ACRP
ASSOCIATION OF CLINICAL RESEARCH PROFESSIONALS

MISSION:
ACRP promotes excellence in clinical research.

99 Canal Center Plaza
Suite 200
Alexandria, VA 22314
USA

T | 703.254.8100
F | 703.254.8101

office@acrpnet.org
www.acrpnet.org

January 22, 2015

Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

In reference to docket number: **HHS-OPHS-2014-0005**

The Association of Clinical Research Professionals (ACRP) is the primary resource for clinical research professionals in the pharmaceutical, biotechnology and medical device industries, and those in hospital, academic medical centers and physician office settings. ACRP was founded in 1976 to address the educational and networking needs of research nurses and others who supported the work of clinical investigations. Almost 40 years later, ACRP is a global association comprised of individuals dedicated to clinical research and development. Our mission is "ACRP promotes excellence in clinical research." The Academy of Physicians in Clinical Research (APCR) is an affiliate of ACRP and is the leading professional organization, exclusive to physicians, that supports and addresses these unique issues and challenges of all physicians involved in clinical research.

ACRP appreciates the opportunity to provide the OHRP with our comments on the Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care draft guidance as this issue has a significant impact on our membership. The attached document provides detailed comments, suggestions, and recommendations on specific sections of the draft guidance.

We applaud the OHRP's efforts on this important issue and hope that our feedback helps improve the final version of the document. Please let me know if you have any questions regarding our comments, or if we may otherwise serve as a resource on issues related to clinical research.

Sincerely,

Jim Thomasell, CPA
Executive Director

HHS-OPHS-2014-0005 : Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care			
Page Number	**Text Line**	**Reference** *(if applicable)*	**Comments**
3	83	Background	Recommend replacing "clinical trials studying" with "research studies evaluating" at this point because a) "clinical trials" may have a different meaning than intended and b) for consistency with other OHRP documents (including this document title) that use the more generalized "research" term; "clinical trial" also appears in another location that may benefit from similar substitution (see line 168 on page 5)
5	176-178	Introduction	Regarding "would be exposed," we are concerned that this statement on standard of care (SOC) risks could be interpreted to mean that identified risks would have to accommodate all possibilities for the potential treatment options, since researchers cannot possibly predict the exact intervention that would have been applied absent the research plan, including the treatment choice for no specific intervention (i.e., watchful waiting). Many factors could be involved in addition to some exposure to a SOC "test article," e.g., patient convenience, insurance coverage, accessibility, and these are not addressed. Given that, routine SOC "treatment consent" would have already addressed such options, making the "research" consent requirements unnecessarily duplicative.
5	178	Introduction	Regarding "outside the study," please clarify whether or not this necessarily means an "additive risk." Existing risks for the available SOC options should already have been fully addressed in a "treatment consent."
5	187-202	Standards of care	We consider it important to clarify and address the issue of a "recognized" SOC and "my" or "their" SOC from the viewpoint of the researcher. Other terminology should also be addressed for contrast or comparison, including "usual and customary" and "preferred practice patterns" that may not fit the current terminology for published SOC from professional societies, etc. Additionally, "studies" and "reports" often are equated with anything "published," which may lend undeserved credence to some publications that advocate or support a particular treatment method. This section should be better clarified to indicate the level of evidence expected in support of a recognized SOC.
5	187-202	Standards of care	Access to a particular SOC should be addressed in terms of whether the existence of a SOC treatment modality is a viable option available to potential study participants. Does the definition presume that the existence of a SOC mean it is also reasonably available to potential study participants (whether by local practice option, financial considerations, logistics, geography, regulatory barriers, etc.)?

5	193	Standards of care	The agency should indicate that the degree of variability in SOC can range widely even between professional societies, and we recommend editing this line to read: "The evidentiary bases for these recognized standards of care vary and some standards may be diametrically opposite of each other or otherwise mutually exclusive." This may improve the recognition for the need to conduct SOC research, when such divergence exists among different recognized standards.
6	198-200	Standards of care	The draft guidance language may be unnecessarily "intervention-centric," in that it may not be appropriate to describe comparative effectiveness study designs where "watchful waiting" is a viable SOC treatment option. We recommend adjusting this sentence to read: "The standard of care being evaluated may be 1) a treatment or procedure involving an intervention or interaction with the human subject; 2) a procedure for obtaining information about that subject; or 3) the withholding or delaying of interventions, interactions or procedures."
6	233-235	Risks of research	While this statement is statistically correct for randomized trials with an equal (1:1) treatment assignment ratio, the statement about what they "would have otherwise received" may not be intuitive and can be confusing. Consider expanding this to explain how this outcome is independent of the non-study treatment preferences (or fate) when considering two treatment options (i.e., what the treatment would have been for any given potential study participant without study involvement).
6	234	Risks of research	Randomization presents several different issues, and while the Draft Guidance remains individual-centric with regard to consent, it is not clear if the Guidance will accommodate issues of cluster randomization, community consent for applicable trials, and randomization schemes that may be staged depending on intermediate outcomes during a trial. These should be addressed.
7	239	Risks of research	Additional emphasis (i.e., Italics) is recommended for "…the risks associated with *any* available standard of care treatment…", as this has important implications in parallel with the emphasis you have in understanding the distinction where "risks of the research do *not* include the risks that are created by the medical condition…."
7	261-262	Research purpose	If one considered a case where no discernable differences in risks were evident based on the research plan (where identifiable risks per se may not be an issue between SOC options, but perhaps treatment costs or efficacy), how should risk disclosure be addressed by the IRB?
8	281-304	Informed consent process	There is concern about "matching" existing information provided in "treatment consent" documentation that is not subject to IRB or FDA oversight, with consent forms that are

			reviewed in a research context by an IRB. What happens when the risks in the treatment form do not match the risks in the research form? This will not only be confusing to the patient/subject but also raise logistical difficulties likely to cause significant delays in study review out of an IRB's fear of not disclosing everything they need to. As noted above, there may be unnecessary duplication between "treatment consent" materials and "research consent" forms, leading to additional administrative burden and potentially lengthy forms. Would it be a rational approach to provide a universal, "one size fits all" form to address collective risks across all treatment arms, rather than trying to delineate the distinct risks of each arm compared to another, especially when the treatment assignment may be masked?
8	281-304	Informed consent process	Will it be considered acceptable to incorporate material by reference in a research study consent form, i.e., as found in existing "treatment consent" materials, in order to describe the reasonably foreseeable risks of the relevant treatment options without extending the length of the research consent form?
8	312	Informed Consent process; example	The single example presents a randomized scenario (again, "research study" may be a better usage here than "clinical trial") and this implies that randomization may be a de facto indicator of research with human subjects. However, there are many other trial designs, in particular for certain observational studies of SOC, which are not suitable for randomization, yet remain very useful. Please clarify if OHRP intended this to apply only to randomized trials.

Page and consecutive line number identification is based on the posted document identified as HHS-OPHS-2014-0005-0002 (Draft 10/20/14).