

AAHRPP ADVANCE

FALL 2009

Enhancing Protection for Research Participants

One Set of Standards Protects Research Participants Worldwide

At the beginning of October, AAHRPP published a revised set of accreditation standards meant to provide equivalent protections wherever research is conducted anywhere around the world—and to address any type of research, whether medical or behavioral and social science.

In addition to a new requirement on conducting transnational research, AAHRPP has developed stricter requirements for managing financial conflict of interest, promoting community-based research, and strengthening data and safety monitoring.

None of the new standards or other changes reflects major revisions in the requirements for accreditation. And they continue to urge behavioral and social scientists to join medical investigators in making human research protection meaningful to their work.

The intent in revising the standards is to strengthen Human Research Protection Programs (HRPPs) and to streamline the accreditation process. The revisions reflect a major regrouping of the standards, laying out a more logical framework for an HRPP and better definition of the primary roles and responsibilities of the entities that make up an HRPP.

Overall, AAHRPP has reduced the number of standards from 22 to 15, and the number of elements, from 77 to 60.

AAHRPP released its Proposed Revised Accreditation Standards on June 1, inviting public comment through July 30.

“We were heartened by the groundswell of support for the Proposed Revised Accreditation Standards,” said AAHRPP President and CEO Marjorie A. Speers, Ph.D.

AAHRPP published the Final Revised Accreditation Standards on October 1, 2009. Current and prospective clients may submit applications using either the current or revised standards between October 1, 2009, and February 28, 2010. Beginning March 1, 2010, all new and renewing applicants must follow the revised standards.

“The Final Revised Accreditation Standards are designed to provide a user-friendly way to better ensure the protection of human research participants, in clinical trials or social science studies, wherever they are conducted,” said Peter Vasilenko, AAHRPP Vice President of Accreditation and the leader of the team that revised the standards.

AAHRPP issued the first Accreditation Standards evaluating research protections for human participants in 2002. Since then, it has used them to accredit 194 research organizations including over 930 entities in hospitals, independent IRBs, universities, VA medical centers, and, most recently, the pharmaceutical industry.

“The Final Revised Accreditation Standards are not any easier to meet than AAHRPP’s original standards,” Dr. Vasilenko said, “but they make it easier to conduct quality, ethical research in many different countries at the same time.” Among other improvements, AAHRPP streamlined the accreditation process by reducing the number of Domains, Standards, and Elements.

You can read and download the Final Revised Accreditation Standards and the new Evaluation Instrument for Accreditation at <http://www.aahrpp.org>. Or you may request a print copy by calling (202) 783-1112 or sending an e-mail for a print or electronic version to accredit@aahrpp.org.

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AAHRPP®

Association for the Accreditation of Human Research Protection Programs, Inc.®

Making Our Social Contract Explicit

Never has it been more salient that our ability to conduct research is based on a social contract: The public trusts government, industry, and researchers to act ethically and to demonstrate fiscal responsibility.

The Final Revised Accreditation Standards make explicit that one set of protections must be applied to every research study, regardless of the type of research, where the study is conducted, or who sponsors the study. These revised standards reflect AAHRPP's vision to have a universal set of standards for conducting research ethically.

As you can see in this issue of *AAHRPP Advance*, the growing demand for human research—and especially multi-site, transnational clinical trials—is in turn fueling the demand for accreditation standards that can ensure public trust in the organizations and companies responsible for keeping participants safe from harm in medical, behavioral, and social science research.

Meanwhile, two articles on the following page illustrate how AAHRPP is increasingly becoming a source of information for improving the ethical oversight of research conducted transnationally, generally, and in Korea, in particular.

Pfizer, after requiring nearly a year ago that IRBs overseeing its U.S. studies be accredited and then earning accreditation for its own phase 1 research units in the spring, held an "Industry Summit" in July to discuss the many issues associated with the globalization of clinical trials, such as accreditation.

Representatives from academia, independent IRBs, and industry, in-

cluding AAHRPP, joined more than 10 other industry sponsors for the summit at Pfizer's Midtown headquarters in Manhattan.

And in Washington, AAHRPP hosted two fellows this summer from the Republic of Korea. They were sponsored by the Korean Association of Institutional Review Boards (KAIRB) and supported by the Korean Ministry for Health, Welfare, and Family Affairs, which would like to have KAIRB prepare the country's IRBs for accreditation.

As more organizations around the world and in the United States achieve accreditation, they produce more examples of innovative practices, such as those featured on pages 4 and 5.

It's no secret that some worry that increasing attention to human research protections might impede quality research, while others say that organizations can have both safety and good science at once.

The University of Colorado Denver and The University of Texas Health Science Center at Houston prove the point that only the most rigorous science yields the most ethical science and, therefore, that only the most ethical research yields the highest-quality research. (See pages 4 and 5.)

At the University of Colorado Denver, every new IRB member, alternate member, and consultant is mentored one-on-one by the board's chair or a senior member of the board.

And at The University of Texas Health Science Center at Houston, funding cannot be released for a study unless the investigator has

attended a course in protecting participants. This is not unique. The health science center, however, not only requires each new investigator to participate actively in a small, interactive seminar; the seminar is taught by the institution's executive vice president for research.

That kind of investment of individuals in their research community is even more important when research participants are children. Last month, AAHRPP awarded accreditation to three independent children's hospitals (pages 6 and 7). Those three institutions joined two others accredited earlier in the year, more than tripling the number of such hospitals in one year.

Just as increasing numbers of clinical trials around the globe are creating pressure to accredit greater numbers of research organizations, continuing demand from government and industry to include children in clinical studies is encouraging children's hospitals to achieve accreditation, according to officials at those institutions.

With all these opportunities to expand protections and improve the research quality required to ensure those protections, for more and more people in more and more places, I'm pleased to tell you that plans to help you "Take Your HRPP to the Next level" at the AAHRPP Annual Conference, April 12-14, 2010, at Atlanta's Omni Hotel at CNN Center, continue to develop apace. We look forward to seeing you there.

— *Marjorie A. Speers, Ph.D.*

Fellows Learn to Apply Accreditation to Korea

AAHRPP fellowship program for KAIRB

AAHRPP worked with the Korean Association of Institutional Review Boards (KAIRB) this summer to host two fellows in Washington, so that they could become familiar with how to conduct the accreditation process in their home country.

Interest in accreditation in Korea began in 2006 when Samsung Medical Center, in Seoul, earned accreditation. Several other Korean medical centers are seeking accreditation, prompting the Korean Ministry for Health, Welfare, and Family Affairs to fund the fellowship program with AAHRPP.

“The fellows program grew out of the ministry’s desire to have KAIRB evaluate all IRBs in Korea and prepare the organizations for accreditation,” according to Marjorie

A. Speers, Ph.D., AAHRPP’s President and CEO.

AAHRPP fellows Byung-In Choe, M.B.A., L.L.M., Ph.D., Associate Professor of Bioethics at the Catholic University of Korea and a member of the Academic Board of KAIRB, and Sang Cheul Oh, M.D., Ph.D., Associate Professor of Oncology at Korea University, worked over the summer with AAHRPP accreditation directors to:

- Gain proficiency in evaluating an application for accreditation.
- Identify the major areas of strengths and weaknesses in applications for accreditation.
- Understand how to conduct a self-assessment and prepare for accreditation.

Drs. Choe and Oh were shown how AAHRPP accreditation directors work with organizations seeking accreditation and how AAHRPP site visitors interact with those organizations to make sure that the policies and procedures identified in the accreditation process are actually put into practice. During their stay, they visited several accredited organizations, as well as government agencies.

In the mid-1990s, the Korean government opened the country to foreign industry sponsors. Recognizing the need to strengthen the research infrastructure, KAIRB has helped Korean IRBs build ethical review capacity to meet international levels of performance. And in recent years, the major clinical trials centers have sought AAHRPP accreditation.

Summit Focuses on Multi-Regional Trials

Industry meets at Pfizer

Representatives from the clinical research enterprise, including AAHRPP, addressed concerns on conducting multi-regional clinical trials at a recent industry summit hosted by Pfizer in New York City.

Critics of such multi-regional studies, according to Justin P. McCarthy, Chief Counsel for Pfizer Global Research and Development, tend to focus on:

- Skepticism about why manufacturers conduct trials in emerging markets, and
- Worries about the standards of quality and ethical oversight applied to such studies.

The summit was convened to address those concerns, McCarthy said.

“We all have a shared responsibility for addressing these issues. And only by working together can we effect meaningful changes that improve trust and credibility in our practices for doing those trials,” he explained.

One factor in moving trials outside Western Europe and the U.S. is that, as in the U.S., “the pharmaceutical industry is not viewed favorably in the emerging markets,” according to Professor Dirceu Greco from Brazil’s Federal University of Minas Gerais, who spoke at the industry summit.

Summit attendees, who agreed to meet again in the fall, included representatives from PhRMA, Merck, AstraZeneca, Abbott, GlaxoSmithKline, Novartis, Bristol Myers Squibb, Hoffman LaRoche, Johnson & Johnson, Schering-Plough, Eli Lilly,

Harvard Medical School, the University of Pennsylvania, Duke University, AAHRPP, Chesapeake Research Review, Western IRB, and Quintiles, among others, in addition to Pfizer.

They took part in panels on “Protocol, Informed Consent, Ethics Committee Review,” “Data Monitoring Committees, Endpoint Adjudication Committees, and Safety Reporting,” “Investigator Training and Selection,” and “Monitoring and Use of Clinical Research Organizations.”

Those who attended concluded that manufacturers and the research industry can and should improve the ethical review process for trials conducted in developing countries, and they discussed accreditation as a way to improve ethical review.

Quality Research IS Ethical Research

Every researcher involved with an incident of serious non-compliance at The University of Colorado Denver may be required to serve six months on one of the school's IRBs.

Most of them ask to serve longer.

At The University of Texas Health Science Center at Houston, research cannot be funded until investigators have taken a course in protecting research participants.

The teacher: the center's Executive Vice President for Research.

The goal at both organizations is to make people feel they are part of an interdependent support community of investigators who do their best research because they do ethical research.

Individual Attention at UC Denver

"A non-compliant investigator has usually made an inadvertent mistake," says Alison Lakin, R.N., L.L.B., L.L.M., Ph.D., and Director of the Colorado Multiple IRB and Human Subject Research Committee at the University of Colorado Denver (UC Denver).

Dr. Lakin believes that exposing individual researchers to the IRB shows them that the review process at UC Denver is not arbitrary, but "collaborative, dynamic, and collegial," aimed at integrating the science of a protocol with researchers' responsibility for participants.

The university has more than 4,000 researchers and five IRBs, four biomedical and one behavioral. And requiring non-compliant

investigators to serve on IRBs is just one example of the individual attention UC Denver gives to key players in its human research protections program.

The same level of attention goes to every new member of an IRB at UC Denver.

When the institution started a program to train new IRB members on the regulations, policies, and procedures regarding human research protection, "people still felt left on their own," Dr. Lakin says.

Today, every new IRB member, alternate member, and consultant goes through a rigorous selection and supportive, one-on-one mentoring process at UC Denver.

When someone shows an interest in serving on an IRB, Dr. Lakin conducts an interview to gauge the depth of that person's interest and

commitment to helping researchers bring their protocols in line with the ethical treatment of research volunteers. If that goes well, the IRB reviews an application from the potential member to serve on the IRB.

If the application is accepted, the potential member must pass the basic and IRB-member modules from the Collaborative Institutional Training Institute before being invited to attend two meetings of an IRB.

"We want them to experience what peer review is actually like," Dr. Lakin says. "We invite them into what many think of as a black box, in order to experience how the IRB is actually an open resource for investigators." After each meeting, the IRB chair or a senior member talks with new members about their questions.

Then the chair or a senior member is matched with each new member for a "mentored primary review" of a protocol, which includes a written and verbal debriefing where the chair and other members comment on the new member's review.

The idea is to provide an intense experience that is both rigorous and supportive, so that no IRB members feel "left on their own" and all members understand that their job is to make it possible for researchers to do high-quality, ethical scientific research.

Dr. Lakin says she looks forward to a time when all investigators at the university are required to attend an IRB meeting, so that they understand how the IRB can help them improve the quality of their research. But, as a former mediator herself, she knows that can happen only over time. "We can't just mandate things if we want to have a collegial, mutually supportive community," she says.

You may contact Dr. Lakin at alison.lakin@ucdenver.edu or (303) 724-1058.

Collegiality from the Top in Houston

Many university presidents and vice presidents are able to spend little time on the human research protection program at their institutions.

But that's not the case with the Executive Vice President for Research at The University of Texas Health Science Center at Houston, Peter J. Davies, M.D., Ph.D. He teaches the small-group seminars on human research protections that all investigators must attend before funding for any of their protocols is released to them.

Investigators at most universities have to attend often large classes taught by HRPP staff, in order to become familiar with regulations, policies, and procedures. But having the leader of the research protection program tell individual investigators, "This is our culture," persuades each investigator to make concern for participants a top priority.

Lots of investigators say, "We want to be in compliance ... but it hurts the quality of the research." Dr. Davies, on the other hand, emphasizes that "high-quality research IS ethical research."

A former investigator himself, Dr. Davies sympathizes with faculty. "They feel piled on and helpless in the face of relentless increases in the number of regulations and requirements they have to meet in order to do their work," he says, "especially when the burden is imposed without their input."

Dr. Davies, for his part, rarely mentions the word "compliance" and never does so in initial meetings with his investigators. "It would be like waving a red flag at a bull," he says. Instead, they start off talking about how investigators can get their research done in ways that meet their responsibilities as ethical members of the university community—and that help them get funded.

"They usually come into the meeting in an oppositional mood, and leave feeling collegial," Dr. Davies says.

Dr. Davies and his team discovered early on that "point-to-mass communications" don't work with large groups of scientists. He had to meet with them in small groups, no larger than 10 and often fewer. "We found that we needed to engage faculty in conversations that often developed into discussions about their concerns," he says. And once their leader proved he could listen, they would listen to him.

In the end, Dr. Davies's faculty members feel they have ownership, with administrators and staff, of every aspect of their research, including their responsibilities to the institution where they conduct it and the people they recruit to participate in their studies.

The University of Texas Health Science Center at Houston devotes a section of its Web site to Dr. Davies's program at <http://www.uth.tmc.edu/orsc/training/InvestigatorResp.html>, which explains that every investigator must go through the training

initially, and every three years after that.

He started the Investigator's Responsibility Training Briefing three years ago, modeling it on the health science center's health and safety program, which ensures that all research meets strict regulations for the disposal of medical and other dangerous waste. "They have a very strong enforcement role," he says, "but the investigators look upon them as friends and helpers."

It's like the story of the researcher who performs high-risk research among adolescents. These children would assent to joining his studies only if their parents didn't know about the nature of the research. Expecting the investigator to be dissatisfied with his IRB, a colleague asked him about his relationship with the IRB.

"I love my IRB!" he exclaimed. "Instead of telling me what I can't do, they say to me, 'Here's how we can work together to make it possible.'"

You may contact Dr. Davies at Peter.J.Davies@uth.tmc.edu or (713) 500-3082.

Informed Consent Toolkit from AHRQ

Researchers can now download the new AHRQ Informed Consent and Authorization Toolkit for Minimal Risk Research free from the DHHS Agency for Healthcare Research and Quality at <http://www.ahrq.gov/fund/informedconsent>.

AHRQ created the toolkit to aid researchers in developing consent forms that will help potential study participants understand what they consent to when they agree to participate in a study and what the study will require of them.

The toolkit helps researchers obtain potential research participants' informed consent and authorization to use their health data in accordance with the Privacy Rule of the Health Insurance Portability and Accounting Act (HIPAA).

Accreditations at Children's Hospitals Follow Rise in Research with Children

Continuing demand from government and industry to include children in more clinical studies, as well as healthy competition for funding for those studies, is stimulating more independent children's hospitals to earn accreditation, according to researchers and HRPP administrators at such hospitals.

Nearly three times as many independent children's hospitals have already earned accreditation in 2009 as were accredited in the previous eight-year history of AAHRPP.

Among all children's hospitals receiving awards from the National Institutes of Health in 2008, more than a third are now accredited.

In September, Miami Children's Hospital, Connecticut Children's Medical Center Corporation, and Children's Healthcare of Atlanta, Inc., joined Nationwide Children's Hospital, accredited in June, and Nemours, which earned accreditation in April 2009.

Cincinnati Children's Hospital Medical Center and Children's Hospital Boston earned accreditation previously, in 2007 and 2005, respectively.

When asked why so many independent children's hospitals were seeking and earning accreditation



The assessment of risk versus potential benefit, the need for parental permission or waiver of permission, and levels of assent from the children themselves make IRBs particularly sensitive to children's need for different kinds of protection.

now, representatives from those hospitals that have been accredited agreed that an emphasis on conducting more research on children is driving the increased interest in accreditation.

Sarah H. Kiskaddon, J.D., M.A., Director of the IRB at Connecticut Children's Medical Center Corporation, says that the number of protocols in pediatric oncology, for example, is increasing faster than those involving adults.

"Accreditation is also a great way to assure patients and parents that everyone who treats them are working closely together," Kiskaddon says, "since the accreditation process brings everyone together around best practices."

And beyond oncology research, according to Amelia Halac, M.D., Assistant Director of the Research Institute at Miami Children's Hospital, accreditation helps parents and children understand that there are rules for conducting clinical research that focus on protecting human research participants.

"Assuring them about protection can be a sensitive issue," especially among pa-

tients who are new to the American health care system. Accreditation builds confidence among participants by providing credibility, Dr. Halac says.

At Children's Healthcare of Atlanta, Inc., "accreditation is a clear sign to our community, patients, and participants that we are among those conducting the highest-quality, most ethical research among children," according to Kristine Rogers, Director of Clinical Research and Research Integrity Officer.

Representatives from accredited independent children's hospitals report that the number of research studies involving children has increased since the 1990s and that the need for accredited research protection programs for children has followed suit.

Robert Frenck, Jr., M.D., Professor of Pediatrics at Cincinnati Children's and Chair of the IRB there, said he thinks peer pressure, and ultimately competition for resources, especially from such outside funders as industry sponsors, is also driving the trend.

Before, according to Susan Kornetsky, M.P.H., C.I.P., Director of Clinical Research Compliance at Boston Children's Hospital, many researchers maintained that protecting children was preventing them from conducting research involving

children. But when the Food and Drug Administration (FDA) published specified additional protection requirements for children enrolled in research in its regulations in 2001 (Subpart D), organizations became more confident that they were conducting research involving children safely and ethically, and they wanted the public to know.

“We need to do more research with children,” according to Kornetsky, because every doctor’s “best guess” for prescribing a drug for children, based on its use in adults, “means that every child receiving the drug is being experimented on.” And children enrolled in research, especially, need protection.

What Kornetsky and other HRPP administrators and investigators call “the rapid increase in children’s research” stimulated many organizations to upgrade their infrastructure for protecting children in research. They say accreditation helps them put that infrastructure in place.

“The standards have to be higher in children’s research,” Kornetsky says, “because we are dealing with children.”

Because children are more vulnerable than competent adults, the Department of Health and Human Services and FDA regulations treat them differently. The assessment of risk versus potential benefit, the need for parental permission or waiver of permission, and levels of assent from the children themselves make IRBs particularly sensitive to children’s need for different kinds of protection.

The accreditation process “confirmed and validated our efforts to protect the children,” according to Brady Reynolds, Ph.D., who conducts behavioral research on smoking cessation among adolescents at Nationwide Children’s Hospital in Columbus, Ohio.

“It was a centering experience,” says Dr. Reynolds, who reports that

accreditation brings researchers and IRB members together around what they have in common: caring for children.

It also strengthens trust in the research enterprise, among parents of patients and the public, according to Dr. Frenck.

At Nemours, the need to ensure public trust in its expanding research enterprise created a major shift in culture, according to Carlos Rose, M.D., C.I.P., chair of one of the organization’s IRBs. Along with seeking accreditation, Nemours formed a single HRPP to oversee each of its separate protection programs in Florida and Delaware, as well as one for pediatric oncology across the organization.

“Seeking accreditation energized

the institution and increased interest in assent issues, and it makes us hyper-compliant,” Dr. Rose says.

Jeremy J. Corsmo, M.P.H., C.I.P. agrees that pediatricians at Cincinnati Children’s, where he directs the Office of Research Compliance and Regulatory Affairs, feel extremely vested in wanting to protect children: “It’s not an afterthought.”

Nationwide’s Dr. Reynolds and Corsmo agree that researchers value the IRB members at their hospitals as colleagues in helping them protect children. “That wasn’t necessarily the case five years ago,” Corsmo says. But the transparency required by accreditation eliminated the perception that “the IRB is just a black box where a researcher submits a protocol and waits for a decision.”

Three Children’s Hospitals Among Seven New Accreditations

Three independent children’s hospitals earned accreditation in September along with four other organizations. They bring the number of accredited organizations to 194, representing more than 930 entities.

Newly Accredited Organizations

Full Accreditation

- **Children’s Healthcare of Atlanta, Inc.**, Atlanta, GA
- **Connecticut Children’s Medical Center Corporation**, Hartford, CT
- **Medical University of South Carolina**, Charleston, SC
- **Miami Children’s Hospital**, Miami, FL
- **Ralph H. Johnson VA Medical Center**, Charleston, SC
- **University at Buffalo—State University of New York**, Buffalo, NY



Qualified Accreditation

- **The University of Texas Medical Branch at Galveston**, Galveston, TX

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NEWS & NOTES

Prepare for what's ahead! At AAHRPP's 2010 conference in Atlanta, April 12-14

Taking human research protection programs to the next level

With practical give-and-take on how to:

- Apply the revised accreditation standards to your program
- Especially the new standards on conflict of interest, transnational research, and community-based participatory research
- Complete the accreditation process
- Meet challenging issues like tissue repositories, contingency planning, multisite research review, community engagement in planned emergency research, and using electronic systems to meet the accreditation standards.

Contact AAHRPP at (202) 783-1112 or accredit@aahrpp.org, or see www.aahrpp.org for more information.