RESEARCH PROTECTIONS UPDATE

News and Comment on the Protection of Human Subjects in Navy and Marine Corps Research

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Commentary

DON HRPP Compliance Specialists Gather Nuggets of Wisdom From the PRIM&R AER 2018 Conference

The Public Responsibility in Medicine and Research (PRIM&R) Advancing Ethical Research (AER) conference was held in San Diego, California, November 14-17, 2018. The annual conference brings together various stakeholders in the human subject protections, research ethics and research oversight arena to discuss, learn and deliberate on issues pertaining to human subject research. Due to the nature and content of the PRIM&R AER conference, Command human research protections personnel are encouraged to attend. Department of the Navy Human Research Protections Program (DON HRPP) Compliance Specialists were also in attendance and returned with insightful bits of information to share:

Patti Yasenchak

In the closing general session, "Research Ethics, Race, and Opioids – the Evolution of the Perfect Epidemic," Brenda L. Curtis, PhD, MSPH discussed the importance of language. When it comes to materials for subjects, such as informed consent forms, we know about the importance of using non-technical language and short sentences and paragraphs. However, this talk included the influence of language in perpetuating stigma and discrimination. For example, a study has shown a bias in treatment professionals when patients are said to "abuse" drugs as opposed to having a "SUD" (Substance Use Disorder). Another example is using the term "recurrence of use" as opposed to "relapse." While "relapse" might be the simpler term, to many people it implies a moral failing. This concept needs to be taken into consideration when creating ma-

(continued on page 3)

Common Rule Buzz

Tips for Navigating FDA-Regulated Studies Under the Revised Common Rule

By Chidima Ioanou

The federal policy for the protection of human research subjects codified in 32 CFR 219 for the Department of Defense (DoD) (also known as the Common Rule) has been revised and is set to take effect on January 21, 2019. However, the U.S. Food and Drug Administration (FDA) regulations for human subject protection codified in 21 CFR Part 50 and 21 CFR Part 56, the regulatory framework that establishes requirements for the rights and safety of human subjects participating in FDA-regulated clinical investigations, at this time remains unchanged. Although FDA and Common Rule regulations share a common foundation, it has been a long held idea that uniformity in both sets of regulations would be highly desirable to reduce administrative burden and redundancy for human subject research that are bound by both regulations. This idea was put into action in 1991 as FDA regulations in 21 CFR Part 50 and Part 56 were amended to harmonize with the Common Rule. The 21st Century Cures Act of 2016 also reinforces this con-

(continued on page 6)

Also in this Issue:

New Roles for Dr. Nancy Dawood and Mr. John Morais

Dr. Nancy Dawood is the Deputy Director for the Department of the Navy Human Research Protection Program (DON HRPP). In this role, Dr. Dawood provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Navy. She assists the Director, DON HRPP, to identify and address new developments related to human subjects research protections. She also provides oversight to all matters related to DoD -Navy engagement in human subjects research and related policy and guidance.

Prior to her appointment as Deputy Director, DON HRPP, Dr. Dawood served as the Program Manager for six years with Armed Forces Services Corporation, providing contract support services to DON HRPP. In this capacity, she served as subject matter expert in the area of research ethics and human subjects research protections to HRPP staff. She also provided guidance to HRPP personnel in the application of human subjects regulations, including 32 CFR 219, DoDI 3216.02, and SECNAVINST 3900-39E CH-1. Dr. Dawood has fourteen years of experience managing human research protections programs and Institutional Review Board (IRB) administration.

Dr. Dawood earned her Doctorate of Education in Organizational Leadership from the Illinois School of Professional Psychology at Argosy University. She holds an M.A. in Psychology from Pepperdine University and dual B.A. degrees (Biology and Psychology) from the University Southern of California.

Mr. John Morais is the Human Research Protections Specialist (Training & Education) for DON HRPP's Research Protections Division at the Office of Naval Research (ONR 343). Mr. Morais joined the Office of Naval Research in October 2018. In his role as a Research Protections Specialist with focus on training and education, he is responsible for the development, organization and implementation of educational programs in human subject research ethics, regulatory compliance, and the responsible conduct of research and research integrity for DON-wide activities engaged in or supporting human subjects research.

Mr. Morais has more than twelve years' experience in the human research protections and research oversight field in a variety of positions with diverse responsibilities. Prior to ONR he held a similar position as a contractor with the Armed Forces Services Corporation (AFSC) supporting the Director, DON HRPP. John holds a B.A. from Mount St. Mary's University in Emmitsburg, Maryland and an M.B.A from the University of Maryland, University College in Organizational Management and is a member of the Phi Kappa Phi Honor Society. He also holds a Certified IRB Professional (CIP) designation and has participated in numerous human research protection continuing education activities.

Retirement Announcement for Ms. Shirley Callan

Ms. Shirley Callan, a treasured member of the DON HRPP community, is retiring on 31 January 2019 after a total of 34 years of Federal service. Out of the 34 years of service, Ms. Callan spent 32 years serving as the HRPP Site Administrator for research programs at Naval Aerospace Medical Research Laboratory, Pensacola, Florida, and Naval Hospital Pensacola, Florida. Ms. Callan has been steadfast and exceptional in her work in human subject protections. We wish her the best!!

Nuggets of Wisdom From The PRIM&R AER 2018 Conference

(continued from page 1)

terials for recruitment as well as consent forms, and applies to both written materials and imagery.

John Morais

It appears that broad consent may be dead upon arrival, or at least the initial reaction to it can be described as less than enthusiastic. Breakout sessions involving tracks on the Revised Common Rule at PRIM&R AER 2018 were predictably well attended. I chose several sessions that focused on research involving data and biospecimens, specifically on the new provisions for broad consent, limited IRB review and their applicability. One such session was titled "Tissue Repositories and Data Banks in the Era of the Revised Common Rule." In what seemed to be universal consensus from each panelist and reinforced by comments from audience members, many of whom were IRB members, institutional officials and other HRPP professionals, there is a 'wait and see' approach to the broad consent provision. In other words, there was no immediate desire or urgency to adopt and update SOPs and local institutional policy to allow for broad consent because the utility and/or burden reducing rationale are not readily apparent. Firstly, broad consent is optional. Secondly, the existing regulatory mechanism for inserting opt-in or opt-out language for secondary research in a main study informed consent document seems to work just fine for many institutions. Thirdly, there are questions and concerns on practical issues of implementing the provision. For example, were the institution to allow for broad consent how would they remain compliant with potential research subjects who wish to opt-out? Can their opt-out be tracked effectively? Does an opt-out of secondary research on data and biospecimens via a broad consent apply to any and all research conducted at that institution for perpetuity? Finally, if there is a renewed emphasis on autonomy and continued adherence to the principles of the Belmont Report in light of "shifts in science, technology, and public engagement and expectations" as described in the Preamble to the revised Common Rule should an opt-out really be final and not applied on a case to case basis?

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Paige Lispcome

"It's Not as New as You Think: Understanding How to Operationalize the Revised Common Rule." Session speakers addressed topics such as limited IRB review, broad consent, and practical approaches for transitioning to the new Common Rule. The definition of limited IRB review was put into simpler terms and it was also made known that some institutions are already conducting limited IRB review; it is simply a mechanism to involve the IRB in certain exemption determinations. Broad consent is not required and IRBs cannot waive broad consent if a subject has refused broad consent for use of their data and/or specimens in secondary research. Speakers recommended conducting quality assurance (QA) processes on IRB operations within the first year of the general compliance date to ensure compliance with the revisions to the Common Rule. Speakers also recommended highlighting the following changes to the Common Rule as a practical approach for educating HRPP and IRB staff: 1- Continuing Review, 2- Exempt Research, 3-Single IRB, 4-Informed Consent, 5-Broad Consent, and 6-Limited IRB Review.

Kristin Jones

"The Seven Habits of Highly Effective and Flexible IRBs." This session outlined what the speakers felt were seven habits of highly effective IRBs:

- Appoint a strong Institutional Official
- Create an educational/collaborative relationship with investigators and research staff
- Continuously update SOPs
- Incorporate flexibility in reviewing minimal risk research
- Limit the IRB's authority to the regulations
- Require the IRB to follow the regulatory criteria for approval
- Create operational flexibility for the IRB and administrative support office.

It was recommended that SOPs should be considered "living documents" which need to be looked at and revised regularly so that IRB staff will follow them. IRBs should also make an

(continued on page 4)

Nuggets of Wisdom From The PRIM&R AER 2018 Conference

(continued from page 3)

effort to stick to reviewing protocols using the criteria for IRB approval (32 CFR 219.111). They are frequently guilty of "mission-creep"… focusing on the scientific review or questioning decisions made in radiation safety or at the Data and Safety Monitoring Board (DSMB). When the IRB takes on too much, the review loses focus and you end up with less protection for the subjects. In doing this the IRB also takes on more of the responsibility and liability. An interesting concept introduced during the session was the idea of "flexible IRBs." Institutions have a collection of IRB members and members can sign up for which meetings they can attend. This has been implemented at a few large institutions and IRB members like the flexibility.

"They [the IRB] are frequently guilty of "mission-creep"…focusing on the scientific review or questioning decisions made in radiation safety or at the Data and Safety Monitoring Board (DSMB). When the IRB takes on too much, the review loses focus and you end up with less protection for the subjects."

Amber Gunn Westland

"Celebrities, Science-y, and Pseudoscience: Tackling Misinformation in the Era of Health Noise." In this session, Timothy Caulfield, LLB, LLM, FRSC, FCAHS, Canada Research Chair in Health Law and Policy, and documentary TV presenter, drew attention to the growing trend of exploiting faulty science and misinterpretation of research for profit. He shared numerous examples of celebrities touting the "scientifically proven" properties of useless, and sometimes dangerous, products and treatments which have enjoyed an enormous following amounting to billions of dollars of annual profits, particularly with the explosion of the internet and "fake news." The FDA is, for the most part, not regulating these treatments and products, and the modern-day snake oil salesman is operating largely unchecked. While some of the treatments and products Mr. Caulfield highlighted simply do not work, others have sent trusting customers to the emergency room, and even the grave. It is clear that the FDA, and other regulatory bodies in the U.S. and abroad, need to step in and have more of a presence in this wild frontier where it can be nearly impossible to separate fact from fiction.

Nora Livengood

"Ideas and Practices for Compliance and Auditing of Single IRB Studies." The presentation was largely about how to track and maintain oversight of studies that are being reviewed by an IRB external to the institution, and how to review studies for other institutions. This is a relatively new hurdle for the civilian world but has always been an important topic for the DoD, where many institutions rely on other IRBs. Of particular interest, was a discussion about SMART IRB, an online reliance system that is increasingly being used in the civilian world for hundreds of institutions to collaborate on their single IRB review.

Derek Englis

"The Revised Common Rule: Operational Considerations for the IRB Chair." This session focused on the aspects of IRB review that need to be updated to prepare for the changes in the Revised Common Rule. The session was presented by two IRB Chairs who have been updating forms, checklists, and processes in preparation for the change. Topics of discussion included, transitioning to the revised Common Rule, changes to the exempt categories, changes to the continuing review, and the limited IRB review. Related to the changes to continuing review, one of the speakers talked about how his institution will beef up post-approval monitoring and require a status update for studies that no longer require continuing review. Another speaker talked about the obvious and subtle changes to the exempt categories, and went over examples of studies to show how the new categories might be applied. Overall, this session was useful in conceptualizing the specific changes that need to be made by command human research protections programs.

"Related to the changes to continuing review, one of the speakers talked about how his institution will beef up post-approval monitoring and require a status update for studies that no longer require continuing review."

Pictured Highlights from PRIM&R AER 2018

PRIM&R 2018 AER DoD Session:

"A Dialogue with the Department of Defense (DOD): Updates for DOD and DOD-Sponsored Research Protections Personnel"

Session speakers from left to right; Ms. Monique Hawkins, Deputy Director, Research Protections Division, Office of Naval Research, Ms. Stephanie Bruce, Director, Office of Human Research Protections, Department of Defense, and Ms. Kim London, Deputy, Research Regulatory Affairs, Air Force Research Laboratory.

In this session speakers highlighted DoD specific updates on human research protections to various DoD stakeholders in attendance at the conference.

Fom left to right: the panelists; Mr. Douglas Osborne, Human Subjects Protections Advisor, TMC Global Professional Services, Mr. Derek Englis, DON HRPP Program Manager, Armed Forces Services Corporation, Ms. Roxana Lescano, Head Research Administration Program, NAMRU-6, Ms. Sophea Sout, HRPP Administrator, NAMRU-2 and moderator, Mr. Edward Bartlett, International Human Subjects Liaison, Office for Human Research Protections.

Congratulations!

Kudos to Ms. Roxana Lescano of NAMRU-6, Ms. Sophea Sout of NAMRU-2, and Mr. Derek Englis of DON HRPP for a successful and informative panel discussion at the 2018 PRIM&R AER conference held in San Diego, California.

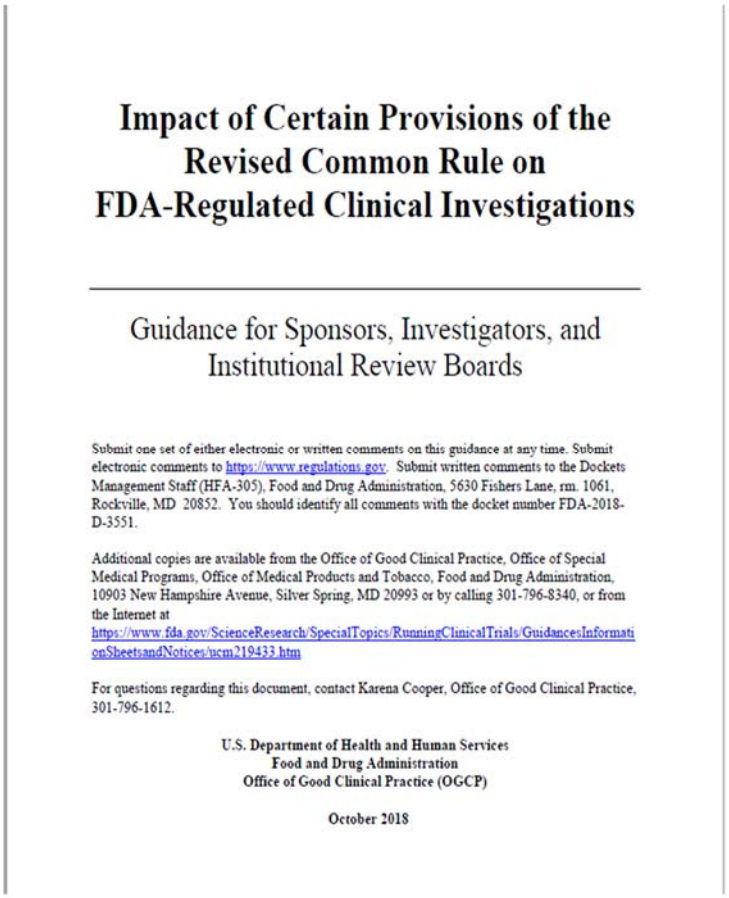
In the session titled "Applying U.S. Human Research Protection Regulation and Embedded Cultural Values to Research Conducted in Different Cultures: Challenges, Cultural Considerations, Collaborations, and Experiences", panelists discussed possible strategies for HRPP staff who are tasked with ensuring U.S– based human research protection requirements within diverse cultures.

Tips for Navigating FDA-Regulated Studies Under the Revised Common Rule

(continued from page 1)

cept by establishing legislation that calls for the harmonization of the Common Rule and FDA regulation for the protection of human subjects. Per this requirement, the FDA has stated that it intends to undertake a rule-making process to revise, to the extent applicable, its regulation governing the protection of human subjects to be harmonious with the revised Common Rule. In the interim, the FDA has published a guidance document titled "Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations." This guidance document does not put forth binding requirements but proposes recommendations on how institutions, sponsors, IRBs and other stakeholders might address the differences in FDA and Common Rule requirements.

IRBs reviewing Common Rule-regulated research and FDA-regulated research studies bound by both sets of regulation will find the guidance document helpful in addressing the differences in the regulations. Below are highlights from the guidance document demonstrating the FDA's current thinking on differences in informed consent requirements, expedited review, and IRB continuing review:



Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations

Guidance for Sponsors, Investigators, and Institutional Review Boards

Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number FDA-2018-D-3551.

Additional copies are available from the Office of Good Clinical Practice, Office of Special Medical Programs, Office of Medical Products and Tobacco, Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993 or by calling 301-796-8340, or from the Internet at https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm219433.htm

For questions regarding this document, contact Karena Cooper, Office of Good Clinical Practice, 301-796-1612.

U.S. Department of Health and Human Services
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Office of Good Clinical Practice (OGCP)

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Informed Consent

The revisions to the Common Rule includes changes to the informed consent requirements (written and oral). These changes consist of a requirement to have the informed consent begin with a concise and focused presentation of key information that is likely to assist a prospective subject or legally authorized representative in deciding whether to participate in research. Other changes include revisions to the basic and additional elements of informed consent. The FDA's current thinking on these differences in regulation is that the new Common Rule requirements are not inconsistent with the FDA's requirements. Thus, there is no need for two separate consent forms/processes to be developed to satisfy both sets of regulations.

Expedited Review Procedures and List

A list of categories of research that can undergo an expedited IRB review was published by the FDA in the Federal Register on November 9, 1998. On that same date, the Office for Protection from Research Risks (OPRR), now known as Office of Human Research Protections (OHRP), published an identical list of research categories that could undergo expedited review. Current FDA regulations (section 56.110(b)) states that as appropriate, IRB reviewer(s) may use the expedited review procedure to review some or all of the research appearing on the list and found by the reviewer to involve no more than minimal risk. The revised Common Rule regulation (section 46.110(b)) states that an IRB may use the expedited review procedure to review some or all of the research appearing on the list unless the reviewer determines that the study involves more than minimal risk. On this matter the FDA has stated via the guidance document that IRBs must continue to comply with FDA regulation at 21 CFR 56.110(b) and use the 1998 list for FDA-regulated clinical investigations, including those that are subject to both the Common Rule and FDA regulations. Presently, the FDA and OHRP have identical lists of research that can undergo expedited IRB review so at this time there is no conflict. Provisions are established under each regulation for the amendment, as applicable, of the lists. However, since both lists are maintained by separate entities, IRBs should pay close attention to any amendments that could lead to potential differences in the lists of research categories eligible for expedited IRB review.

(continued on page 7)

Tips for Navigating FDA-Regulated Studies Under the Revised Common Rule

(*continued from page 6*)

IRB Continuing Review

The revised Common Rule has eliminated the requirement, unless the IRB determines otherwise, for continuing review of research that has met the following criteria: research eligible for expedited review, research reviewed by the IRB in accordance with a limited IRB review, and research that has progressed to the point that it involves only data analysis and/or accessing of follow-up clinical data from procedures undergone as part of clinical care. The FDA has not revised its regulation on continuing review and IRBs must continue to comply with current requirements. So for FDA-regulated research, IRBs are still required to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. This means that IRBs reviewing studies that are bound by both sets of regulations might "determine otherwise" and conduct continuing review of research that no longer requires such under the revised Common Rule because it still remains a requirement under FDA regulation.

The guidance document is a great tool that provides clarification and insight on the FDA's current stance on how to address the impact of the revisions to the Common Rule on FDA-regulated research. The recommendations in the guidance document maintains the FDA's longstanding position concerning the protection of human subjects in that, where the regulations differ, the regulation that offers the greater protection should be followed.

Resources

1. https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/ucm118893.htm
2. https://www.fda.gov/RegulatoryInformation/Guidances/ucm623197.htm
3. https://www.federalregister.gov/documents/2007/10/26/E7-21126/protection-of-human-subjects-categories-of-research-that-may-be-reviewed-by-the-institutional-review
4. https://www.fda.gov/downloads/drugs/guidances/ucm436811.pdf

DON HRPP News!!

The Department of Defense (DoD) Human Research Protection Program (HRPP) Training Days regarding the implementation of the draft DoD Instruction 3216.02 and the Revised Common Rule were conducted on 9-10 January 2019. The DoD training sessions were held in Arlington, VA at the Defense Advanced Research Projects Agency (DARPA) Conference Center. Please note that OUSD(R&E) plans to hold another DoD training session in Fall 2019 which will reflect on the best practices observed during this year of change.

Should you have any questions or comments regarding the DoD training session, please contact Ms. Stephanie Bruce of OUSD(R&E) directly at 571-372-6442 (DSN 372-6442) or Stephanie.A.Bruce4.civ@mail.mil.

We Need Your Help!

Get a BZ from RPU

Have a "Good News" story or picture from your Research Protection Program? Don't keep it to yourself! Why not share it with the DON Research Protection community? We're looking for material to publish in the *Research Protections Update* newsletter. Send your research news, success stories, tips, pictures, lessons learned, or other material related to the ethical conduct of human research to usn.ncr.bumedfchva.mbx.don-hrpp@mail.mil

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