paid for by insurance groups," Bazemore says. "Also, many insurers will not allow patients to be repaid for standard of care treatment if they're also receiving investigational treatment."

More than 90% of oncologists and medical directors surveyed reported they already treat patients with a personalized medicine approach. On average, 40% of their patients are treated this way, and breast cancer was the most common tumor type treated with a personalized medicine approach, the survey found.

About 58% of those surveyed said the most likely factor to increase the number of patients participating in clinical trials would be mandated health plan coverage of treatments.

Kind of a drag

Also, 86% of oncologists said they think the clinical trial approval process takes more than a year due to regulatory red tape. Other factors they reported slowed the CR process are as follows:

- Inefficiency of initiating organization - 51%;
- Lack of funding - 44%;
- Excessive analysis - 29%;
- Targeting wrong patient population - 20%;
- Asking wrong clinical question - 15%.

"Of the 1,300 physicians in the network, approximately 750 pay very strict and close attention to clinical research," Bazemore says. "Close to 60% have a very detailed approach to clinical research, and about 150 or 20% of them are heavy adopters of personalized or precision medicine in a trial."

The survey's data show that oncologists would like to get involved in personalized medicine research, but they find it quite difficult to navigate, Bazemore says.

"It distracts them and takes them away from other trials that might be easier to navigate and which might be as relevant to the patient," he adds. ■

Improve your research contract, negotiation skills

Understand everyone's motivations

Each clinical trial administrator and investigator needs to understand the motivations of all

parties involved — including his or her own — before beginning a clinical trial contract negotiation process.

"One main thing in any clinical trial is the principal investigator wants to see if he'll benefit in any way," says **Theresa Jacob**, PhD, MPH, director of the clinical trials unit and translational research at Maimonides Medical Center in Brooklyn, NY.

"One thing they're stuck on is publication rights," Jacob says. "They're usually eager to publish the results, so publication rights is a huge thing for many of the clinical investigators that I work with."

For instance, an investigator often would like to know if his or her name will be on a study's final paper. This is a negotiating point because some studies only include the names of key investigators, Jacob says.

Investigators also might want to know if they can publish some part of the work or present a piece of the research at a convention.

The other side of the negotiation table has the sponsor who has different goals and motives when it comes to publication rights, Jacob says.

"During contract negotiation, the investigator needs to make sure the contract has what he wants, and if it doesn't, then he shouldn't sign the contract," Jacob says. "That's if it's absolutely non-negotiable. Most of the time there's leeway, and since sponsors are interested in having investigators involved in the study, they'll listen."

Jacob offers these additional negotiation tips:

1. Do your budget before signing the contract.

Investigators often are not aware that various sites have different budgets for the same study because of contract negotiations, Jacob says.

Clinical trial sites should determine their budget for a particular study based on the protocol and their own infrastructure expenses. And then they need to negotiate for payment that would more than cover their anticipated budget, she suggests.

"It's better if you don't lose any money on a study, and it's best to get something out of the study for the hospital or facility," Jacob says. "But you should at least break even."

Investigators sometimes make the mistake of thinking a study will provide have access to the same resources physicians have when treating patients.

"The investigator expects all these things to be done in the study too," Jacob notes.

But including every procedure and detail costs time and money, and a study budget might not have room for frills. So it's best to stick with the protocol's interventions and procedures when both designing and following a budget.

2. Remember the goal is quality data.

Sponsors want high quality clinical data, Jacob says.

"The main objective of any pharmaceutical or medical device is to conduct a clinical trial to collect high quality clinical data and to obtain FDA approval of the product so they can market it," she says. ■

CNE/CME Objectives / Instructions

The CNE/CME objectives for *Clinical Trials Administrator* are to help physicians and nurses be able to:

- **review** pertinent regulatory mandates;
- **develop** practical clinical trial oversight strategies;
- **review** best practices shared by facilities that successfully conduct clinical trials.

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you. ■

COMING IN FUTURE MONTHS

- ■ Improve CT recruitment by understanding motivations
- ■ Research office has excellent GCP templates to share
- ■ Here's how site handles protocol deviations
- ■ Institution creates extensive research patient data warehouse
- ■ Include all of these elements of successful informed consent

CNE/CME *questions*

9. Which of the following is not a strategy to reduce regulatory burden and ethics review board "mission creep?"
   A. Reduce the number of IRB reviews per protocol
   B. Move more reviews from expedited category to full review category
   C. Improve IRB member/staff recruitment, retention, and reward systems
   D. Build culture of trust

10. A Good Clinical Practice checklist for regulatory documents might list which of the following items?
    A. FDA 1572 current, signed, dated, complete, correct
    B. Financial disclosure forms completed by all listed investigators and sub-investigators
    C. Protocol and accompanying instruction manual
    D. All of the above

11. The University of Pittsburgh research office has developed an informed consent checklist with questions for CR sites. Which of the following is not one of the questions they've included on the list?
    A. Was a copy of the consent document provided to the subject?
    B. Who explained the details of study participation?
    C. How much is the subject being paid to participate?
    D. Does the subject appear to understand all terms of participation and agree to enrollment?

12. True or False: When clinical research investigators negotiate with sponsors over a study contract, they should keep in mind that sponsors' chief goal is to obtain quality data that will help lead to FDA approval for marketing a new drug or device.
    A. True
    B. False

Answer: 9. B; 10. D; 11. C; 12. A.