AAHRPP ADVANCE
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SUMMER 2018

Improving Communication Between CIRBs and DSMBs

In May 2017, the StrokeNet CIRB took the unprecedented action of suspending enrollment of a specific group of patients in the DEFUSE 3 trial based on data that was available but not yet published. A recent AAHRPP conference session took a look at this decision and the relationship between CIRBs and DSMBs. **LEARN MORE**

K. Sue Haddock: Council Chair and AAHRPP Ambassador

Get to know Council on Accreditation Chair K. Sue Haddock, PhD, RN, FAAN. The Associate Chief of Staff for Research & Development at WJB Dorn VA Medical Center in South Carolina, Dr. Haddock leads council discussions on accreditation, is a site visitor, and presents at AAHRPP conferences. **LEARN MORE**

Highlights from the 2018 AAHRPP Conference

Representatives of accredited and non-accredited organizations, plus our federal and founding organization friends, turned out in force for the 2018 AAHRPP conference, which featured some of the nation's most respected experts on the Common Rule and other complex research protection issues. Check out a sample of photos from the event.
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From the President and CEO

AAHRPP President and CEO Elyse I. Summers, JD, discusses the value of AAHRPP accreditation during uncertain times. As organizations wrestle with changes to the Common Rule—and shifting dates for implementation—AAHRPP standards continue to provide an assurance of quality. **LEARN MORE**

Upcoming Webinars

July 24 and 26: Successful Strategies for Adjusting to the New Rule
October 9 and 11: A key HHS official will share insights on pressing issues. (Title TBD.)
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SUMMER 2018

INSIDE

LATEST ACCREDITATIONS

- **Avera Health,** Sioux Falls, South Dakota
- **The Board of Regents of the University System of Georgia,** by and on behalf of the University of Georgia, Athens, Georgia
- **Loma Linda University Health,** Loma Linda, California
- **The Rector and Visitors of the University of Virginia,** Charlottesville, Virginia
- **Temple University of the Commonwealth System of Higher Education,** Philadelphia, Pennsylvania

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SAVE THE DATE

2019 AAHRPP Conference: May 21–23
Ritz Carlton, New Orleans

Improving Communication Between CIRBs and DSMBs

When, if ever, should a central IRB (CIRB) stop enrollment in a clinical trial without agreement or coordination with the trial's data safety monitoring board (DSMB)?

That was the question faced last year by the University of Cincinnati CIRB, which serves as the central IRB for the National Institutes of Health (NIH) StrokeNet, a stroke trials network.

On May 24, 2017, the StrokeNet CIRB answered that question by taking the unprecedented action of suspending enrollment of a specific group of patients at all trial sites based on results from a separate but related trial that were available but not yet published. The action was taken independent of a recommendation of the DSMB.

"The data was presented as an abstract at a meeting. That's not the same as publishing it in a journal," says Michael Linke, PhD, CIP, CIRB Chair and Associate Professor of Medicine, University of Cincinnati. "The decision to use those data was controversial, but it was very clear that the outcomes were better for one study group. The CIRB felt there was no longer equipoise."

In the past, when study review involved multiple IRBs, such a decision most likely would have affected enrollment at only a single site. Instead, because the study review was handled by a CIRB, enrollment was halted at sites nationwide.

"As we move more and more to central IRB review, CIRBs will have more power and more responsibility," Dr. Linke says.

He was one of four presenters of "Overlapping Roles of DSMBs and IRBs in the Protection of Human Research Participants," a session at the 2018 AAHRPP conference in Denver in April. Dr. Linke's presentation focused on the University of Cincinnati/StrokeNet CIRB's experience with a DSMB from the StrokeNet DEFUSE 3 study and reported results from an independent but related industry-sponsored trial called DAWN. Although the two trials had different eligibility criteria for subject participation, both studies were testing the effectiveness of blood clot removal in stroke patients who presented for treatment more than six hours from initial onset of symptoms.

Todd W. Rice, MD, MSc, Associate Professor of Medicine and Medical Director, Vanderbilt University HRPP, who serves on DSMBs, covered the current DSMB-IRB relationship. Megan Kasimatis Singleton, JD, MBE, CIP, Assistant Dean for Human Research Protections & Director of the HRPP at Johns Hopkins University School of Medicine, shared a case example on "The Existing Model-What Can an IRB at a Single Site Do?" Robert Silbergleit, MD, Professor, University of Michigan, provided recommendations for improving DSMB-CIRB interactions.

"The decision to use those data was controversial, but it was very clear that the outcomes were better for one study group. The CIRB felt there was no longer equipoise."

— Michael Linke, PhD, StrokeNet CIRB

"The key is to think of the DSMB-CIRB relationship as a partnership," Dr. Silbergleit says. "Everyone has the same goal of protecting human subjects. With a little bit of planning and willingness to communicate and coordinate, that partnership can work most effectively."

The AAHRPP conference session was so well-received that the presenters were asked to repeat it at a Society for Clinical Trials meeting and at the 2019 AAHRPP conference in New Orleans.

The DAWN and DEFUSE studies—and the CIRB decision

Previous studies had demonstrated that removing a blood clot in the brain (endovascular thrombectomy) in combination with standard medical therapy was more effective than medical therapy alone for patients who presented for treatment within six hours of stroke onset. The DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes) trial enrolled a subset of patients between six and 24 hours after the start of stroke symptoms who were selected by an advanced stroke imaging strategy. The DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3) study enrolled patients between six and 16 hours from the time of symptom onset, who were selected by an alternative but similar strategy.

Both studies enrolled patients whose imaging scans showed a large-vessel blockage and salvageable brain tissue. Both studies randomly assigned patients to receive either the combination clot removal and medical therapy or medical therapy alone. DAWN had more narrow enrollment criteria, focusing on patients with smaller core lesions and more severe stroke symptoms. As a result, about half of DEFUSE 3 patients were not eligible for DAWN.

Improving Communication Between CIRBs and DSMBs (cont.)

On May 16, 2017, Dr. Linke and the other StrokeNet CIRB members faced a dilemma when the DAWN trial findings were presented at the European Stroke Organisation Conference in Prague. Patient enrollment in DAWN had ended early, in March 2017, when the interim review of data found a significant benefit to one group of patients—those receiving the combination therapy.

> **"The key is to think of the DSMB-CIRB relationship as a partnership. … With a little bit of planning and willingness to communicate and coordinate, that partnership can work most effectively."**
>
> **— Robert Silbergleit, MD, University of Michigan**

Despite the similarity between the DAWN and DEFUSE 3 trials, the DEFUSE 3 DSMB did not call for changes to DEFUSE 3 enrollment. Instead, the DSMB cited the potential impact on DEFUSE 3 participants who were ineligible for DAWN, and recommended that any decisions regarding DEFUSE 3 be made after the DAWN results were published. The DSMB also scheduled an urgent meeting May 26, 2017, to consider these issues.

The StrokeNet CIRB disagreed. After discussion with the principal investigator, the CIRB suspended enrollment of patients who met the DAWN criteria but permitted continued enrollment of DAWN-ineligible patients.

"The CIRB determined that the rights and welfare of DEFUSE 3 participants who did not meet the DAWN criteria remained favorable," Dr. Linke explains.

The CIRB decision was not made lightly, in part because such decisions typically are the purview of the DSMB.

"There was a lot of discussion and a lot of angst. We knew we could be shutting down a multimillion-dollar study," Dr. Linke says. "But it was an emergent situation, and the results clearly were better for one group of patients."

In fact, once the results for both studies were published, the combination therapy became the new standard of care.

Recommendations for DSMB-CIRB interactions

For Dr. Silbergleit, a principal investigator for the new NIH-funded Strategies to Innovate Emergency Care Clinical Trials Network (SIREN), the StrokeNet CIRB experience with DEFUSE 3 underscores the need to establish best practices for CIRB-DSMB interactions.

Because SIREN is still laying the groundwork for CIRB and DSMB roles and responsibilities, Dr. Silbergleit sees an opportunity for the network to learn and try to anticipate and address potential CIRB-DSMB differences. He also emphasizes the critical contributions of the investigator as the liaison to help the CIRB and DSMB coordinate decisions and recommendations.

The place to start, Dr. Silbergleit says, is with an understanding of the roles of the CIRB and DSMB, recognition that they inevitably have overlapping responsibilities, and appreciation of the strengths, resources, and expertise that distinguish the two entities from one another.

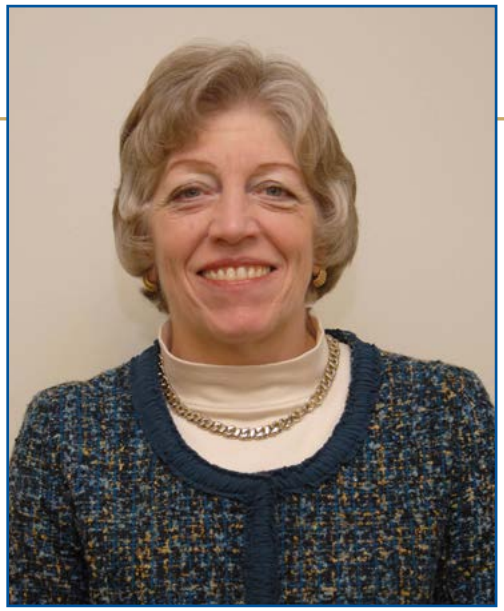
"There are going to be times when an IRB or DSMB will have to recognize that the other body is simply better-equipped than they are for a particular area of shared responsibility," he says. "In those cases, you need to be prepared to allow somebody else to take the lead on a decision because they have the capacity and the resources that you don't."

He sums up his recommendations as follows:

- Acknowledge resources
- Delineate shared responsibility
- Designate leads for areas of overlap
- Plan to talk

For Dr. Linke, that last recommendation could have made all the difference during the DEFUSE 3 trial. "There was no route for communication," he says. "If I could have just called the chair of the DSMB, that could have really helped."

K. Sue Haddock: Council Chair and AAHRPP Ambassador



K. SUE HADDOCK, PHD, RN, FAAN

Seven years ago, K. Sue Haddock, PhD, RN, FAAN, accepted an invitation to become a subject matter expert on the AAHRPP standards and serve as an AAHRPP site visitor. The more she learned, the more Dr. Haddock increased her commitment to AAHRPP and accreditation.

Today, the Associate Chief of Staff for Research & Development at WJB Dorn VA Medical Center in South Carolina chairs AAHRPP's Council on Accreditation, the group of experts responsible for decisions on organizations' accreditation status. She remains a site visitor and presents at AAHRPP conferences, covering topics such as quality improvement and common site-visit findings.

"I find joy and satisfaction in helping people and organizations take the next step or see things in a new way," Dr. Haddock says. During a site visit, for example, "helping organizations understand the essence of the AAHRPP standards and elements, and providing ideas on how to meet them, is an important part of improving that organization's human research protection program and the field of research protections as a whole."

With her colleagues on the Council on Accreditation, Dr. Haddock reviews applications for accreditation and site visitor reports and recommendations on accreditations. All council members are experienced site visitors. They include physicians, researchers, university administrators, and heads of IRBs, human research protection programs (HRPPs), and research compliance programs.

"Each person's perspective is a little bit different, which is why it's important that everyone has the opportunity to voice any concerns they might have," Dr. Haddock says. "As chair, it's my responsibility not only to lead the discussion on the review but also to ensure that every voice is heard."

As a site visitor in the field, Dr. Haddock's approach reflects AAHRPP's emphasis on helping organizations recognize and apply the flexibility in the AAHRPP standards and, ultimately, achieve accreditation. She views the two-step accreditation process—with its input and back-and-forth exchange after the self-evaluation, followed by the site visit—as instrumental in helping organizations improve the quality of their HRPPs and the science that results from research.

"Our goal is to help every organization reach a standard that protects human subjects going forward," Dr. Haddock says. "The process has become a lot more consultative and supportive. We don't tell the organizations what to do, but we do share what's worked for others."

She is an ideal ambassador for AAHRPP in part because WJB Dorn has gone to great lengths to maintain accreditation. The VA medical center attained accreditation in December 2008 and was reaccredited for the first time in 2011. A year later, when the U.S. Department of Veterans Affairs ended its contract with AAHRPP, many VA facilities found themselves financially unable to continue with AAHRPP accreditation. But Dr. Haddock successfully appealed to WJB Dorn's affiliated research foundation to cover accreditation costs.

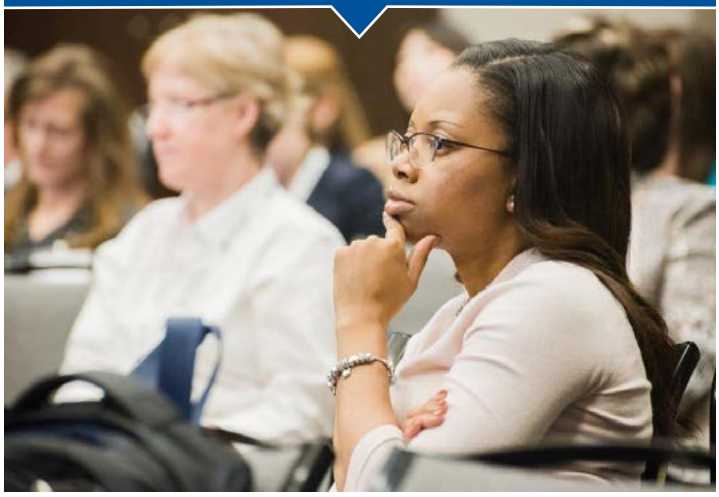
"We know how important it is to maintain our accreditation," she says, "to be able to say to partners in pharmaceutical and other industries that, if you invest your research dollars here, you can be assured we meet AAHRPP's high standards."

Connecting at the 2018 AAHRPP Conference in Denver

AAHRPP President and CEO Elyse I. Summers, JD, (at podium) during the opening address.

Megan Kasimatis Singleton, JD, MBE, CIP, Assistant Dean for Human Research Protection and Director of the HRPP, Johns Hopkins University School of Medicine

Focused on the presentation



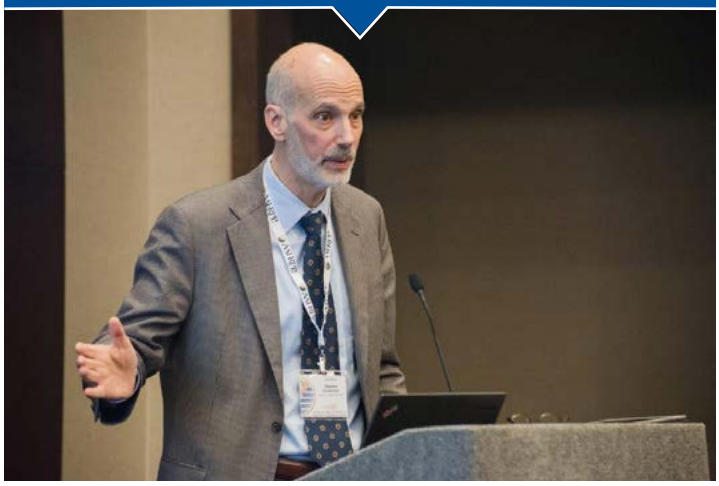
Robert Hood, PhD, AAHRPP Director of Accreditation, during one of the many breakout sessions

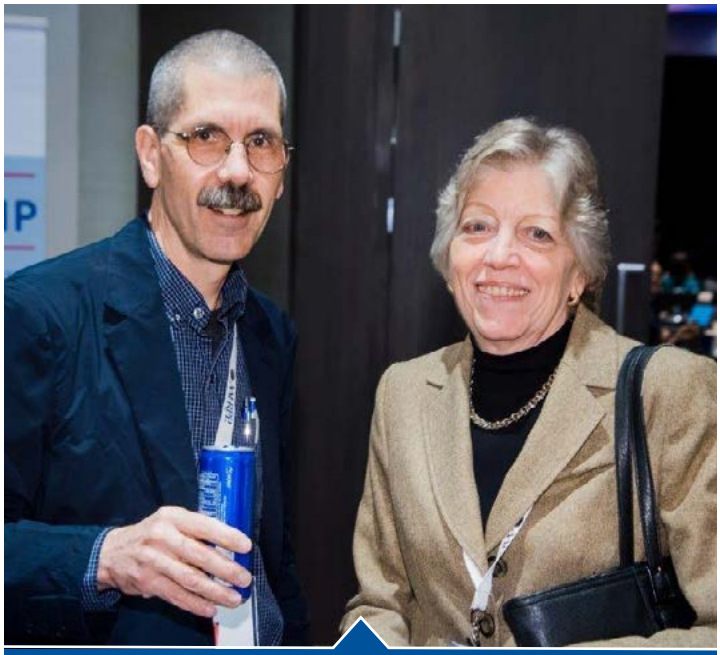
Ivor Pritchard, PhD, Senior Advisor to the Director of the Office for Human Research Protections

Conferring over a poster presentation

Connecting at the 2018 AAHRPP Conference in Denver

Stephen Rosenfeld, MD, MBA, of Quorum Review; Chair, Secretary's Advisory Committee on Human Research Protections



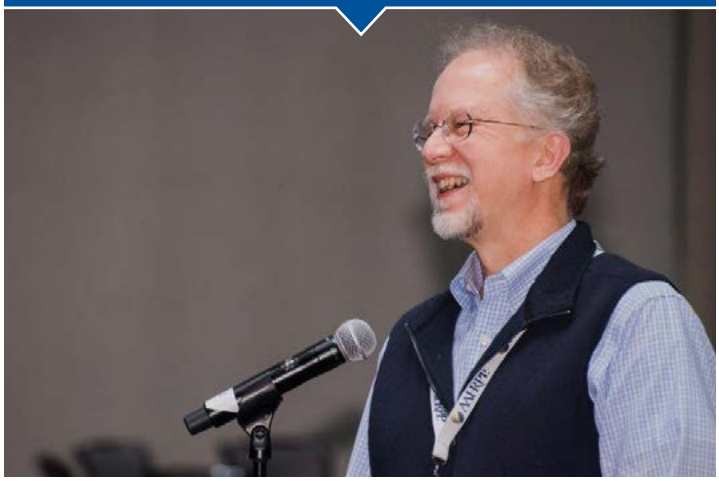


Wesley Byerly, PharmD, Associate Vice President for Research Compliance at University of Connecticut Health Center, and AAHRPP site visitor, with K. Sue Haddock, PhD, RN, FAAN, Associate Chief of Staff for Research & Development at WJB Dorn VA Medical Center, and Chair, AAHRPP Council on Accreditation

From left, Nichelle Cobb, PhD, Director, Health Sciences IRBs, University of Wisconsin- Madison, recipient of AAHRPP's Distinguished Site Visitor Award, with AAHRPP President and CEO Elyse I. Summers, JD

The AAHRPP team, *from left*: Front row, Rob Withrow, Director of Operations; Marianna Suleymanova, Operations Coordinator; Robert Hood, PhD, Director of Accreditation; Elyse I. Summers, JD, President and CEO; Lori Kravchick, Office Manager; and Lindsey Lucente, Program Assistant. Back row: Harry Frazier, Controller; Oscar Platero, Assistant Director of Operations; Michelle Feige, MSW, LCSW-C, Executive Vice President; and Kate Vulakovich, Assistant Director of Accreditation

Daniel Nelson, MSc, Director, Human Research Protocol Office, U.S. Environmental Protection Agency



From the President and CEO

The value of AAHRPP standards in times of uncertainty

ELYSE I. SUMMERS, JD

For those of us concerned with human research protections, the months since the approval of the updated Common Rule have often seemed marked by uncertainty. As you recall, the new rule was published January 19, 2017, with an implementation date of January 2018. Early this year, the U.S. Department of Health and Human Services and 15 other federal agencies delayed implementation by six months to July 2018. In June, the implementation date was postponed again—to January 21, 2019.

At AAHRPP, we understand the reasons for these delays. We also are doing everything possible to minimize their impact on accredited and not-yet accredited organizations, as well as on all stakeholders in the research enterprise.

Perhaps our most significant contribution is the AAHRPP standards themselves. With one notable exception related to single IRB review of multisite research—which itself was created to provide foundational guidance in this time of uncertainty—AAHRPP standards remain constant. They are a beacon of sorts for all who are committed to protecting research participants and advancing high-quality, ethical research.

In the months since the first announcements about the new rule, AAHRPP standards have continued to have a significant, positive impact on research protections in the U.S. and around the world. AAHRPP-accredited organizations have maintained their commitment to AAHRPP standards, providing essential assurances of quality to research participants, sponsors, and other partners. Organizations that are in the process of attaining accreditation have remained focused on that goal and continue to strengthen their programs and align their policies with AAHRPP's requirements.

At the same time, AAHRPP has taken significant steps to prepare for the provisions of the new rule—and to help research organizations do the same. For starters, we have revised our **Evaluation Instrument** to reflect the new rule, which, among other things, includes three burden-reducing provisions that organizations can opt to implement this month. AAHRPP guidance and processes allow our accredited organizations to exercise this option.

Notably, our 2018 AAHRPP conference featured numerous sessions on the provisions of the new rule. In addition, we continue to offer webinars on new-rule-related topics. In fact, later this month, Dave Borasky, MPH, CIP, Vice President of IRB Compliance for WIRB-Copernicus Group, and Monika Markowitz, PhD, MA, MSN, RN, Director of the Office of Research Integrity and Ethics for Virginia Commonwealth University, will be the featured speakers for our **webinar** on "Successful Strategies for Adjusting to the New Rule." There's still time to **register**.

In other words, we're ready. And so are many of you.

Elyse I. Summers, JD
AAHRPP President and CEO

Of Note

AAHRPP senior staff recently contributed to a book chapter and journal article on issues related to research involving human participants.

- President and CEO Elyse I. Summers, JD, and Executive Vice President Michelle Feige, MSW, LCSW-C, co-authored Chapter 5, "Accreditation of Human Research Protection Programs" in *Principles and Practice of Clinical Research*, Fourth Edition, Academic Press (an imprint of Elsevier), 2018.

- Feige co-authored "**Broad Consent for Research on Biospecimens: The Views of Actual Donors at Four U.S. Medical Centers**," published February 1 in the *Journal of Empirical Research on Human Research Ethics.*