IRB ADVISOR

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INSIDE

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Reanimation Study a Step Toward Brain-death Breakthrough?

Gray matter: Brain death 'is not black and white'

By Gary Evans, Senior Staff Writer

Though met with the inevitable zombie jokes — in part because the human research subjects are officially categorized as "living cadavers" — a new reanimation study of brain death has many compelling and hopeful aspects to its principal investigator in India and biotech sponsor in the U.S.

"As someone who started my career in orthopedic traumatology and who has ventured into neurology, spinal cord injury, and regenerative medicine due to the related overlap between the disciplines, this represents a unique opportunity to explore interventions in the most serious of central nervous system [CNS] indications: brain death," says **Himanshu Bansal**, MD, who is conducting the research at Anupam Hospital in Rudrapur, India.

A NEW REANIMATION STUDY OF BRAIN DEATH HAS MANY COMPELLING AND HOPEFUL ASPECTS TO ITS PRINCIPAL INVESTIGATOR IN INDIA AND BIOTECH SPONSOR IN THE U.S.

In an email interview with *IRB Advisor*, Bansal says he is in the process of recruiting 20 human subjects from area hospitals between the ages of 15 and 65 that have been declared brain dead from a traumatic brain injury having diffuse axonal injury — one of the most common and devastating brain traumas — on MRI. The living cadavers must not be indicated for organ donation, have no cranial implants, and cannot be pregnant.

"Patients will be recruited through neuro-intensivists and through family introductions at regional ICUs in the northern India area," he says. "We have created a special long-term acute care

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unit at the Anupam facility where the patients recruited for the study will be transported and placed."

Sponsored by Bioquark Inc. in Philadelphia, the study is registered with the National Institutes of Health as a clinical trial but it has IRB approval only to be conducted in India. The study will use a variety of interventions from stem cells, biologics, laser therapy, and nerve stimulation to see if there are any favorable signs for brain regeneration. There is no expectation that any patient will be brought back from brain death in this initial research.

"There have been a lot of zombie jokes, but we're not near that at this point in time," says **Ira S. Pastor**, BS, MBA, Bioquark CEO and director of the affiliated ReAnima Project. "We do not anticipate any reanimation event in terms of someone jumping up and walking around the ICU."

Quest for Fire

Instead, the investigators are looking for the stir of a spark — any signs of neurogenic or vasculargenic activity that could mean formation of new neurons or blood vessels where there was no pre-existing activity in the brain stem.

"We are sort of taking a step with this living cadaver model to merge together biologic tools that have been used in neuroregenerative medicine and some of the same tools that are basically used in the ICU to try to wake up coma patients," Pastor says.

The study is registered on ClinicalTrials.gov as a "Non-randomized, Open-labeled, Interventional, Single Group, Proof of Concept Study With Multi-modality Approach in Cases of Brain Death Due to Traumatic Brain Injury Having Diffuse Axonal Injury." *(http://1.usa.gov/25JIxNi)*

The primary outcome measure is reversal of brain death as noted in clinical examination or by electroencephalogram (EEG) test to detect electrical activity of the brain. The time frame is six weeks, and of course the patients will have to be kept on life support to allow the study to proceed over that period. As approved by an IRB in India, informed consent must come from family members of the research subject. Depending on the results, some families may be asked if they would like to continue into a second phase of the trial.

"The IRB was quite open to the study design and ethical dynamics surrounding such research, [allowing] informed consent to be supplied by family members," Bansal says. "Families that have contacted us to date realize and understand that this is much more of an early stage, exploratory research endeavor at this point. It is not easy to recruit for, but we are not promising miracles as a result of this first study. This is a basic open label design and all patients will be given the same set of interventions."

Secondary outcome measures include analysis of cerebrospinal fluid for color consistency, cell counts, and microbial evaluation to signify any signs of aseptic or bacterial meningitis, pulse, O_2 saturation, blood pressure, and respiration changes.

The study has been questioned for the perception of exploiting some regulatory loophole between the living and the dead. It certainly raises questions about the boundary between the two and invites contemplation of some utterly unknown aspects of consciousness. You cannot work

with living cadavers in research that involves harvesting organs, but other than that it is an essentially new, unregulated frontier in both the U.S. and India, Pastor says.

Long-range, this line of research holds great promise for a variety of devastating conditions, Bansal says.

"This area has been quite off the radar for most pharma companies and healthcare institutions," he says. "[This research] could potentially effect change that can apply to millions of patients with other disorders of consciousness, brain injuries as well as chronic degenerative conditions of the CNS."

Salamanders and 'Terminal Lucidity'

There are existing examples in nature that have regenerative powers unavailable to humans. For instance, the salamander can regenerate whole limbs and brain matter.

"We as a company are making the bet that [human] memory and mind will be recoverable," Pastor says. "We base that assessment on many things, not the least of which is the fact that non-human species that go through complete brain regeneration can be trained to do something, and have their brains destroyed, only for the memories of the mind to come back. We are really trying to mimic what happens, for example, when you cut out a brain of a salamander, how it reforms from the remaining tissue in the spinal column."

We may think of the human brain as a static organ, but we are able to maintain function and memories over years while "burning up a 100,000 neurons in the course of day," he says. "Then there are many conditions we don't have answers to."

Those include the bizarre but documented phenomenon of "terminal lucidity," in which people with severe Alzheimer's and other degenerative brain conditions astonish their caregivers by becoming completely coherent and communicative for a brief period before they die.

"We also cannot explain why we see consciousness in children who are born without a cortex," Pastor says. "There have been cases in the literature in the past few decades of very young children who have been considered brain dead that have recovered. These are controversial and they never had a [documented] prognosis, but they show that when there is still an active neurogenic piece persisting, like in an infant, things aren't as black and white as they seem." ■

Adopt the 'Not a Success Until You Find a Successor' Philosophy

Planning next generation of leadership begins today

It might very well be a baby boomer problem, or it could be a perennial issue. But with a huge chunk of the nation's IRB leadership about to retire, now is the time to do succession planning, long-time IRB leaders say.

The IRB world cannot ignore this dilemma as 30%-40% of the workforce will be eligible for retirement in the next five years, says **Candice Yekel**, MS, associate vice president for research and the director for the office for research protections at The Pennsylvania State University in University Park.

"That's a staggering number," Yekel says. "I'm 57, and probably in three to five years, I'll be ready for retirement."

A thrown-into-the-deep-end-of-the-pool type of succession is not ideal, notes **Charlotte Coley**, MACT, CIP, education and training manager in the Office of Human Research Ethics at the University of North Carolina in Chapel Hill. Both Coley and Yekel spoke about succession planning at the Association for the Accreditation of Human Research Protection Programs (AAHRPP) 2016 Annual Conference, held April 19-21, 2016, in Long Beach, CA.

"Trial by fire doesn't work very well; everybody ends up being burned," Coley says. "A lot of offices now are creating a deputy director position, which allows someone to learn at the feet of another person and not be thrown in the deep end."

Yekel has had succession planning on her mind for some time. Like other IRB leaders in the baby boom generation, Yekel's career path led her to human subjects research, although it wasn't an early career choice. "I love it, but in graduate school I would have said, 'No way,'" she says. "I had not thought to move in that direction."

A large proportion of IRB leaders have been in this field since the 1980s or 1990s, and now they're looking ahead to the next transition into

retirement, Yekel notes.

There currently is a two-decade gap between this older generation of leaders and the younger group of IRB professionals who moved into the field within the last decade or so as part of a deliberate career track, she adds.

Both Yekel and Coley work in IRB offices that, unlike many IRBs, have attracted younger staff.

"My office is rather young," Yekel says.

Coley works with a number of IRB professionals in their 20s and 30s. "Living in North Carolina has been a very attractive draw to younger professionals, and it's given us a [demographic] mix," Coley says. "At my last IRB job, the average age was 55."

"It's a more deliberate decision for people in their 20s and 30s," Yekel says. "I've met several young professionals, and they know early on that this is what they want to do."

Finding or developing IRB leaders from the ranks of people in their 40s or early 50s might be more of a challenge, they note.

"Since the IRB world started to explode and a lot of young professionals were coming into it, there's been a gap," Yekel says. "We have people who are quite senior and looking to transition into retirement."

Then there are the younger IRB professionals who may not have the years of experience that would be ideal in successors to today's IRB leadership, she adds.

IRB leaders face several challenges when planning for tomorrow's leaders: First, they need to attract younger workers to their offices and develop advancement and growth strategies that will retain them; second, they need to groom the most experienced staff to become the next generation of leaders; and third, they need to have an emergency succession plan in the event they have to take off several months or longer at little to no notice. *(See story on creating a career track for younger staff, page 77.)*

Yekel and Coley offer the following suggestions for succession planning:

• **Hire people who have leadership skills.** New IRB professionals should have a college degree because this at least suggests the job applicant has good writing, critical thinking, analytical, and communication skills, Coley says.

"IT'S NONSTOP HECTIC; PEOPLE NEED TO THINK QUICKLY AND MOVE FAST AND NOT GET OVERWHELMED AND DEPRESSED BY THE WORKLOAD BECAUSE EVERY IRB HAS MORE WORK THAN THEY CAN HANDLE."

"They need to pay attention to details; a comma in the regulations makes a difference sometimes," she adds.

"We expect folks in the office to be analysts, to think in a much more scientific way," Yekel says. "They need to use good judgment, to not be afraid to make a decision, and to enjoy working with people."

IRB professionals help researchers navigate the complexities of human research, so they need to have refined communication skills and a service mentality, she adds. "And you need to have someone who can handle all of the stress because it is time-driven work."

Coley compares work in an IRB office to having a job in Grand Central Station on a holiday weekend's Friday afternoon. "It's nonstop hectic; people need to think quickly and move fast and not get overwhelmed and depressed by the workload because every IRB has more work than they can handle," she says.

"I once had an employee who wanted a clean and neat desk and wanted to be able to clear her desk of all open projects each day," Coley recalls. "But you can't be in control working in the IRB office; you may have a plan for what you want to do today, but things pop up and you have to go with the biggest bonfire."

The tidy employee did not last long in the office, but found another job in which having a perpetually clean desk was possible, Coley adds.

• **Create opportunities for staff to work with other departments.** The next step in succession planning is to create opportunities for staff to work with other human research protection program departments and non-IRB individuals, Coley suggests.

"If you could set up an internship where IRB staff would work for one or two days or a week in another office, like the conflict of interest office or ethics office or even the pharmacy service, then they'd have a better understanding of other areas," she says.

IRB professionals can learn more about human research as they interact with different offices on campus or in a hospital, Coley says.

"They also can develop a relationship with people in these other offices," she adds. "It takes

more than an IRB to have a culture of compliance and get everyone working together."

Working with other departments also helps staff improve their communication skills and network. For example, Coley had her institution's conflict of interest office do a presentation for the IRB analysts, giving analysts a chance to meet and talk about what's going on in each office and where the two offices interact.

"We can identify ways to create synergy between all these different offices," Coley says.

• **Groom the best and brightest for future leadership.** Grooming or mentoring staff with leadership skills for future positions of authority might resolve one of the problems IRBs have in growing leadership, which is their flat organizational structure, Coley notes.

"With a flat structure, people eventually have to leave your office to get a promotion or move up," she explains. "Recently, there's been a lot of effort to create opportunities for professional growth within the IRB offices."

An IRB director can ask motivated employees with help on special projects or strategic planning and coach them in the new role. While this isn't the same as a promotion, it does give the professional the opportunity to learn new leadership and organizational skills, Yekel adds.

• **Prepare for leadership succession emergencies.** It's always possible that a current IRB leader will need to leave on short notice because of a health problem or family emergency, so IRB succession planning should prepare for this contingency as well.

For example, an IRB could create back-up positions and train staff to be able to jump into a leadership role if needed, Coley says.

"Most institutions have a back-up plan in place where if somebody leaves, people take vacations, or if they get sick, there is a back-up for their position," she says. "Others can step up and fill in or divide up the work until they get back."

If the person who leaves abruptly is a long-time IRB leader, then the gap could be difficult to fill. It's best if the IRB leader has an emergency successor — someone who has been trained by the leader to take over some of the leader's responsibilities, Coley adds. ■

Add Some Climbs and Hills to Typically Flat Career Path

Use creativity to make office structure less flat

It might require creativity, but there are ways to make the IRB office structure less flat.

"There's a movement away from flat IRB structures," says **Candice Yekel**, MS, associate vice president for research and the director for the office for research protections at The Pennsylvania State University in University Park.

"Those of us in the field in leadership roles need to think about what type of career track we're giving our people coming into IRB work," Yekel says.

"I was reading a statistic recently about how a young professional will go to five or six different jobs, jumping every couple of years," she adds. "It would be smart for IRB leaders to make sure there's a career track in our field to hang onto as long as we can."

The Penn State IRB has started that process, creating analyst jobs, team leader positions, an administrative coordinator job, as well as the director position, she notes.

"Three years ago, we went through a transformation, reorganizing the IRB program," Yekel says. "Within the program, there is some natural progression people can make."

Another strategy in adding career tracks to an IRB office is to put positions at different levels, such as an analyst I, analyst II, and analyst III, suggests **Charlotte Coley**, MACT, CIP, education and training manager in the office of human research ethics at the University of North Carolina in Chapel Hill.

"You could have senior positions versus entry level and have people like me who are managers of compliance or quality improvement or education," Coley says.

Changes in federal regulations also leave openings for new ways to advance staff. For example, IRBs could create new positions with leadership growth potential. IRB leaders could create new job descriptions to fit some of the work that will change under the Notice of Proposed Rulemaking (NPRM) for the Common Rule.

For instance, the NPRM, if made final, will mandate that research institutions rely on a single IRB for U.S. research. This means that IRBs will need someone to handle the multiple Federalwide Assurances (FWAs) and IRB Authorization Agreements (IAAs), as IRBs from each institution involved in a research project will have its own FWA, Coley says.

IRBs at sites that will rely on a coordinating center or central IRB will also have to let the central IRB know what their state laws and institutional requirements are with regard to informed consent and reporting adverse events and handling continuing reviews, Coley says.

"That role is going to be an opportunity for growth in an IRB office," she adds.

The main goal is to give staff opportunities to grow within the office so they can get more IRB knowledge and leadership experience, Coley says.

Even with a flat IRB structure, an IRB leader can at least have conversations with employees about their goals and ambitions, Yekel suggests. "Ask, 'What is your long-term plan? What would you like to do?'"

Any kind of strategy to recognize employees' work as they gain more experience will help with staff retention, and every IRB office wants good employees to stay, Yekel and Coley say.

"You have to invest an awful lot of time in training people; it takes a year, at least, before people start hitting their stride on effectiveness, and then it sometimes takes years in the trenches, looking at all different kinds of protocols," Coley says. "But if your entry-level and mid-level folks have to leave after three to five years to get a promotion, then maybe they'll come back, and maybe they won't." ■

FDA Discusses New Guidance on Using EHRs for Clinical Investigations

Stresses importance of verifiable data

The U.S. Food and Drug Administration (FDA) issued in May draft guidance titled, "Use of Electronic Health Record [EHR] Data in Clinical Investigations."

The guidance advises sponsors and clinical investigators to adhere to best practices, including the planning and management of using EHRs in research, modifying EHR data, providing audit trails, including statements about confidentiality in informed consent, and maintaining privacy and securing data.

IRB Advisor asked the FDA to respond, in writing, to a few questions about the draft guidance in this Q&A. The FDA's responses were made by **Cheryl Grandinetti**, PharmD, Health Science Policy Analyst in the Office of Medical Policy at FDA's Center for Drug Evaluation and Research, and **Leonard Sacks**, MD, Associate Director of Clinical Methodology, also in the Office of Medical Policy.

IRB Advisor: What kinds of issues have arisen that led to the need for the new draft guidance related to EHR data in clinical trials?

FDA: In general, EHRs are not under the control of FDA-regulated entities (e.g., sponsors, clinical investigators), because in most instances these systems belong to healthcare organizations and institutions. FDA has stated in previous guidance that we do not intend to assess compliance of EHRs with 21 CFR part 11. However, FDA's acceptance of data from clinical investigations for decision-making purposes depends on FDA's ability to verify the quality and the integrity of data during on-site inspections and audits (see 21 CFR parts 312 and 812). Sponsors are responsible for assessing the validity, reliability, and integrity of any data used to support a marketing application for a medical product. Therefore, best practices on the use of the data in clinical investigations from these systems are needed and this guidance clarifies our expectations when EHRs are used as a source of data in clinical investigations.

IRB Advisor: How does the guidance ensure that EHR data meets FDA's requirements (i.e., what are some of the common problems related to recordkeeping and record retention)?

FDA: This guidance describes the critical information that should be captured for audit trails as well as other controls, like access controls and the ability to retain and copy records. These are important attributes of an electronic system when used as a source of data in FDA-regulated clinical investigations,

and necessary to ensure the reliability, integrity, and confidentiality of the data.

IRB Advisor: With so many different EHRs in use, how are organizations doing with interoperability? How have things improved over where they were five years or a decade ago?

FDA: Issues pertaining to EHR interoperability are being addressed by the adoption of data standards and through standardization requirements as part of the ONC Health Information Technology Certification Program.

IRB Advisor: In the draft guidance's informed consent section, the document refers to foreseeable risks with the use of EHRs. Besides the risk of data breaches, what other types of risks might there be?

FDA: The risks associated with the use of electronic health records stem primarily from data breaches. The consequences that arise from such data breaches include risks to the subject's insurability or employability, and could also stigmatize the subject. Additionally, data breaches increase the likelihood of the subject being a victim of medical identity fraud.

Editor's note: A copy of the new draft guidance is available online at: http://1.usa.gov/1OG8996. ■

NIH Explains its Draft CT Protocol Template

47-page protocol template

A draft clinical trial template tool might help investigators design and submit better protocols.

"It's a tool for investigators that allows them to prepare protocols for Phase II and Phase III trials in a way that is efficient and will result in timely review," says **Carrie Wolinetz**, PhD, associate director for science policy and director of the Office of Science Policy at the National Institutes of Health (NIH) in Bethesda, MD.

The draft protocol template, published March 17, 2016, arose out of discussions between NIH and the FDA. Changes will be made after comments are reviewed, and it could be made final later this year, Wolinetz says.

"We wanted to streamline IRB reviews and help investigators more easily get through the FDA regulatory process," Wolinetz says.

There's a high turnover rate in the clinical trial industry, with as many as 85% of investigators who submitted a new drug application in 2007 having only participated in a single clinical trial.[1]

Standardized templates can help first-time investigators write protocols that can make it through the IRB review process more easily, Wolinetz suggests.

The National Cancer Institute provides a template for studies it funds and its template can serve as one example, but researchers in other fields may not have access to protocol templates, she notes.

This is why there is a great variation in terms of what investigators are submitting to the FDA, and that's the problem NIH and FDA wanted to solve, Wolinetz says.

The 47-page protocol template suggests the following main sections:

- key roles, introduction, objectives and purpose,
- study design and endpoints, study enrollment and withdrawal, study agent, study procedures, and schedule,
- assessment of safety,
- clinical monitoring,
- statistical considerations,
- source documents and access to source data/documents,
- quality assurance and quality control,
- ethics/protection of human subjects,
- data handling and recordkeeping,
- study administration,
- conflict of interest policy, and
- literature references.

The protocol template provides definitions, sample charts, diagrams, and graphs, as well as explanations and examples.

For example, the template includes a sample flow diagram of a randomized controlled trial. The top box lists activities that are done prior to enrollment, such as obtaining informed consent and screening potential subjects by inclusion and exclusion criteria, as well as obtaining history. Then a triangle represents randomization with one oval for Arm 1 and another oval for Arm 2. Both arms of the study are linked to a box for performing baseline assessments, which links to a box for repeating study intervention, if applicable, and links to two boxes for following up assessments of study endpoints and safety. The last part is a parallelogram for final assessments.

"One thing we are in the process of doing is making an electronic version of this template, which is a PDF," Wolinetz says. "It could be something easily utilized in submitting and entering information."

An electronic version would be useful across different systems. For example, NIH-funded investigators could pull up information from their grant applications and use the electronic data to populate some fields of the electronic protocol, she explains.

"We'd love to see interoperability of all these things so investigators won't have to enter the information over and over again," Wolinetz says.

The protocol template will be made available at no charge for all Phase II and III investigational drug or device trials, regardless of the trial's funding source, she adds.

"One thing we'd like to do is think about whether there would be utility in making other templates, as well," she says. "This is our starting place, and we'll move from there."

The draft protocol template is available online at: http://1.usa.gov/1S3t5CG.

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Education May Overcome Reticence to Join Trials

Cancer advances threatened by resistance to research participation

People in general, and cancer research subjects in particular, are reluctant to participate in clinical trials, a trend that could undermine progress toward treatment, according to a survey of some 1,500 consumers and 600 physicians conducted on behalf of Memorial Sloan Kettering Cancer Center (MSK) in New York City. Only 35% of Americans indicated that they were "likely" to enroll in a clinical trial. Other studies have shown that only 4% percent of cancer patients enroll in clinical trials nationally each year.

That's particularly concerning, since the vast majority of modern advances against cancer were the result of clinical trials. Clinical research is increasingly dependent upon larger numbers of cancer patients participating, says **Paul Sabbatini**, MD, Deputy Physician-in-Chief for Clinical Research at MSK Cancer Center. He recently agreed to an interview with *IRB Advisor* about this critical research issue.

IRB Advisor: It's surprising that only 4% of cancer patients enroll in clinical trials nationally — do you have a have a reference on that?

Sabbatini: That figure has been reported with a slight variation between 3% to 5%. Recently, we've seen Vice President Joe Biden noting 3% to 4% percent participation. *[http://lat.ms/24nlbzM]* At Memorial Sloan Kettering, this figure is higher: Nearly one-third of our patients participate in clinical trials. Yet it is imperative that we increase understanding and participation in clinical trials to fuel the research pipeline moving forward — and to be able to offer the best treatments to our patients, now and in the future.

IRB Advisor: Can you elaborate on this critical point in the survey: "Clinical research is increasingly dependent upon larger numbers of cancer patients participating?" Is that in part to find results that can be extrapolated to larger populations?

Sabbatini: There is an urgent need to have more patients enrolling. In fact, this low participation in clinical research could very well be our Achilles heel in curing cancer as we know it. Thanks to the many advancements in precision medicine, researchers are able to sequence more and more genes and to do it at a faster rate. But we must start by having the necessary volume.

Not only does having more patient participation fuel this knowledge, it also helps us explain "anomalies" or extraordinary responders. For instance, a particular new treatment may not work for most clinical trial participants, but could have an exceptionally positive outcome for one or few. Why is this the case and what can this tell us for future patients? There is much more we can uncover on these topics. Research has the potential to help bring better treatments faster, but we need participants in clinical trials to keep the momentum going.

IRB Advisor: After reading a brief statement defining clinical trials, the number of respondents who had a positive impression of these studies jumped significantly, from 40% to 60%. Can you provide the

educational statement that had this effect?

Sabbatini: It reads, "Clinical trials are research studies in which patients volunteer to help test new ways to treat, diagnose, or prevent diseases. They are used to determine if a new test or treatment works and is safe. These trials are used for thousands of medical conditions, including many types of cancer. By participating in clinical trials for cancer, you have the opportunity to:

• Receive drugs or therapies years before they are available elsewhere.

• Receive the newest treatment being studied (in the majority of cases) in addition to the standard current treatment available.

• Better manage symptoms or side effects from the treatment of cancer or improve your overall well-being.

• Receive a higher level of oversight and care.

• Treatments studied can include new drugs, new surgical procedures, or devices or new ways to use existing treatments or improve them.

• Typically, one group of the study receives the new treatment in addition to the standard treatment, while a comparison group receives the current standard treatment. Note that regardless of the treatment group you are in, you are free to leave a trial at any time. The costs of the new treatment are typically covered by the clinical trial, while the standard treatment is covered by the patient or his/her insurance.

• Clinical trials are key in helping physicians develop medical breakthroughs. Nearly all cancer drugs in use today were first tested and made available to patients through clinical trials."

IRB Advisor: Do physicians respond to education about clinical trials in a similar manner?

Sabbatini: Physicians also reviewed the statement and the majority responded in a positive way, sharing that this type of statement could be helpful/useful; specifically:

• 68% would be likely to use the statement with patients.

• 69% feel it would be effective in educating patients.

IRB Advisor: How can "real-world" concerns, like side effects/safety, insurance, out-of-pocket costs, and trial locations be addressed?

Sabbatini: The survey findings illustrate that there is more work to do to help improve clinical trials on several fronts: in the quality of information/education we provide, in increasing access to treatment, and, of course, in providing quality care. Education early on in the process is vital so participants know all of their options and understand what clinical trials are and are not. For instance, many people worry about costs, but the reality is that most clinical trials present no additional out-of-pocket expenses for the treatment itself. Others worry about getting a placebo, but the vast majority of clinical trials do not use a placebo. The good news is that many of these concerns are simply misperceptions that can be addressed through education.

The location concern, however, is not a misperception, but it is still valid. Memorial Sloan Kettering is pioneering a new model — in the NYC area and beyond — to expand outpatient treatment and surgical centers, as well as to establish partnerships with regional providers. These efforts will enable more people in more locations to have access to best practices in medicine and, in some cases, to the very same clinical trials that were previously only open to patients close to MSK's main facility in Manhattan. Patients want high-quality clinical expertise, but they also want options that are convenient and close by — so we must work to bridge this gap.

IRB Advisor: The "guinea pig" misperception may be rooted in reports of unethical research in the past, but were you surprised that more physicians (53%) were concerned about this than consumers (34%)? What do you think may be the issue there with so many docs having a concern about the experimental aspect of trials?

Sabbatini: To clarify, we asked physicians what they think are the biggest concerns for their patients when considering participation in a clinical trial for cancer treatment. Their responses included side effects/safety (63%) and concern about getting a placebo (63%). Additionally, when we asked consumers about their main deterrents when considering participating in a clinical trial for cancer treatment, they pointed to side effects/safety (55%), potential costs (50%), location of treatment (48%) and worries over getting a placebo (46%).

IRB Advisor: Many physicians seem to also view clinical trials as late-stage or last resort interventions, but you're saying that there are clinical trials being conducted on much earlier stages of cancer?

Sabbatini: Yes, the research stresses the importance of educating both patients and physicians on the benefits of clinical trial enrollment at every/any stage of the diagnosis, not just as a "last resort" option. Of the almost 600 physicians polled, more than half (56%) of physicians said they considered clinical trials late in treatment, with 28% noting them "as a treatment of last resort." Only one-third (32%) said they discuss the topic with their patients at the beginning of treatment. However, it is important to evaluate clinical trial enrollment every time a change in

treatment is considered.

With more than 900 trials underway, Memorial Sloan Kettering runs one of the largest clinical trials programs in the country, with trials available at almost every stage of treatment. To us, the survey data reflects a possible missed opportunity on behalf of patients. Clinical trials can offer our very best thinking on how to discover newer, better ways to treat cancer — especially early on.

IRB Advisor: How can the cancer community specifically address these common myths and misunderstandings around clinical trials, particularly in physicians?

Sabbatini: The burden of education is on all of us within the medical community, but it is not insurmountable. The survey results indicated that only 40% of Americans have positive impressions of clinical trials. Yet once consumers read a brief statement describing their real purpose and function, favorability jumped to 60%. This desire for education is both an opportunity and a challenge that we must embrace. We want to start a national dialogue in which other institutions and providers can take part. Speaking with a collective, collaborative voice is the best way to ensure that the message is being heard. And as we heard from Vice President Joe Biden during his recent visit to MSK [May 26], breaking down barriers to scientific collaboration and being able to share data is critical to achieve the "Cancer Moonshot." Curing cancer as we know it is a larger scale problem that we believe we can solve, working together with other leading cancer centers, researchers, and the most important group: the brave patients who choose to participate in clinical trials. They are the true heroes. ■

State Passes Bill Granting Oversight of UM Psychiatric Research

Will new favorable IRB report sway governor to veto?

Legislators have passed a bill granting oversight of psychiatric drug research at the University of Minnesota in Minneapolis (UM) to an independent state ombudsman's office. The law awaited approval or veto by the governor as this issue went to press.

The action culminates a seemingly endless series of reports and investigations into UM research after the 2004 suicide of a man enrolled in a psychiatric drug trial. *(See the June 2016 issue of* IRB Advisor *for more information.)*

While the university and some members of the Board of Regents have said the oversight is not needed given the many reforms put in place, others hailed state monitoring of clinical drug trials as a much-needed step to ensure the psychiatry department protects human subjects and complies with all IRB requirements. The university has been subjected to withering criticism of its psychiatric research program in various reports, but a recent update by the state auditor[1] found positive improvements in the IRB that could sway the governor's decision. The auditor's finding included the following:

"The University has implemented and will continue to implement a wide range of changes to strengthen the oversight capacity of its IRB. In addition, the University is in the process of establishing a new Research Compliance Office to investigate certain allegations about research projects, a function previously performed by the IRB.

We think the following four changes are particularly significant:

• Expansion of the IRB's Membership and Structure:

The University is in the process of revamping its IRB approval process to increase the number of IRB members, panels, and expertise. One of the problems with the current IRB system was that it has been understaffed. According to University officials we interviewed, it was difficult to get people to participate because IRB members were overworked, unpaid, and received no recognition from their department or the medical school for serving on an IRB.

Instead of having four medical panels focused on a particular topic, there will be eight panels with a variety of experts on each of them. If some projects require special expertise and none of the panels have appropriate experts, the University will supplement the panels with a roster of consultants or people within or outside the University who can serve as objective reviewers. Serving on an IRB will also be recognized as a service to the University and members will be paid.

• Creation of a Research

Compliance Office:

In 2015, the University Vice President for Research created the Research Compliance Office (RCO) to consolidate the University's oversight of research compliance with pertinent regulations. Previously, such oversight occurred in various parts of the University, depending on where funds for the research came from, or whether the research involved humans, animals, biosafety, or other areas of focus. The RCO has also assumed responsibility for some investigations — known as 'for-cause' investigations — that the IRB previously conducted. 'For-cause' investigations examine concerns about research compliance in response to a specific allegation. These investigations are not part of routine monitoring of compliance with regulations; they may reflect cases in which researchers have not adequately addressed compliance problems or in which University officials want more information on a particular problem. In addition, the RCO will track the ongoing compliance of research projects with regulations and develop accountability measures for approved projects. The University expects to approve policies and procedures for this office in July 2016.

• Use of an External IRB:

Since we issued our reports last year, the University has outsourced the oversight of 12 psychiatry studies involving human subjects. Previously, the University's IRB reviewed the research protocols for these studies and provided ongoing oversight. In 2015, the University entered into an agreement with a private IRB. For studies selected by the University, this IRB (Quorum) has independently examined the research protocols. In 2015, Quorum recommended that one study the University's IRB had already approved be discontinued, due to what it considered an inadequate study protocol submitted by the principal investigator.

Electronic IRB Tracking of Research Studies:

The University is investing approximately $5 million in a new system to make its entire IRB submission, approval, and review process electronic. Part of the expense is to acquire software packages … for researchers and IRB staff and members to communicate, submit, and review documents. The University expects the new system to streamline the current process which University officials characterize as extremely inefficient and ill-suited for the volume and complexity of research the Human Research Protection Program oversees.

The program receives approximately 10,000 unique submissions annually. According to an official in the program, under the current system, '[S]ubmissions are emailed to our office. Each email and all attachments must be downloaded to PDFs and details about the submission must be added by staff into our database (a system implemented in 2005). Each submission and all subsequent communication must also be added to our document routing system and the online file sharing site reviewers use to access materials. Our database feeds minimal information to a system transparent to researchers. They are able to check basic status information but little else. They may be able to see that a submission is under review, but they are unable to view the documents or communication related to that review.'

IRB staff and reviewers will start using some elements of the software in July 2016. But some elements that researchers will use, such as standard operating procedures, templates, worksheets, and an investigator manual, will not be available until the end of the year." ■

REFERENCE

1. Office of the Legislative Auditor. Protections for Human Subjects in Research Studies at the University of Minnesota Department of Psychiatry: A Preliminary Assessment of Reforms. May 16, 2016: http://bit.ly/1YbaxHe.

CME/CE OBJECTIVES

The CME/CE objectives for IRB Advisor are to help physicians and nurses be able to:

1. establish clinical trial programs using accepted ethical principles for human subject protection;
2. apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
3. comply with the necessary educational requirements regarding informed consent and human subject research.

COMING IN FUTURE MONTHS

- Educating IRB members, A through Z
- Urban health center solves dilemma with centralized review functions
- Study initiation program receives positive feedback
- IRB shares best practices in pre-review process

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. Scan the QR code to the right or log on to AHCMedia.com, then select "MyAHC" 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. What were the human research subjects categorized as in a reanimation trial?

A. Alive
B. Dead
C. Living cadavers
D. Clinically subconscious

2. According to FDA officials in discussing the May draft guidance on the "Use of Electronic Health Record [EHR] Data in Clinical Investigations" and its informed consent section, which of the following is the most important foreseeable risk?

A. Subjects sharing personal information about their study participation on social media
B. Data breaches
C. Natural disaster resulting in lost data
D. False medical data

3. The NIH and FDA issued in March a draft protocol template that would help streamline IRB reviews and help investigators navigate the FDA regulatory process. Which of the following is included in the 47-page protocol template?

A. Study design and endpoints, study enrollment and withdrawal, study agent, study procedures and schedule
B. Assessment of safety
C. Source documents and access to source data/documents;
D. All of the above

4. Of almost 600 physicians polled in a cancer research survey, what percent had the misperception that clinical trials should be considered only as a treatment of last resort?

A. 28%
B. 35%
C. 52%
D. 56%